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AccuTOF LC series with DART bibliography (May 2016)
Introduction

Mass Spectrometry (MS) is one of the fastest-growing areas in analytical instrumentation. The use of mass spectrometry in support of synthetic, organic, and pharmaceutical chemistry is well established. Mass spectrometry is also used in materials science, environmental research, and forensic chemistry. It has also evolved into one of the core methods used in biotechnology. However, currently available ion sources place extreme restrictions on the speed and convenience of sample analysis by mass spectrometry. Here we report a method for using mass spectrometry to instantaneously analyze gases, liquids, and solids in open air at ground potential under ambient conditions.

Traditional ion sources used in mass spectrometry require the introduction of samples into a high vacuum system. Traditional ion sources operated in vacuum include electron ionization (EI)[1], chemical ionization (CI)[2], fast atom bombardment (FAB)[3], and field desorption/field ionization (FD/FI)[4]. These techniques have been used successfully for decades. However, the requirement that samples be introduced into a high vacuum for analysis is a severe limitation. Gas or liquid samples must be introduced through a gas chromatograph or a specially designed inlet system. Solid samples must be introduced by using a direct insertion probe and a vacuum lock system. Direct insertion probes can result in vacuum failure and/or contamination of the ion source if too much sample is introduced.

Atmospheric pressure ion sources such as atmospheric pressure chemical ionization (APCI)[5], electrospray ionization (ESI)[6-8], matrix-assisted laser desorption ionization (MALDI)[9-10] and atmospheric pressure photoionization (APPI)[11] have broadened the range of compounds that can be analyzed by mass spectrometry. However, these ion sources require that samples be exposed to elevated temperatures and electrical potentials, ultraviolet irradiation, laser radiation, or a high-velocity gas stream. Safety considerations require that the ion source be fully enclosed to protect the operator from harm.

The new ion source reported herein overcomes these limitations. The new technique, referred to as Direct Analysis in Real Time (DART™), has been coupled to the AccuTOF-LC™ atmospheric pressure ionization mass spectrometer to permit high-resolution, exact mass measurements of gases, liquids, and solids[12,13]. DART successfully sampled hundreds of chemicals, including chemical agents and their signatures, pharmaceuticals, metabolites, pesticides and environmentally significant compounds, peptides and oligosaccharides, synthetic organics, organometallics, drugs of abuse, explosives, and toxic industrial chemicals. These chemicals were detected on a variety of surfaces such as concrete, human skin, currency, airline boarding passes, fruits and vegetables, body fluids, cocktail glasses, and clothing. The composition of drug capsules and tablets was directly analyzed.

Background and Principle of Operation

DART grew out of discussions at JEOL USA, Inc. between two of the authors (Laramée and Cody) about the possibility of developing an atmospheric pressure thermal electron source to replace the radioactive sources used in hand-held detectors for chemical weapons agents (CWAs), drugs, and explosives. The discovery that DART could be used for positive-ion and negative-ion non-contact detection of materials on surfaces, as well as for detection of gases and liquids, led to the development of a commercial product.

DART is based on the atmospheric pressure interactions of long-lived electronic excited-state atoms or vibronic excited-state molecules with the sample and atmospheric gases. The DART ion source is shown in Figure 1. A gas (typically helium or nitrogen) flows through a chamber where an electrical discharge produces ions, electrons, and excited-state (metastable) atoms and molecules. Most of the charged particles are removed as the gas passes through perforated lenses or grids and only the neutral gas molecules, including metastable species, remain. A perforated lens or grid at the exit of the DART provides several functions: it prevents ion-ion and ion-electron recombinations, it acts as a source of electrons by surface Penning ionization, and it acts as an electrode to promote ion drift toward the orifice of the mass spectrometer’s atmospheric pressure interface.

Several ionization mechanisms are possible, depending on the polarity and reaction gas, the proton affinity and ionization potential of the analyte, and the presence of additives or dopants. The simplest process is Penning ionization [14] involving transfer of energy from the excited gas $M^+$ to an analyte $S$ having an ionization potential lower than the energy of $M^+$. This produces a radical molecular cation $S^{+}+e^-$ and an electron $e^-.$

$$M^+ + S \rightarrow S^{+} + M + e^-$$

Penning ionization is a dominant reaction mechanism when nitrogen or neon is used in the DART source. Nitrogen or neon ions are effectively removed by the electrostatic lenses and are never observed in the DART back-
ground mass spectrum.

When helium is used, the dominant positive-ion formation mechanism involves the formation of ionized water clusters followed by proton transfer reactions:

\[ \text{He}(2S) + H_2O \rightarrow H_2O^+ + \text{He}(1S) + \text{electron} \]

\[ H_2O^+ + H_2O \rightarrow H_2O^+ + OH^- \]

\[ H_2O^+ + n \times H_2O \rightarrow [(H_2O)nH]^+ \]

\[ [(H_2O)nH]^+ + M \rightarrow MH^+ + nH_2O \]

The helium 2S state has an energy of 19.8 eV. Its reaction with water is extremely efficient [15] with the reaction cross section estimated at 100 Å². Because of this extraordinarily high cross section, DART performance is not affected by humidity.

Negative-ion formation occurs by a different mechanism. Electrons (e⁻) are produced by Penning ionization or by surface Penning ionization:

\[ M^+ + \text{surface} \rightarrow M + \text{surface} + e^- \]

These electrons are rapidly thermalized by collisions with atmospheric pressure gas

\[ e^- + \text{gas} \rightarrow e^-_{\text{slow}} \]

Thermal electrons undergo electron capture by atmospheric oxygen

\[ e^-_{\text{slow}} + O_2 \rightarrow O_2^- \]

to produce O₂⁻, which reacts with the analyte to produce anions. The DART negative-ion reagent mass spectra are virtually identical for nitrogen, neon, and helium. However, negative-ion sensitivity increases for DART gases in the following order:

nitrogen < neon < helium

This is due to the increased efficiency in forming electrons by Penning ionization and surface Penning ionization as the internal energy of the metastable species increases.

The polarity of the DART ion source is switched between positive-ion mode and negative-ion mode by changing the polarity of the disk electrode and grid. The polarity of the discharge needle is not changed, so the plasma is not interrupted. This permits rapid switching between positive and negative modes.

Other reactions are possible. The presence of traces of dopants such as ammonium (e.g. from ammonium hydroxide headspace vapor) or chloride (e.g. from methylene chloride vapor) can modify the chemistry allowing the chemist to tailor the experiment for specific analyses.

DART produces relatively simple mass spectra characterized by M⁺ and/or [M+H]⁺ in positive-ion mode, and M⁻ or [M-H]⁻ in negative-ion mode. Fragment ions are observed for some compounds. The degree of fragmenta-
tion can be influenced by the choice of gas, the temperature, and the AccuTOF orifice 1 potential. Alkali metal cation attachment and double-charge ions are not observed.

The mechanism involved in desorption of materials from surfaces by DART is less well characterized. Thermal desorption plays a role if the gas stream is heated. However, the analysis by DART of inorganic materials such as sodium perchlorate or organic salts having little or no vapor pressure is evidence of other processes. It is postulated that the transfer energy to the surface by metastable atoms and molecules facilitates desorption and ionization.

In contrast with other ion sources that use metastable species [16-23], the DART ion source does not operate under reduced pressure, apply a high electrical potential to the analyte, or expose the analyte directly to the discharge plasma. Argon, used in many of these ion sources, is not well suited for use with DART because argon metastables are rapidly quenched in the presence of water vapor [20] by a reaction involving homolytic cleavage of the water bond without concomitant ion formation. None of these ion sources are designed for direct analysis of gases, liquids, and solids in open air under ambient conditions.

**Experimental**

A DART™ source [24] was installed on a JEOL AccuTOF LC™ time-of-flight mass spectrometer. The DART source replaces the standard electrospray ionization (ESI) source supplied with the AccuTOF. No vacuum vent is required. The ion sources can be exchanged and made operational within minutes.

