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Increasing the rate of sample vaporization in an open air desorption ionization source by using a heated metal screen as a sample holder

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Rapid vaporization of sample into the ionizing gas exiting a direct analysis in real time (DART[®]) source has been enabled by directing a high electrical current through a metal wire screen to which sample has been applied. This direct heating of the screen enables rapid vaporization of sample as the wire temperature rises from room temperature to greater than 400°C in less than 20s. Positioning the screen between the DART source and atmospheric pressure inlet of the mass spectrometer ensures that the ionizing gas is in close proximity to the sample molecules, resulting in efficient ionization while significantly reducing the time required for mass spectrometric analysis. The capability to modulate the electrical current flow through the wires facilitates either rapid desorption for the determination of single component samples or slower desorption where analysis of mixtures might be desired. The technology also enables deployment of strategies for the determination of chemicals present as powders that might otherwise require dissolution prior to analysis. Results from the use of this thermally assisted DART ('TA-DART') system for the analysis of pure compounds, simple mixtures, solids and low vapor pressure samples are presented. Copyright © 2011 John Wiley & Sons, Ltd.

Analysis using a direct analysis in real time (DART) open air desorption ionization source starts with placing a small quantity on a solid support and inserting that support into the heated carrier gas containing metastable atoms that both desorb and ionize the analyte. The typical solid support material is a glass capillary tube that can be heated to temperatures exceeding 400°C without changing composition. The carrier gas is heated to a temperature sufficient to desorb molecules into the vapor phase by using a cartridge heater inside the DART source. Because gas-phase ionization is the predominant means for generating protonated or deprotonated molecules with DART, vaporization is a critical step to successful analysis.^[1] In practice, nearly instantaneous ionization of molecules of interest including those generated as products of chemical synthesis,^[2,3] pharmaceuticals,^[4–6] and foodstuffs^[7,8] is achieved by starting with a moderately high temperature carrier gas and manually positioning samples on the solid support in the ionization region for a few seconds. The skilled analyst can manage the rate of desorption by monitoring the production of ions while manipulating the distance of the sample from the heated gas source. For high vapor pressure molecules the sample-coated surface is positioned several millimeters from the heated gas source, while the surface coated with low vapor pressure molecules is subject to direct gas flow to facilitate the maximum transfer of heat to the surface. One can imagine that the automation of this process is not easy as it

is difficult to know the vapor pressure of a molecule prior to analysis. Thus, a solution that relies less on the heated gas for desorption is desirable.

As an alternative to knowing the vapor pressure of a sample before analysis, an experimental protocol involving repeat analysis of the same sample at successively higher gas temperatures is used to complete the differential desorption of the individual components present in a sample. The mass spectra acquired at different temperatures provide a thermal profile of the chemicals present in a sample. In practice, heating the flowing gas to a specific temperature and holding it at that temperature requires a relatively short period of time. However, as the thermal profiling experiment requires analysis at a series of different temperatures the time necessary to heat and then cool the gas becomes longer. In order to decrease the time between the measurements of different mass spectra necessary for the thermal profile analysis, we decided to investigate devices for separating the heating of the sample support from the gas-phase ionization.

Investigations involving the use of porous materials as the desorption ionization surface appeared in the literature shortly after the development of DART. The determination of chemicals by open air surface desorption directly from non-conducting screens and fabrics positioned in-line between the DART source and the atmospheric pressure inlet (API) of the mass spectrometer has been documented by several groups. These investigations included the examination of the quantity and type of antimalarial chemical distributed on mosquito netting^[9] and the retention of various chemicals on fabric.^[10] In their discussion of the in-line sampling process where the DART gas flowed through the screen resulting in both desorption and ionization, Fernandez and co-workers coined the term 'transmission-mode DART'.^[9]