The mass spectrometer operates at a constant resolving power of approximately 6000 (FWHM definition). Typical atmospheric pressure interface conditions are: orifice 1 = 30V, and both orifice 2 and ring lens are set to 5V. The AccuTOF ion guide voltage is varied as needed depending on the lowest m/z to be measured. Orifice 1 temperature is typically kept warm (80 degrees C) to prevent contamination. Although there is some electrical potential on the exposed orifice 1, the voltage and current are so low that there is absolutely no danger to the operator, even with prolonged direct contact.

The DART source is operated with typical gas flows between 1.5 and 3 liters per minute. Gas temperature is programmable from ambient temperature up to approximately 350 degrees C (gas heater temperature from OFF to a maximum of 350 degrees C). Typical potentials are: discharge needle 2 kV to 4 kV, electrode 1: 100V, grid: 250 V. Gas, liquid, or solid samples positioned in the gap between the DART source and mass spectrometer orifice 1 are ionized.

Because the mass spectrometer orifice is continually bathed in hot inert gas, the DART source is remarkably resistant to contamination and sample carryover. Mass scale calibration is easily accomplished by placing neat poly-
ethylene glycol average molecular weight 600 (PEG 600) on a glass rod or a piece of absorbent paper in front of the DART source. In positive-ion mode, this produces a series of \([M+H]^+\) and \([M+H_2O]^+\) peaks from \(m/z\) 45 up to beyond \(m/z\) 1000. By including background peaks, the calibrated mass range can be extended down to \(m/z\) 18 or 19. Negative-ion spectra of PEG are characterized by \([M+O_2-H]^\) and \([(\text{C}_2\text{H}_4\text{O})n+O_2-H]^\) ion series.

The reference spectrum can be acquired within seconds. There is no memory effect or carryover of the reference compound -- the PEG peaks do not persist after the reference standard is removed. For these reasons, a full reference mass spectrum can be quickly and easily included in each data file, and accurate mass measurements are routinely acquired for all samples.

Applications

The DART ion source has been used to analyze an extremely wide range of analytes, including drugs (prescription, over-the-counter, veterinary, illicit, and counterfeit) in dose form or in body fluids or tissues, explosives and arson accelerants, chemical weapons agents and their signatures, synthetic organic or organometallics compounds, environmentally important compounds, inks and dyes, foods, spices and beverages. An important benefit of DART is that materials can be analyzed directly on surfaces such as glass, TLC plates, concrete, paper, or currency without requiring wipes or solvent extraction.

Drugs can be detected in pill form by placing the pill in front of the DART source for a few minutes. An example is shown below (Figure 2) for the rapid detection of illicit drugs in pills confiscated by a law-enforcement agency. The intact pills were simply placed in front of the DART source and analyte ions were observed within seconds. Exact mass and isotopic measurements confirmed the elemental compositions of the labeled components. All labeled assignments in the following examples were confirmed by exact mass measurements.

Drug counterfeiting is becoming a serious and widespread public health problem. Counterfeit drugs are not only illegal, but dangerous; they may contain little or no actual drug content, or they may contain completely different drugs with potentially toxic consequences.

DART can be used to rapidly screen for counterfeit drugs. An example is shown below in Figure 3 where DART was used to analyze a sample of a real drug containing the anti-malarial dihydroartemisinin, and a counterfeit drug containing no active ingredients.

DART has been applied to the direct detection of drugs and metabolites in raw, unprocessed body fluids, including blood, urine, perspiration, and saliva. An example is shown below in Figure 4 for the negative-ion analysis of the urine of a subject taking prescription ranitidine. No extraction or other processing was used: a glass rod was dipped in raw urine and placed in front of the DART source.

For easy viewing, only abundant components are labeled in this figure. A more complete list of assignments is given in Table 1. Assignments are made for compounds com-
Table 1: Assignments for Compounds Detected in Negative-Ion DART Mass Spectrum of Raw Urine.

<table>
<thead>
<tr>
<th>Name</th>
<th>Meas.</th>
<th>Calc.</th>
<th>Diff(u)</th>
<th>Abund.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBL</td>
<td>85.0295</td>
<td>85.0290</td>
<td>0.0006</td>
<td>11.0317</td>
</tr>
<tr>
<td>Pyruvic_acid</td>
<td>87.0084</td>
<td>87.0082</td>
<td>0.0002</td>
<td>7.1700</td>
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<tr>
<td>Lactic_acid</td>
<td>89.0236</td>
<td>89.0239</td>
<td>-0.0002</td>
<td>8.3658</td>
</tr>
<tr>
<td>Cresol</td>
<td>107.0492</td>
<td>107.0497</td>
<td>-0.0004</td>
<td>9.2946</td>
</tr>
<tr>
<td>Uracil</td>
<td>111.0153</td>
<td>111.0195</td>
<td>-0.0041</td>
<td>14.3328</td>
</tr>
<tr>
<td>Creatinine</td>
<td>112.0513</td>
<td>112.0511</td>
<td>0.0002</td>
<td>81.6851</td>
</tr>
<tr>
<td>Purine</td>
<td>119.0354</td>
<td>119.0358</td>
<td>-0.0004</td>
<td>31.9510</td>
</tr>
<tr>
<td>Niacin</td>
<td>122.0277</td>
<td>122.0242</td>
<td>0.0035</td>
<td>3.1489</td>
</tr>
<tr>
<td>Dihydro_methyluracil</td>
<td>127.0486</td>
<td>127.0508</td>
<td>-0.0021</td>
<td>23.3773</td>
</tr>
<tr>
<td>pGlu</td>
<td>128.0353</td>
<td>128.0348</td>
<td>0.0006</td>
<td>59.2337</td>
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<tr>
<td>Methylmaleic_acid</td>
<td>129.0212</td>
<td>129.0188</td>
<td>0.0024</td>
<td>37.1191</td>
</tr>
<tr>
<td>Me_succinate/diMe_malonate</td>
<td>131.0368</td>
<td>131.0358</td>
<td>0.0010</td>
<td>19.3593</td>
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<tr>
<td>Deoxyribose</td>
<td>133.0489</td>
<td>133.0501</td>
<td>-0.0012</td>
<td>28.3521</td>
</tr>
<tr>
<td>Hypoxanthine</td>
<td>135.0306</td>
<td>135.0307</td>
<td>-0.0001</td>
<td>100.0000</td>
</tr>
<tr>
<td>Adipic_acid</td>
<td>145.0469</td>
<td>145.0501</td>
<td>-0.0032</td>
<td>11.7389</td>
</tr>
<tr>
<td>Methyl_hypoxanthine</td>
<td>149.0454</td>
<td>149.0463</td>
<td>-0.0009</td>
<td>37.5243</td>
</tr>
<tr>
<td>Hydroxymethyl_methyl_uracil</td>
<td>155.0453</td>
<td>155.0457</td>
<td>-0.0003</td>
<td>55.5832</td>
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<tr>
<td>a-aminoacidic_acid</td>
<td>160.0568</td>
<td>160.0610</td>
<td>-0.0042</td>
<td>9.5885</td>
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<tr>
<td>Methionine_sulfoxide</td>
<td>164.0419</td>
<td>164.0381</td>
<td>0.0037</td>
<td>11.7609</td>
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<tr>
<td>Methylxanthine</td>
<td>165.0408</td>
<td>165.0412</td>
<td>-0.0004</td>
<td>32.4341</td>
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<tr>
<td>Formiminoglutamic_acid</td>
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<td>173.0562</td>
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<td>12.3531</td>
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<td>Ascorbic_acid</td>
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<td>175.0243</td>
<td>0.0042</td>
<td>23.1998</td>
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<tr>
<td>Hippuric_acid</td>
<td>178.0513</td>
<td>178.0504</td>
<td>0.0009</td>
<td>66.4487</td>
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<tr>
<td>Glucose</td>
<td>179.0552</td>
<td>179.0565</td>
<td>-0.0004</td>
<td>39.7499</td>
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<tr>
<td>Dimethylxanthine</td>
<td>179.0552</td>
<td>179.0569</td>
<td>-0.0017</td>
<td>39.7499</td>
</tr>
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<td>Pyridoxinecarboxylic_acid</td>
<td>182.0479</td>
<td>182.0453</td>
<td>0.0026</td>
<td>34.7913</td>
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<tr>
<td>Hydroxyindoleacetic_acid</td>
<td>190.0542</td>
<td>190.0504</td>
<td>0.0037</td>
<td>5.4133</td>
</tr>
<tr>
<td>Dimethyluric_acid</td>
<td>195.0527</td>
<td>195.0518</td>
<td>0.0009</td>
<td>23.7577</td>
</tr>
<tr>
<td>AAMU (caffeine metabolite)</td>
<td>197.0667</td>
<td>197.0675</td>
<td>-0.0007</td>
<td>79.6617</td>
</tr>
<tr>
<td>Cinnamalidinemalonic_acid</td>
<td>217.0483</td>
<td>217.0501</td>
<td>-0.0017</td>
<td>60.5399</td>
</tr>
<tr>
<td>AAMU (caffeine metabolite)</td>
<td>217.0483</td>
<td>217.0501</td>
<td>-0.0017</td>
<td>60.5399</td>
</tr>
<tr>
<td>Dimethylxanthine</td>
<td>217.0483</td>
<td>217.0501</td>
<td>-0.0017</td>
<td>60.5399</td>
</tr>
<tr>
<td>Hydroxyindoleacetic_acid</td>
<td>225.0643</td>
<td>225.0624</td>
<td>0.0019</td>
<td>21.1156</td>
</tr>
<tr>
<td>Dimethyluric_acid</td>
<td>225.0643</td>
<td>225.0624</td>
<td>0.0019</td>
<td>21.1156</td>
</tr>
<tr>
<td>Adenosine</td>
<td>263.1332</td>
<td>263.1322</td>
<td>-0.0010</td>
<td>4.7459</td>
</tr>
<tr>
<td>Adenosine</td>
<td>263.1332</td>
<td>263.1322</td>
<td>-0.0010</td>
<td>4.7459</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>349.0113</td>
<td>349.1101</td>
<td>0.0011</td>
<td>11.7296</td>
</tr>
<tr>
<td>Ranitidine+Cl</td>
<td>349.0113</td>
<td>349.1101</td>
<td>0.0011</td>
<td>11.7296</td>
</tr>
</tbody>
</table>

Fig. 5 Rapid quantitative analysis by DART of promazine in urine. Chlorpromazine was added as an internal standard.

DART: Promazine in Urine

\[
y = 0.0397x - 0.2301 \\
R^2 = 0.9952
\]

Conclusion
A new ion source has been developed that permits the analysis of gases, liquids, and solids in open air under ambient conditions. No solvents or high-pressure gases are used. The sample is not directly exposed to high voltages, laser beams or radiation or plasma. The combination of this source with a high-resolution time-of-flight mass spectrometer permits rapid qualitative and quantitative analysis of a wide variety of materials.

Acknowledgment
Technical assistance and keen scientific insight were unselfishly provided by (in alphabetical order) Daniel Banquer, Ted Boileau, William Creasy, Daniel Evans, Drew McCrady, Michael McKie, Michael Nilles, Edward Owen, Gary Samuelson, Philip Smith, John Stuff, and Dean Tipple. The authors would like to thank Prof. Facundo Fernandez of Georgia Tech University for the dihydroartemisinin and counterfeit drug sample.

Additional Information
Additional applications and digital videos showing DART analysis are available on the internet at http://www.jeolusa.com/ms/msprod-
References

[25] IonSense, Inc., 11 Dearborn Road, Peabody, MA USA 01960.

Fig. 6 3 ppm explosives spiked into muddy water. 1=DNT, 2=amino-DNT, 3=trinitrotoluene, 4=TNT, 5=RDH+TFA, 6=Tetryl, 7=HMX+TFA, 8=palmitate in the water background (used as lock mass). Headspace vapor from a 0.1% aqueous solution of trifluoroacetic acid was used to produce TFA adducts.

Fig. 7 Positive-ion DART mass spectrum of triacetone triperoxide (TATP). Ammonium hydroxide headspace vapor provided a source of NH4+.

Fig. 8 Exact-mass analysis of trace simazine and propazine in a sample of the herbicide atrazine.

Table 2  DART measured masses for [M+H]+ from atrazine and trace impurities.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Composition</th>
<th>Measured</th>
<th>Calculated</th>
<th>Diff. (mmu)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrazine</td>
<td>C9H14N5Cl</td>
<td>216.10159</td>
<td>216.10160</td>
<td>-0.01</td>
</tr>
<tr>
<td>Propazine</td>
<td>C6H7N5C</td>
<td>230.11760</td>
<td>230.11725</td>
<td>+0.35</td>
</tr>
<tr>
<td>Simazine</td>
<td>C7H13N5Cl</td>
<td>202.08440</td>
<td>202.08595</td>
<td>+1.60</td>
</tr>
</tbody>
</table>
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The AccuTOF® Atmospheric Pressure Interface: an Ideal Configuration for DART® and Ambient Ionization

Introduction
The DART ion source was developed on the JEOL AccuTOF time-of-flight mass spectrometer which allows the exit of the DART source to be positioned within millimeters of the sampling orifice (orifice 1) of the mass spectrometer atmospheric pressure interface (API). The AccuTOF vacuum system is robust, highly resistant to contamination, and capable of pumping helium DART gas without assistance.

The AccuTOF API
Figure 1 shows a schematic diagram of the AccuTOF atmospheric pressure interface. The API consists of two off-axis skimmers (designated “orifice 1” and “orifice 2”) with an intermediate ring lens, followed by a bent RF ion guide. The off-axis skimmer design traps contamination -- ions are electrostatically guided upward toward orifice 2 whereas neutral molecules are pumped downward. Any contamination that enters the API is either pumped away into the rough pump (RP) or trapped on the lower part of orifice 2. The bent RF ion guide provides an additional level of protection. This makes the AccuTOF an ideal mass spectrometer for DART analysis of dirty “real-world” samples such as mud, biological fluids, melted chocolate, polymers, and even crude oil. In addition, orifice 1 is easily accessible and is operated at low voltage and current, making it a convenient platform for ambient ionization sources.

Figure 1. Schematic diagram of the AccuTOF atmospheric pressure interface (API)

AccuTOF® is a registered trademark of JEOL Ltd. (Akishima Japan)
DART® is a registered trademark of JEOL USA, Inc. (Peabody, MA USA)
Figure 2 shows the DART source mounted on the AccuTOF with the exit of the ceramic insulator positioned approximately 1 cm from the apex of orifice 1. This is the optimal positioning of the DART source for normal operation.

**The Vapur® Interface**

**Description**

The vacuum systems of other mass spectrometer systems are not capable of handling the additional pumping burden and may shut down if the DART is operated with helium. The Vapur® interface allows the DART source to be used with non-JEOL mass spectrometers. It consists of a ceramic tube mounted on a custom flange and an auxiliary pumping stage (Figure 3 and Figure 4) that is used as an interface for mounting the DART on ALL non-JEOL mass spectrometers and for mounting certain DART accessories that require additional clearance.

**Figure 3. Schematic diagram of Vapur interface. On the AccuTOF, the gap between orifice 1 and the exit of the Vapur ceramic tube should be 2 mm for optimal performance.**

Vapur® is a registered trademark of IonSense LLC (Saugus, MA USA)
Loss of signal
The large diameter of the Vapur interface’s ceramic tube improves reproducibility for some analyses by reducing gas turbulence and it provides space for mounting some accessories such as the IonSense 3+D Scanner. However, increasing the gas flow path increases the likelihood of ion-molecule reactions occurring, which can cause a loss of signal for samples that do not have a high proton affinity. Figure 5a shows the normal DART positive-ion low-mass background without the Vapur installed. The dominant reagent ions are protonated water and proton-bound water dimer. Figure 5b shows the background measured with the Vapur installed. Protonated water is barely visible, even at a magnification of 25X. The other peaks are trace impurities in the gas lines and in the background that have a higher proton affinity than water.