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More recently, the transmission DART experiment was utilized for the detection of various pesticides on fruits and vegetables by Edison *et al.*^[12] where a polyethylene foam swab was used to directly sample pesticide residues from the surface of food and then serve as the desorption support. In those experiments a sample holder was designed to permit automatic positioning of the swab in the ionization region for an extended period of time so that the metastable-containing carrier gas traveled directly through the foam. The temperature of the carrier gas was gradually increased over a 2-min period from 150°C to 400°C for each sample, allowing for the desorption and subsequent detection of hundreds of chemically diverse pesticides. This experiment, like others where the temperature of the gas is varied, requires an analysis time of several minutes per sample because the DART system needs to heat the carrier gas to several hundred degrees Celsius for each sample. The need for the gas to cool down again before the next sample further increases the time required for the analysis. While this experiment still takes advantage of the speed of analysis of DART, shortening the heating and cooling time would allow for a much higher throughput and expand the potential real-world uses of this method.

Understanding that these non-conducting porous surfaces provided a surface that could promote desorption/ionization when used in transmission mode DART, we decided to conduct experiments using heat-conducting materials including wire screens. Our initial evaluation of the utility of metal screens for DART analysis was to investigate the feasibility of their use as desorption ionization surfaces. Knowing that metal surfaces can be reactive we wanted to compare mass spectra of molecules obtained with sample presented on glass and metal. The results of these studies demonstrated that desorption from metal screens was completed at a significantly lower temperatures than from the glass capillary. As a result, we focused our investigation on methods that enable heating of the metal screen. Understanding that application of electrical current across it would rapidly increase the heat applied to the sample we subsequently fabricated the thermally assisted transmission DART device described in this communication.

EXPERIMENTAL

Materials

Woven wire screens were purchased in the following mesh sizes from the McMaster-Carr Supply Company (Elmhurst, IL, USA): 165 × 165 mesh, 0.0019" diameter wire; 74 × 74 mesh, 0.0037" diameter wire; 60 × 60 mesh, 0.0045" diameter wire; and 32 × 32 mesh, 0.0065" diameter wire.

Reagents

The following high-performance liquid chromatography (HPLC) grade solvents were purchased from VWR (West Chester, PA, USA) and used without further purification for dissolving samples: methanol, acetone, and methylene chloride.

Chemicals

Quinine, methyl paraben, and acetaminophen were purchased from TCI America (Portland, OR, USA) and dimethoate, phenylephrine hydrochloride, and dextromethorphan hydrobromide were purchased from Sigma Aldrich (St. Louis, MO, USA).

Development of the Thermal-Assist DART device

A device was designed that held a woven wire screen at a fixed distance between a ceramic transfer tube leading to the atmospheric pressure inlet of the mass spectrometer and the outlet of the DART source. The screen was attached to clean paper cards, allowing it to be handled without touching and becoming contaminated. Once a sample had been applied to the screen, the card was placed in the holder and electrical leads were clamped down on either side of the sample. The DART gas was turned on and the power supply was switched on, causing the circuit to close and current to flow across the mesh screen, thus heating the sample. The power supply was programmed to function at three settings: 'low', 'medium', and 'high', which correspond to 2.0, 2.5, and 3.0 V, respectively, at a current of ~8 A. A schematic of the DART and screen setup is presented in Fig. 1.

Instrumentation

Mass spectrometer

Analysis was performed using a Finnigan LCQ Deca (Thermo Electron Corp., Waltham, MA, USA) ion trap mass spectrometer. The capillary temperature was set to 200°C. In positive-ion mode the capillary voltage was set to 15 V and in negative-ion mode it was set to -15 V.