Figure 5. (a) positive-ion low-mass DART background without the Vapur installed, showing the dominant reagent ions with trace laboratory solvent peaks and (b) the low-mass background observed with the Vapur installed.
Nonpolar compounds are particularly susceptible to signal loss due to ion-molecule reactions at atmospheric pressure. Figure 6 illustrates the signal loss for a roughly equimolar mixture of epitestosterone and quinine with trace levels of methyl stearate as the Vapur is installed. The methyl stearate signal is completely lost, epitestosterone’s signal reduced by a factor of 6, and even the relatively polar quinine is attenuated by a factor of 2.

![Figure 6. Comparison of signal for quinine, epitestosterone, and methyl stearate (a) without the Vapur interface and (b) with the Vapur interface.](image)

**Differences in ionization chemistry**

Samples such as ethers and carbonyls measured with the Vapur interface installed tend to form ammonium adducts preferentially. This results from ion-molecule reactions occurring during sample transport through the Vapur, which favor ammonium over hydronium due to the high proton affinity of trace atmospheric ammonia. Samples without a strongly basic site that normally produce proton adducts by DART without the Vapur may be observed as ammonium adducts if the Vapur is installed. Figure 7 shows the comparison of the DART mass spectra measured for a polyethylene glycol (PEG) sample measured without the Vapur (Figure 7a) and with the Vapur (Figure 7b). Proton and ammonium adducts are observed in both spectra, but the proton adducts dominate in Figure 7a, whereas ammonium adducts dominate in Figure 7b.
Sample Carryover

Sample carryover in the Vapur is a problem for some samples. Therefore it is important to limit sample quantity when using the Vapur and to check for cross-contamination between samples. Figure 8 shows an example for the analysis of a sample containing 1% diisobutyl phthalate in isopropanol. Samples were introduced by depositing them onto the sealed end of a melting point tube and positioning the tube in the DART gas stream for several seconds. Three replicate measurements were made for the sample, followed by a mass reference standard (Jeffamine® M-600, Huntsman Corporation). Figure 8a shows the results of the sample measurement without the Vapur installed, and Figure 8b shows the results of the same measurements with the Vapur installed. The red arrows indicate the time at which each sample was introduced into the DART gas stream. Note that the total ion current and reconstructed ion current chronogram (RIC) for diisobutyl phthalate show increasing contamination in Figure 7b as the DiBP is adsorbed onto the ceramic tube. The results obtained without the Vapur do not show any sample carryover and it is easy to determine when each sample was measured.

Figure 8. Chronograms for three replicate measurements of a sample containing diisobutyl phthalate (DiBP) (a) with no Vapur and (b) with the Vapur installed.
Vapur Summary

• **Features**
  - Assists weaker vacuum systems to pump helium.
  - Improves reproducibility by reducing effects of turbulence.
  - Provides a universal EART interface.

• **Problems**
  - Required for DART on ALL mass spectrometers **EXCEPT THE JEOL AccuTOF.**
  - Ion-molecule reactions occur as ions are transported over a longer distance.
  - Loss of non-polar and reactive compounds including the air peaks.
  - Ammonium adducts dominate over M+.
  - Increased oxidation.
  - Problems with sample carryover if compounds stick to the Vapur ceramic tube.
  - Requires an extra vacuum pump.

**Conclusion**

The AccuTOF mass spectrometer atmospheric pressure interface is an ideal platform for use with the DART and ambient ionization sources. It permits the use of the DART without additional pumps, interfaces, or hardware that can cause sample carryover, loss of signal, or changes in the DART ionization chemistry.
Drug counterfeiting is becoming a serious and widespread public health problem. The number of FDA open investigations into drug counterfeiting rose sharply from 2000 to 2001 and has remained high in recent years. Counterfeit drugs are not only illegal, but dangerous; they may contain little or no actual drug content, or they may contain completely different drugs with potentially toxic consequences. The problem is worldwide; it has been reported that nearly 50% of all anti-malarial drugs in Africa are thought to be counterfeit.

Direct Analysis in Real Time (DART™) offers a simple solution to screening for counterfeit drugs. DART can detect the presence or absence of drugs in medicines within seconds by simply placing the pill or medicine in front of the mass spectrometer. In combination with the AccuTOF, DART provides exact masses and accurate isotopic patterns that provide elemental compositions for known and unknown substances.

The top spectrum (below left) shows a sample of a genuine drug containing the anti-malarial compound “Guilin B” containing artesunate (structure below right), and the bottom spectrum shows a counterfeit drug containing only binders (stearate and palmitate) and no active ingredient. The samples were placed in front of the DART with no sample preparation and the mass spectra were obtained within seconds.

It is noteworthy that the peak at m/z 283.15476 in the genuine drug is assigned the composition C_{19}H_{28}O_{8}^- (dihydroartemisinin or a fragment from artesunate). The measured m/z differs from the calculated m/z by only 0.2 millimass units and is easily distinguished by its exact mass measurement from the peak at m/z 283.26405 (C_{18}H_{35}O_{2}^- or stearate) in the phony drug. This illustrates the value of AccuTOF’s exact mass measurements in making correct assignments for compounds having the same integer mass.

2. Samples were provided courtesy of Prof. Facundo Fernandez, Georgia Institute of Technology.
Direct Analysis of Drugs in Pills and Capsules with No Sample Preparation

The AccuTOF™ equipped with Direct Analysis in Real Time (DART™) is capable of analyzing drugs in pills and capsules with no sample preparation. In most cases, the pill can simply be placed in front of the DART and the active ingredients can be detected within seconds. This application note shows a wide variety of pills that have been analyzed by using DART. The examples include prescription drugs, over-the-counter medicines, and illicit drugs that were confiscated by a law-enforcement agency.

Examples of Pills and Medicines that Have Been Analyzed Directly by DART

**OTC Medicines**
- Ibuprofen (anti-inflammatory)
- Naproxen sodium (anti-inflammatory)
- Aspirin (anti-inflammatory)
- Acetaminophen ("Tylenol®" painkiller)
- Sudafed® (pseudoephedrine decongestant)
- Melatonin (sleep aid)
- Chlortrimeton (antihistamine)
- Cough syrup (guaifenesin and dextromethorphan)
- Codeine with Tylenol® (painkiller)

**Prescription Drugs**
- Generic Wellbutrin® (Bupropion antidepressant)
- Zantac® (ranitidine: histamine H 2 -receptor antagonist) Sealed capsule.
- Lipitor® (atorvastatin: treatment of hypercholesterolemia)
- Endocet® (oxycodone plus acetaminophen)
- Levsin® sublingual tablet (Hyoscyamine anticholinergic)

**Dietary Supplements and Herbal Medicines**
- Coenzyme Q10 with Vitamin E and Di- and Triglycerides
- Magnolia Bark (Chinese herbal medicine)
- Conjugated Linoleic Acid ("CLA" weight-loss formulation)

**Confiscated Illicit Drugs**
- Dimethoxyamphetamine plus methamphetamine
- Methylendioxymethamphetamine ("Ecstasy" or MDMA)
- OxyContin®

All brand names are registered trademarks of their respective manufacturers.
Introduction
Recent events have led to the recall of both pet food and dairy food products from international consumer markets. In both cases, melamine was added to these products to show a higher chemical signature for proteins, which in turn would increase the reported quality of the food. Unfortunately, the effect of this melamine addition caused the death of both pets and babies that consumed these tainted products. As a result, there is growing government and consumer concern towards the presence of melamine in food products.1, 2 Because of this concern, there is a need for a rapid and accurate test to quickly determine the presence of melamine in these food products. Previously, the JEOL AccuTOF-DART was shown to be an effective technique for determining the presence of melamine in pet food.3 In this work, we extend the application of AccuTOF-DART to show that melamine can be rapidly detected when it is present in dry nonfat milk.