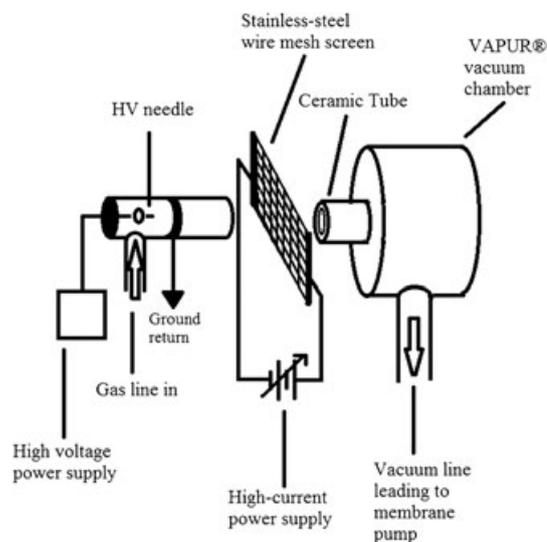


Figure 1. A stainless steel wire mesh was placed between the DART gun (to the left of the mesh) and a ceramic transfer tube and IonSense VAPUR®. The high-current power supply is switched on and current flows through the screen, causing it to rapidly heat. Helium metastables are emitted from the gun and ions are formed after interaction with the gas-phase analyte that has been desorbed off of the screen's surface due to the heat. The vacuum pressure of the VAPUR® and mass spectrometer pull the ions into the atmospheric pressure inlet.

The instrument parameters used during data acquisition were as follows: polarity, positive or negative, depending on the analyte of interest; scan range, m/z 100–500; capillary temperature, 200°C; capillary voltage, 25V.

DART ionization source

The ionization source used was a DART SVP-A model (IonSense, Inc., Saugus, MA, USA). The gap between the DART source and the ceramic tube leading to the atmospheric pressure inlet was set at 8mm.

For all the described experiments, the DART heater was set to 'OFF' and the heater temperature readback remained at less than 30°C. Helium was used as the ionization gas and the polarity of the grid voltage was set to positive 350V for positive-ion mode and –350V for negative-ion mode.

Power supply

A Systron-Donner (Concord, CA, USA) model HR40-7C Trygon power supply (0–40V, maximum output of 7A) provided the current to heat the screens.

Sample preparation

Screen preparation

Prior to use as sampling supports, the wire screens were placed in a furnace at 500°C and left to bake for 3h to remove industrial contaminants. After cooling, rectangular pieces of wire screen approximately ½ inch in length and 1/8 inch in width were cut from the screens. Leads were attached to opposite ends of longest length of the screens.

Analysis of chemical standards

Quinine, methyl paraben, and dimethoate were prepared by dilution in an equal mixture of HPLC-grade methanol and water (1:1 v/v).

Operational method

Liquids were pipetted onto the center region of the rectangle-shaped metal screen and allowed to dry for several minutes. For semi-solid materials, a small quantity was transferred by spatula and pressed onto the center region of the diamond-shaped metal screen. Electrical leads from the positive and negative poles of the power supply were attached to opposite ends of longest length of the rectangle-shaped piece. The DART SVP controller was switched from 'OFF' mode directly to 'RUN', which turns on the high-voltage power supply and initiates the flow of gas through the DART source. The screen was positioned between the outlet of the DART source and the API inlet. After verifying that no ions of interest were being generated at ambient temperature, the power supply was switched on to apply current through the wire screen, resulting in the rapid rise of its temperature. The output current reached its maximum after approximately 5s. The heating of the wire lagged slightly behind the current, probably due to the resistivity of the metal decreasing as the temperature increases. The power supply providing current was turned off after a period of less than 10s since no additional ions were generated after this time.

Ions produced through the use of metal screens are transferred to the API source through use of a gas ion separator interface device, the VAPUR® (IonSense, Inc.), which incorporates a vacuum chamber with a ceramic tube at its entrance. The ceramic tube draws a vacuum of approximately

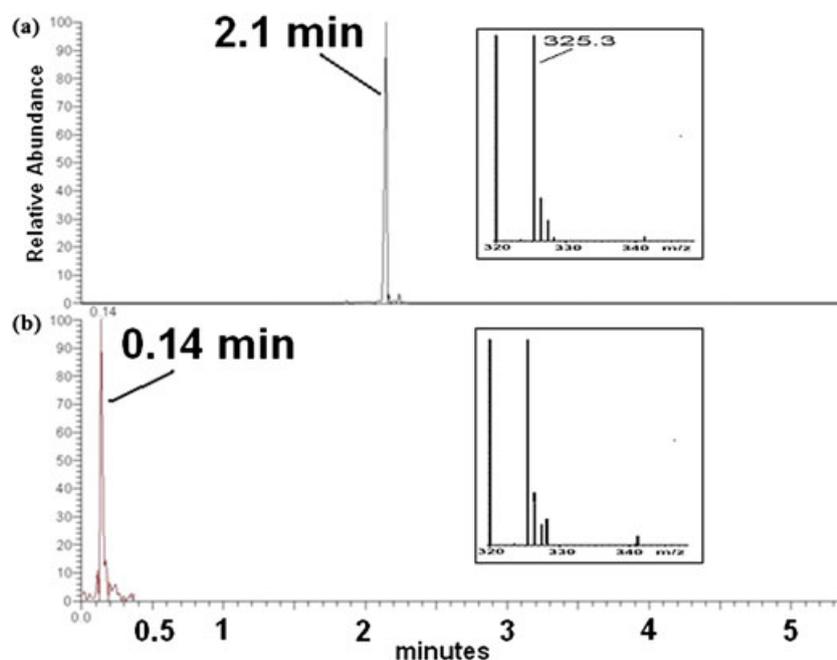


Figure 2. A comparison of the time required for (a) a 'conventional' DART-MS analysis of a quinine solution off of a glass capillary with (b) the time required to complete desorption and ionization of the same quinine solution off of a current-heated metal mesh. The time required for full analysis, including warm-up and cool-down time, is reduced from 5min down to less than 12s.

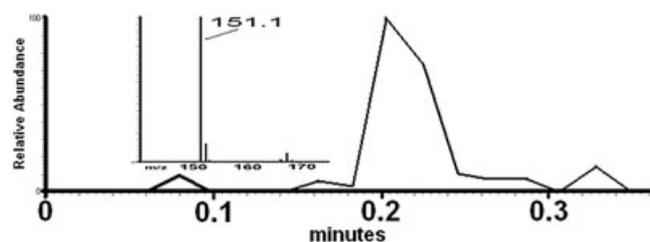


Figure 3. The extracted ion chromatogram for methyl paraben, along with an insert of the mass spectrum. These data demonstrate the utility of the method in negative-ion mode.

200mTorr, which results in a higher volume of carrier gas containing ions being transmitted through to the API region. The balance of gas entering the API source is modulated by adjusting the flow of gas to the membrane pump using a needle valve.^[11]

RESULTS AND DISCUSSION

Improving desorption ionization throughput

Figure 2 shows two mass spectra for quinine along with their corresponding extracted ion chromatograms for the protonated molecule of quinine (m/z 325.4). The bottom mass spectrum and chromatogram were produced using the current-heated screens in less than 10s. By comparison, previous investigations using the conventional DART method had documented that the temperature of the heated gas had to

be 350°C for quinine to completely desorb. The top mass spectrum and chromatogram were produced using the conventional DART method of analysis with the DART gas starting at room temperature and rising as fast as possible to the set point of 350°C. In the extracted ion chromatogram the entire analysis time is shown, including the 2min required to heat the gas to a temperature sufficient to desorb the quinine and the 3min required to cool-down the gas after the sample was inserted. The results from desorption/ionization using the current-heated screen are shown in the bottom panel. The desorption and ionization process is completed in under 15s and, once the current is removed, the metal screen temperature returns to ambient in a similar time period. In this comparison, the potential for a more rapid and complete analysis of sample for both content and potentially purity is demonstrated.

In Fig. 3, the negative-ion spectrum for methyl paraben was notable for the absence of significant quantities of typical DART background ions. At low gas temperatures very few atmospheric molecules are desorbed and ionized, reducing the potential for isobaric interference, and enabling better signal-to-noise (S/N) values. This offers the potential for more efficient negative-ion DART analysis, which has traditionally been much less effective than operation in positive-ion mode.