Experimental
Solid melamine granules were artificially spiked into commercially available dry nonfat milk at levels between 1000 ppm and 500 ppb. These samples were then pulverized with a mortar and pestle to homogenize the mixtures. For analysis, the AccuTOF-DART system was set to the following parameters: needle voltage 3500V, discharge electrode 150V, grid electrode 40V, Helium temperature 150 degrees C, and He flowrate 2.3 L/min. A melting point tube was dipped and swirled through the melamine/milk mixture and then placed in the Helium stream between the DART and the AccuTOF atmospheric pressure interface. The data was collected in a matter of seconds from the moment the samples were introduced into the DART stream. A representative mass spectrum is shown in Figure 1 that shows the high resolution and isotopic data for the melamine [M+H]+. Additionally, a semi-quantitative calibration curve was constructed to show the ability of the AccuTOF-DART to measure melamine in dry milk over a dynamic range of concentrations (Figure 2). Furthermore, using this methodology, the AccuTOF-DART was able to detect 1 ppm of melamine in dry milk, which is below the United States Food and Drug Administration’s maximum allowable concentration of 2.5 ppm.1

Conclusion
Unlike other analytical techniques, the AccuTOF-DART methodology described above does not require time consuming extractions or chromatographic methods to detect melamine in dry milk. Additionally, within seconds of sampling the tainted milk, the AccuTOF-DART provides high resolution and isotopic data to identify melamine.

References


Tomatoes are rich in lycopene, a hydrocarbon antioxidant that is the source of the red coloring in ripe tomatoes. The potential benefits of nutritional antioxidants such as lycopene have received a great deal of attention in the popular media.

A piece of tomato skin was placed in front of the DART and the positive-ion mass spectrum was recorded. Peaks were quickly observed at the expected exact masses for lycopene and [M+H]+ (C_{40}H_{57}^+, m/z 537.4460) and phytoene [M+H]+ (C_{40}H_{65}^+, m/z 545.5086).
Instantaneous Detection of Opiates in Single Poppy Seeds

Poppy seed is a common flavoring ingredient that is known to contain small amounts of opiates. Maximum morphine and codeine concentrations are estimated to be about 33 and 14 micrograms respectively per gram of seed. Consumption of typical amounts of baked goods containing poppy seeds has not been shown to cause any ill effects. However, ingestion of poppy seeds may result in false positives from drug tests.

Single poppy seeds from different sources were analyzed independently in two different laboratories by using the DART™/AccuTOF™ combination. The resulting mass spectra were nearly identical.

**Distribution of Capsaicin in Chili Peppers**

Capsaicin (C\textsubscript{18}H\textsubscript{27}NO\textsubscript{3}) is the molecule that causes the hot, burning sensation when you eat chili peppers. Capsaicin, dihydrocapsaicin (C\textsubscript{18}H\textsubscript{29}NO\textsubscript{3}), and a related compound, nonivamide (C\textsubscript{17}H\textsubscript{27}NO\textsubscript{3}) are found in different concentrations in different parts of the pepper pod.

We examined different parts of a hot pepper to determine which part of the pepper contains the highest concentration of capsaicin. Different sections of the pepper were placed between the DART and the AccuTOF orifice. Little capsaicin was found in the fleshy part of the pepper; higher concentrations were found in the pepper seeds. The highest concentration of capsaicin was found in the membrane inside the pepper pod onto which the seeds are attached.
Detection of Unstable Compound Released by Chopped Chives

Every cook knows that chopping onions releases chemicals that cause eye irritation. The lachrymator released by chopped onions and related plants is formed by the action of a pair of enzymes on a cysteine derivative to ultimately form propanethial S-oxide (C₃H₆SO), the compound that causes eye irritation. This compound is reactive and unstable and is therefore difficult to analyze by conventional mass spectrometry techniques. However, DART was easily able to detect propanethial S-oxide when a freshly cut chive bulb was placed in front of the mass spectrometer. The sample was analyzed at atmospheric pressure under ambient conditions and no sample preparation was required, other than cutting into the chive bulb. The compound was detected as [M+H]+ (C₃H₆SO+, m/z 91.0139).

Lachrymator detected from freshly chopped chive bulbs placed in front of the mass spectrometer.
Rapid Detection of Fungicide in Orange Peel

Thiabendazole is an anthelmintic and a highly persistent systematic benzimidazole fungicide that is widely used for controlling spoilage in citrus fruit. It is considered a General Use Pesticide (GUP) in EPA Toxicity Class III – Slight Toxicity.

A small piece of orange peel (a few square millimeters in size) from a Florida orange was placed in the DART sampling region. Compounds present in the peel were detected within seconds. Among these were the familiar orange-oil flavor components such as limonene and sinensal as well as polymethoxylated flavones that are attributed with antioxidant and cholesterol-reducing properties.

An enlarged view of the region near m/z 202 is shown below. The large peak at m/z 205.1949 has the elemental composition C_{15}H_{24}, assigned as the [M+H]^+ for farnesene. Residual thiabendazole was detected as [M+H]^+ at m/z 202.0444, which differs by only 0.0005 from the theoretical m/z of 202.0439.

Conclusion: DART was used for the rapid detection of trace pesticides on fruit.
Detection of Oleocanthal in Freshly Pressed Extra-Virgin Olive Oil

According to a recent report in *Nature*¹, freshly pressed extra-virgin olive oil contains a compound, oleocanthal, that has properties similar to the common anti-inflammatory drug, ibuprofen.

We used DART to rapidly examine cooking oils for the presence of this compound. Fresh-pressed extra-virgin olive oil from a specialty food store was compared with a medium-quality grocery-store brand. Sesame oil and a low-quality spray-on cooking oil were also examined. No sample preparation was required. Glass melting point tubes were dipped into the oil samples and then placed in front of the DART source for analysis. The DART source was operated with helium in positive-ion mode at a gas heater temperature of 350°C. A cotton swab dipped in dilute aqueous ammonium hydroxide was placed nearby to permit the formation of [M+NH₄]⁺ for triglycerides and other oil components. A mass spectrum of neat PEG 600 on a glass rod was acquired and stored in the same data file to provide an external calibrant for exact mass measurements.

The oleocanthal was readily observed in the fresh-pressed oil as [M+H]⁺ and [M+NH₄]⁺. The measured masses confirmed the expected composition with excellent mass accuracy.

**Figure 1.** Positive-ion DART mass spectra of two olive oils. Enlarged view of the region where oleocanthal peaks are observed.

**Conclusion**
DART can detect the presence of natural products in cooking oils. Analysis is rapid (within seconds) and no sample preparation is required.

**Reference**
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Introduction

Dietary fats are categorized according to the level of unsaturation. Oils are a mixture of triglycerides and free fatty acids. Olive oil contains a high concentration of monounsaturated fatty acids, while other oils such as Canola and safflower oil contain larger amounts of polyunsaturated fatty acids. Characterizing the type of lipids present is important for quality control and for detecting adulteration of more expensive oils (e.g., olive oil) with cheaper products. Analysis by HPLC is time-consuming and requires solvents and consumables. DART provides a convenient alternative: no solvents are required and the analysis can be completed in seconds.

Experimental

Analysis was carried out by using a JEOL AccuTOF-DART™ mass spectrometer operated in positive-ion mode at a resolving power of >6000 (FWHM). The DART source was operated with helium and the gas heater was set to 375°C. Melting point tubes were dipped in oil samples and placed in front of the DART ion source for a few seconds. A cotton swab dipped in dilute ammonium hydroxide was placed nearby to enhance formation of [M+NH₄]⁺ from triglycerides. A spectrum of PEG 600 was measured between samples to permit exact mass measurements.

Results

Figure 1 shows the DART mass spectrum of a grocery-store olive oil and Figure 2 shows a comparison of mass spectra for different cooking oils. Free fatty acids (Figure 3), squalene and di- and triglycerides (Figure 4) are detected as [M+NH₄]⁺. The relatively high abundance of free fatty acids in Figure 1 (bottom) is a result of thermal decomposition and is only observed at higher gas temperatures for large amounts of (neat) oil. However, the abundant peaks for the free

![Image of mass spectra](https://example.com/image.png)

Figure 1. Medium-quality grocery store olive oil. Top: dilute solution of olive oil in hexane, bottom: neat oil (DART at 375°C).
fatty acids under these conditions make it easy to see differences in the overall fatty acid content of the oil. Of the C$_{18}$ fatty acids, oleic acid (O) comprises 55-85% of olive oil, while the Omega-6 fatty acid linoleic acid (L) is present at about 9% and the Omega-3 fatty acid linolenic acid (Ln) is present at less than 1.5%. Other fatty acids including the C$_{16}$ palmitic acid (P) are also detected.

The triglycerides are readily detected (Figure 4) and their elemental compositions confirmed by exact mass measurements (Table 1) and isotope pattern matching. Triolein (OOO) is the major component in olive oil, while increasing unsaturation is observed for the Canola/safflower oil blend and the sesame oil.

Elemental compositions were confirmed for the triglyceride [M+NH$_4$]$^+$ peaks by exact mass measurements and isotope pattern matching. Examples for triolein (OOO) and OOP are shown in Table 1. Figure 5 shows the DART mass spectrum of an olive oil sample to which 50% of the Canola/safflower oil blend has been added. In comparison with the unadulterated olive oil (Figures 3 and 4), the adulterated oil is easily recognized by the higher degree of unsaturation and the relatively higher abundance of linoleic and linolenic acids.
Figure 3. Enlarged view of free fatty acid region

Figure 4. Enlarged view of triglycerides in cooking oils
### Table 1. Elemental compositions from exact mass measurements

<table>
<thead>
<tr>
<th>Meas. mass (um)</th>
<th>Abund. (%)</th>
<th>Difference (mmu)</th>
<th>Unsaturation</th>
<th>Compositions</th>
</tr>
</thead>
<tbody>
<tr>
<td>876.801270</td>
<td>25.14</td>
<td>-0.75</td>
<td>3.5</td>
<td>C55 H106 O6 N1 (OOP)</td>
</tr>
<tr>
<td>902.816040</td>
<td>35.62</td>
<td>-1.61</td>
<td>4.5</td>
<td>C57 H108 O6 N1 (OOO)</td>
</tr>
</tbody>
</table>

**Figure 5. DART mass spectrum of adulterated olive oil**

**Conclusion**

DART can characterize lipids such as fatty acids and mono-, di-, and triglycerides in cooking oils and detect adulterated olive oil within seconds and with no sample preparation.

**Reference**

Flavones and Flavor Components in Two Basil Leaf Chemotypes

The chemical composition of herbs and spices can vary dramatically between different species and different growing conditions. Herbs grown under different conditions that have different essential oil compositions are referred to as chemotypes. 

Basil is an herb that has widely varying chemotypes\(^1,2\). The difference between basil leaves from two different sources was easily observed by using DART. A leaf from a basil plant purchased at a grocery store was compared with a leaf from a Vietnamese restaurant. A small particle from each leaf was analyzed placed in front of the DART source. Mass spectra were obtained within seconds. Elemental compositions were confirmed by exact masses and accurate isotopic abundance measurements.

The resulting mass spectra (Figure 1) show dramatic differences between the two leaves. The basil leaf from the Vietnamese restaurant has a pleasing licorice-like flavor and a fragrant licorice-and-lemon aroma whereas the grocery store basil has a very mild clove flavor and a weak aroma. Both leaves contain terpenes and sesquiterpenes. The mass spectrum of the restaurant basil leaf (top figure) shows an abundant estragole (methyl chavicol, or \(p\)-allyl anisole) peak and a smaller citral peak. The grocery-store basil shows a weak eugenol peak. Furthermore, the restaurant basil leaf shows an abundance of hydroxymethoxyflavones. Flavones and related compounds are of interest because of possible antioxidant activity or other health benefits\(^3,4\). The grocery store basil shows only weak peaks for these compounds.

![Figure 1. DART analysis of two different basil leaves.](image)

**Conclusion**

DART can rapidly detect flavor components and antioxidants in herbs and spices and can be used to discriminate between different chemotypes.

**References**

1. [http://www.plantphysiol.org/cgi/content/full/136/3/3724](http://www.plantphysiol.org/cgi/content/full/136/3/3724)
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Direct analysis of caffeine in soft drinks and coffee and tea infusions

Caffeine (Figure 1), a xanthine alkaloid acting as psychoactive stimulant and mild diuretic in human, is an integral part of diet of many people. It is often found in natural products such as tea, coffee and cocoa beans, cola nuts and many others. Analysis of caffeine in various foods and beverages is an important task for analytical laboratories, as its content is considered in assessment of product quality (coffee, cocoa beans and tea). Due to its physiological effect, the amount of caffeine is regulated in selected foods in EU. Maximum limits are set for some soft drinks to which caffeine is added. HPLC methods employing UV detection are commonly used for its control. While for soft drinks and coffee/tea infusions, the sample preparation is not too much time demanding, LC separation of sample components becomes a limiting step in laboratory throughput. Employing AccuTOF-DART system offers straightforward examination of caffeine content in tens of samples per hour, thanks to omitting separation step. Isotope dilution is used for target analyte quantification.

Figure 1 Structure of caffeine (1,3,7-trimethylxanthine, CAS Number: 58-08-2).

![Structure of caffeine](image)

Experimental

Samples

The samples were prepared for analysis in following way:

(i) Soft drinks (ice tea, cola drink, energy drink) were decarbonized by sonication.
(ii) Soluble coffee 2 g were diluted in 100 mL of boiling water.
(iii) Ground coffee beans and tea leaves (5 g) were extracted with 100 mL of boiling water under shaking (1 min).

All liquid samples were diluted 50 times and 5 µL of aqueous solution containing 5 µg of isotope labeled internal standard (13C3-caffeine) were added to 1 mL of each diluted sample.

Lukáš Václavík, Jakub Schürek and Jana Hajišlová. Department of Food Chemistry and Analysis, Institute of Chemical Technology Prague, Technická 5, 166 28 Prague 6 – Dejvice, Czech Republic. Phone: +420 220 443 185, e-mail: jana.hajislova@vscht.cz
DART-TOFMS measurements

The DART ion source was operated in positive ion mode with helium as the ionizing medium at a flow rate of 2.7 L/min. The gas beam was heated to 350°C, discharge needle voltage set to 3000 V, perforated and grid electrode voltages were +150 V and +250 V, respectively. Accurate mass spectra were acquired in a range of m/z 50–500 employing 0.2 s recording interval; the peaks voltage value was set to 1000 V. A solution containing a mixture of polyethylene glycol (PEG) 800 and 200 was introduced at the end of each sample analysis to compensate any mass drift.

The examined samples were introduced automatically with the use of an AutoDart sampler and Dip-aTM tips. Following steps were involved: (i) sampling tip immersed into the sample; (ii) placing of tip in front of the DART gun exit close to the ion source – mass spectrometer axis; (ii) sampling tip disposed. Five replicate measurements were carried out on examined samples.

Results

As shown in Figure 3, both caffeine and isotope labeled internal standard were detected as [M+H]⁺ ions. The differences between exact and measured masses were as low as -0.7 mmu and -0.6 mmu, respectively.

In Figure 4 calibration plot of caffeine is shown. Each data point is an average of five repeated analyses measured over a period of five days, good linearity was obtained (R² = 0.989). Table 1 summarizes the results of analyses obtained by analyses of the above samples. The repeatability of measurements was less then 8% (RSD) within an experimental series for all examined matrices. Good agreement with data obtained by reference HPLC/UV method was obtained.

Conclusions

DART-TOFMS technique was demonstrated to be suitable for accurate determination of caffeine in various beverages including coffee and tea infusions. The requirements on sample preparation are minimal: only dilution, sonication and internal standard addition are needed. The results of preliminary experiments have shown the potential of DART-TOFMS to detect also other regulated compounds in soft drinks (artificial sweeteners, acidulants, preservation agents, etc.).