Analysis of a chemical mixture

The method also demonstrates great utility for the analysis of compounds with widely varying chemical properties. Under conventional DART analysis, such a mixture would

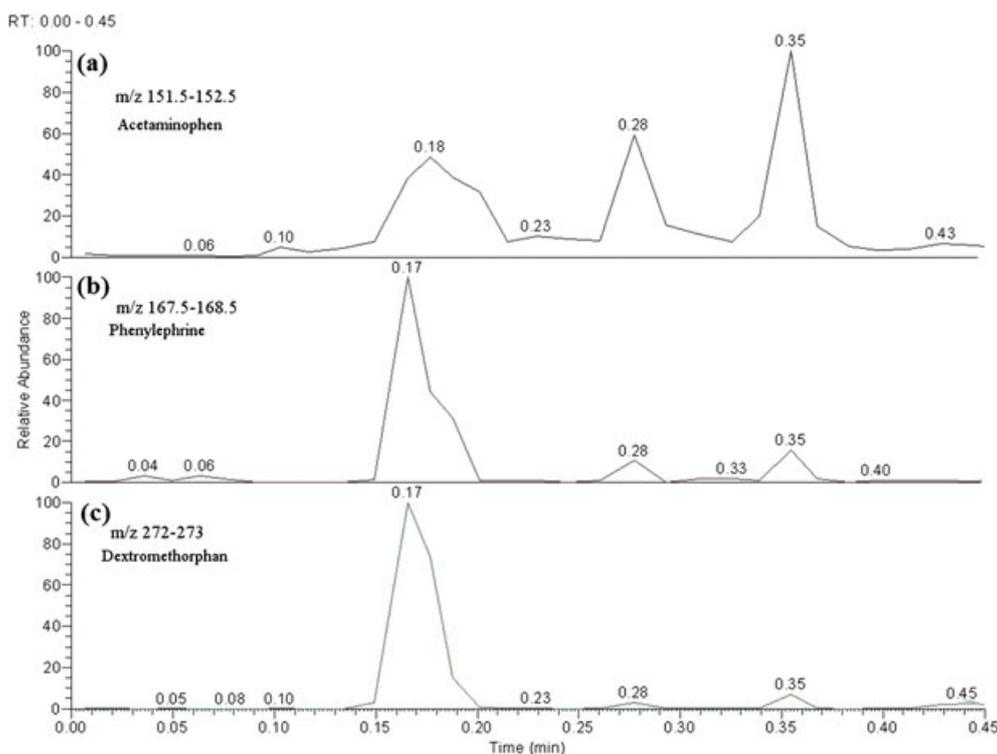


Figure 4. Extracted ion chromatograms for (from top to bottom) (a) protonated $[M+H]^+$ molecules of acetaminophen (mw 151Da), (b) phenylephrine (mw 167Da), and (c) dextromethorphan (mw 271.5Da). All three compounds were desorbed instantaneously when current was applied to a metal mesh substrate. The high relative quantity of acetaminophen resulted in multiple peaks before the signal dissipated.

require multiple analyses at differing desorption temperatures. Figure 4 shows the extracted ion chromatograms for three active pharmaceutical ingredients in a mixture that was ionized and observed as the following three protonated molecules: acetaminophen $[M+H]^+$ at m/z 152, phenylephrine at m/z 168, and dextromethorphan at m/z 272. The three components have widely varying physical characteristics and desorb at differing DART gas temperatures. Earlier efforts at analyzing this mixture noted that acetaminophen desorbed at an optimal temperature of 250°C, while dextromethorphan gave an optimal signal at 450°C. Placing the mixture on the metal screen and heating rapidly through all the temperatures allows for the desorption of all three compounds in a matter of seconds, versus over 5 min for the full thermal profile necessary to obtain spectra for all three compounds using the conventional DART method.

CONCLUSIONS

The development of this 'Thermally Assisted' DART (TA-DART) system demonstrates the potential to significantly reduce the time required to complete a DART experiment. Its functionality has been successfully demonstrated on a wide variety of liquid chemical standards, chemicals in solution, and powders. Furthermore, its ability to rapidly ramp through different desorption temperatures removes the need to optimize temperature, an improvement that leaves the DART as a true 'on-or-off' source. This combination of speed and simplicity suggests that this new electrically assisted DART source would be ideal in an open-access environment.

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