Table 1 Caffeine concentrations in examined samples.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Caffeine concentration (µg/ml)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee infusion</td>
<td>250</td>
<td>7.9</td>
</tr>
<tr>
<td>Black tea infusion</td>
<td>103</td>
<td>4.2</td>
</tr>
<tr>
<td>Green tea infusion</td>
<td>71</td>
<td>3.1</td>
</tr>
<tr>
<td>Ice tea</td>
<td>44</td>
<td>5.6</td>
</tr>
<tr>
<td>Cola drink</td>
<td>95</td>
<td>4.5</td>
</tr>
<tr>
<td>Energy drink</td>
<td>230</td>
<td>3.5</td>
</tr>
</tbody>
</table>

* calculated to undiluted beverage. n = 5
Rapid screening of strobilurins in crude solid materials (wheat grains) using DART-TOFMS

Direct control of solid materials for pesticide residues is a challenging task enabling fast contamination screening. In our study, we investigated direct analysis of strobilurin fungicides in milled wheat grains. Strobilurins, systemic pesticides originated from natural fungicidal derivatives, play an important role in control of various plant pathogens.\textsuperscript{1,2,3} Because of their unique protective properties, significant yield enhancements and longer retention of green leaf tissue, strobilurins have been widely used in agriculture since their introduction on the market in 1992.\textsuperscript{3} As other pesticides, these compounds are involved in control and monitoring surveys undertaken by regulation authorities.\textsuperscript{4} Some characteristics of strobilurins are shown in Table 1.

\textbf{Table 1} Strobilurins: physico-chemical characteristics.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>log Kow</th>
<th>water solubility (mg l\textsuperscript{-1})</th>
<th>molecular weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoxystrobin</td>
<td><img src="image1" alt="Structure" /></td>
<td>2.5</td>
<td>6.0</td>
<td>403.4</td>
</tr>
<tr>
<td>Kresoxim methyl</td>
<td><img src="image2" alt="Structure" /></td>
<td>3.4</td>
<td>2.0</td>
<td>313.4</td>
</tr>
<tr>
<td>Pyraclostrobin</td>
<td><img src="image3" alt="Structure" /></td>
<td>4.0</td>
<td>4.6</td>
<td>387.8</td>
</tr>
</tbody>
</table>

AccuTOF-DART system was used for examination of milled wheat grains containing incurred residues of azoxystrobin, kresoxim methyl and pyraclostrobin.

The DART ion source was operated in positive ion mode with helium as the ionizing medium at flow a rate of 2.7 L/min. The gas beam was heated to 130°C and the distance between the exit of the DART gun and inlet of the mass spectrometer was 12 mm. The discharge needle voltage of the DART source was set to positive
potential of 2400 V, perforated and grid electrode voltages were +150 V and +250 V, respectively. Accurate mass spectra were acquired in a range of m/z 100-500, spectra recording interval was 0.2 s; the peaks voltage value was set to 850 V. A mixture solution of polyethylene glycol PEG 600 and 200 was used for calibration. The same calibrant was also introduced at the end of each sample analysis to perform mass drift compensation. The mass resolution of the mass spectrometer was typically 6000 ± 500 (FWHM).

Samples were introduced manually with the use of in-hand made filtering paper envelopes containing approximately 1 g of homogenous sample. The sample was spread across the edge of the envelope (see Figure 1) and placed into the DART gas stream to ionize target analytes and detect the respective peaks.

**Figure 1** The only items needed for fast analysis of strobilurins in milled wheat grain are: a) incurred wheat grain sample, b) filtering paper, c) spatula, d) PEG solution.

In Figures 2, 3 and 4 a positive-ion DART mass spectrum of directly analyzed wheat grains samples showing the tested strobilurins as [M+H]+. The ion identity was confirmed by elemental composition calculations as documented in Table 2 and also shown in respective Figures.

**Figure 2** a) Mass spectrum of wheat grains containing incurred residues of azoxystrobin. b) Estimation of an element composition from exact mass measurement. The highlighted column stands for target analyte.

**Figure 3** a) Mass spectrum of wheat grains containing incurred residues of pyraclostrobin. b) Estimated element composition from exact mass measurement. The highlighted column stands for target analyte.

**Figure 4** a) Mass spectrum of wheat grains containing incurred residues of kresoxim-methyl. b) Estimated element composition from exact mass measurement. The highlighted column stands for target analyte.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Exact mass (m/z)</th>
<th>Measured mass (m/z)</th>
<th>Difference (m/z)</th>
<th>Elemental composition</th>
<th>Concentration (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoxystrobin</td>
<td>314.13023</td>
<td>314.13864</td>
<td>-0.24</td>
<td>C19H19NO6</td>
<td>45</td>
</tr>
<tr>
<td>Kresoxim methyl</td>
<td>388.15641</td>
<td>388.15890</td>
<td>-0.49</td>
<td>C19H19O11</td>
<td>202</td>
</tr>
<tr>
<td>Pyraclostrobin</td>
<td>398.15035</td>
<td>398.15011</td>
<td>0.02</td>
<td>C19H19O11</td>
<td>43</td>
</tr>
</tbody>
</table>

The quantification was performed using DART-TOFMS for the analysis of dried outside samples of wheat grains (propiconazole was used as internal standard).

In this study, DART-TOFMS system has been demonstrated as a suitable tool for rapid screening of strobilurin fungicides, time and money consuming sample preparation and purification steps can be omitted. The exact mass measurements provide high degree of confirmation, enabled by elemental composition calculation of target analytes.

**References**
Analysis of strobilurins in wheat grains using DART-TOFMS

Strobilurins, systemic pesticides originated from natural fungicidal derivatives, play an important role in control of various plant pathogens.\textsuperscript{1,2,3} Because of their unique protective properties, significant yield enhancements and longer retention of green leaf tissue, strobilurins have been widely used in agriculture since their introduction on the market in 1992.\textsuperscript{3} As other pesticides, these compounds are involved in control and monitoring surveys undertaken by regulation authorities.\textsuperscript{4} Some characteristics of strobilurins are shown in Table 1.

\begin{table}[h]
\centering
\begin{tabular}{llc}
\hline
\textbf{Compound} & \textbf{CAS number} & \textbf{Structure} & \textbf{MRL (mg/kg) in wheat} \\
& & & \textbf{UK} & \textbf{Codex} & \textbf{EU} \\
\hline
Azoxystrobin & 131860-33-8 & \includegraphics[width=0.2\textwidth]{Azoxystrobin.png} & 0.3 & none & 0.3 \\
Kresoxim methyl & 143390-89-0 & \includegraphics[width=0.2\textwidth]{Kresoxim_methyl.png} & 0.05 & 0.05 & 0.05 \\
Pyraclostrobin & 175013-18-0 & \includegraphics[width=0.2\textwidth]{Pyraclostrobin.png} & 0.2 & none & none \\
Trifloxystrobin & 141517-21-7 & \includegraphics[width=0.2\textwidth]{Trifloxystrobin.png} & 0.02\textsuperscript{a} & none & none \\
Dimoxystrobin & 149961-52-4 & \includegraphics[width=0.2\textwidth]{Dimoxystrobin.png} & 0.05\textsuperscript{b} & none & none \\
Picoxystrobin & 117428-22-5 & \includegraphics[width=0.2\textwidth]{Picoxystrobin.png} & 0.05\textsuperscript{b} & none & 0.05\textsuperscript{b} \\
\hline
\end{tabular}
\caption{Strobilurins: structure and MRLs in wheat.}
\end{table}

\textsuperscript{a} proposed MRL, \textsuperscript{b} temporary MRL
The AccuTOF-DART system equipped with an AutoDart HTC PAL autosampler was used for the analysis of strobilurin residues (listed in Table 1) in wheat grain extracts. Crude extracts were prepared by shaking 12.5 g of sample with 50 mL of ethyl acetate and 5 mL of Na₂SO₄ suspension was then filtered and the volume was made up to 25 mL by rotavapour. Within the validation, extracts spiked with strobilurins in the range from 12 to 1200 ng/g were analyzed. For quantitative analysis, prochloraz was used as an internal standard (samples were spiked with this internal standard at a level of 250 ng/g).

The DART ion source was operated in positive ion mode with helium as the ionizing medium at a flow rate of 2.7 L/min. The gas beam was heated to 300°C, and the optimal distance between the exit of the DART gun and inlet of the mass spectrometer was 12 mm. The discharge needle voltage was set to positive potential of 3000 V, perforated and grid electrode voltages were +150 V and +250 V, respectively. Accurate mass spectra were acquired in a range of m/z 100-500 employing 0.2 s recording interval; the peaks voltage value was set to 1000 V. A solution containing a mixture of poly(ethylene glycol) PEG 600 and 200 was used for mass calibration. The same calibrant was introduced at the end of each sample analysis to compensate any mass drift. The mass resolution of the mass spectrometer was typically 6000 ± 500 (FWHM).

The examined samples were introduced automatically with the use of an AutoDart sampler and Di-electroTM tips. A sampling tip was immersed into the sample and then placed in front of the DART gun exit close to the source – mass spectrometer axis. Each sample was examined in six repeated runs. The TIC chromatogram of spiked wheat sample is shown in Figure 1. Due to the variability of absolute responses, the use of internal standard is obviously essential for quantitative measurements.

**Figure 1** TIC chromatogram: “on-line” 6 repeated injections of spiked wheat extract followed by PEG mixture.

Figure 2 shows a positive-ion DART mass spectrum of crude ethyl acetate wheat extract spiked with strobilurins. Under those experimental conditions, both strobilurins and internal standard were detected as [M-H]⁻. In Table 2, measured and exact masses are compared, the differences ranged from 1.95 to 2.51 mmu.

**Figure 2** Strobilurins (240 ng/g) and prochloraz (250 ng/g) in wheat extract.

As Figure 3 shows, acceptable linearity was obtained for the analytes in the range from 12 to 1200 ppb.

The repeatability of measurements at a spiking level of 60 ng/g was in the range 8–15% (n = 6), limits of quantification (LOQs) ranged from 12 to 30 ng/g depending on the particular analyte. To prove the trueness of generated data, wheat grains with incurred strobilurin residues (reference material) were employed. Table 3 documents good agreement between the data obtained by DART-TOFMS and accredited LC-MS/MS method.

**Table 1** Strobilurins identified in wheat extract by exact mass

<table>
<thead>
<tr>
<th>Compound</th>
<th>Exact mass (m/z) [M-H]⁻</th>
<th>Measured mass (m/z) [M-H]⁻</th>
<th>Difference (mmu)</th>
<th>Elemental composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoxystrobin</td>
<td>304.1265</td>
<td>304.1263</td>
<td>0.95</td>
<td>C₂₃H₂₅N₄O₁₀</td>
</tr>
<tr>
<td>Kresoxyn methyl</td>
<td>314.1323</td>
<td>314.1411</td>
<td>0.98</td>
<td>C₂₃H₂₅N₄O₁₀</td>
</tr>
<tr>
<td>Pyraclostrobin</td>
<td>388.1964</td>
<td>388.1957</td>
<td>0.94</td>
<td>C₃₂H₃₀N₄O₁₀</td>
</tr>
<tr>
<td>Triklosyenethyl</td>
<td>459.1372</td>
<td>459.1389</td>
<td>0.51</td>
<td>C₃₂H₃₀N₄O₁₀</td>
</tr>
<tr>
<td>Dimethoxytrobin</td>
<td>327.1758</td>
<td>327.1715</td>
<td>0.71</td>
<td>C₂₃H₂₅N₄O₁₀</td>
</tr>
<tr>
<td>Picoxytrobin</td>
<td>308.1197</td>
<td>308.1162</td>
<td>0.85</td>
<td>C₂₃H₂₅N₄O₁₀</td>
</tr>
<tr>
<td>Prochloraz</td>
<td>370.0884</td>
<td>370.0892</td>
<td>0.28</td>
<td>C₂₃H₂₅N₄O₁₀</td>
</tr>
</tbody>
</table>

As Figure 3 shows, acceptable linearity was obtained for the analytes in the range from 12 to 1200 ppb.

**Table 3** Comparison of DART-TOFMS and LC–MS/MS method: analysis of wheat grain reference material.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>DART-TOFMS Conc. (ppb)</th>
<th>LC–MS/MS Conc. (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoxystrobin</td>
<td>100</td>
<td>182</td>
</tr>
<tr>
<td>Kresoxyn methyl</td>
<td>40</td>
<td>52</td>
</tr>
<tr>
<td>Pyraclostrobin</td>
<td>200</td>
<td>170</td>
</tr>
</tbody>
</table>

Compared to conventional LC–MS/MS method, DART-TOFMS allowed significant decrease of analysis time, thus, enabled increase of sample throughput. Although the detection limits are somewhat higher employing this new strategy as compared to the LC–MS/MS method, the DART-TOFMS enables convenient control of MRLs set for strobilurins residues in wheat grains which are in the range from 0.05 to 0.3 mg/kg.

**References**

**Analysis of deoxynivalenol in beer**

Mycotoxins, toxic secondary metabolites of several fungal species, represent food safety issue of high concern. Deoxynivalenol (Figure 1), the most abundant trichothecene mycotoxin, can be found world-wide as a contaminant of wheat, barley, maize and other cereals.\(^1\)\(^2\) The transmission of deoxynivalenol from barley into beer has been reported in several studies.\(^3\)\(^4\) Therefore, its levels should be controlled.

*Figure 1* Structure of deoxynivalenol, trichothecene B *Fusarium* toxin.

The AccuTOF-LC time-of-flight mass spectrometer equipped with a DART ion source and AutoDart HTC PAL autosampler, was used for examination of beer in this study. Donprep® immunoaffinity columns (R-Biopharm) was employed for selective isolation of target analyte from the sample. Briefly, 10 mL of beer with added internal standard ((\(^{13}\)C\(^{15}\))-deoxynivalenol, 500 ng/ml) were passed through the cartridge, which was then washed with 5 mL of water. Deoxynivalenol was subsequently eluted with 4.5 mL of methanol. Calibration standards containing deoxynivalenol in the range from 100 to 1500 ng/mL and fixed amount of internal standard (500 ng/mL) were prepared for quantification.

Introduction of the sample \((n = 5)\) into the gas beam was carried out automatically with the use of autosampler. Beer extract was placed in the sampling hole, Dip-it\(^{\text{TM}}\) sampler stick was immersed into the sample and introduced in front of the DART ion source (Figure 2). After each sample analysis, PEG mixture solution was injected for mass drift compensation. TIC chromatogram of beer sample analysis is shown in Figure 3.
To enhance negative ionization of target analytes, vial containing methylene chloride was placed beneath DART gun exit — MS office axis. After sample introduction, both deoxyxynivalenol and $^{13}$C$_6$-deoxyxynivalenol were immediately detected as [M+Cl]$^-$ (see Figure 4) under parameters setting shown in Table 1. Good mass accuracy was obtained (see Table 2).

**Table 1 Optimized DART ion source parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Setting</th>
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</thead>
<tbody>
<tr>
<td>Polarity</td>
<td>negative</td>
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<tr>
<td>Helium flow rate</td>
<td>2.7 L/min</td>
</tr>
<tr>
<td>Discharge needle voltage</td>
<td>3000 V</td>
</tr>
<tr>
<td>Perforated electrode voltage</td>
<td>-150 V</td>
</tr>
<tr>
<td>Grid electrode voltage</td>
<td>-250 V</td>
</tr>
<tr>
<td>Gas beam temperature</td>
<td>300 °C</td>
</tr>
</tbody>
</table>

**Figure 4** Positive DART spectrum: deoxyxynivalenol and internal standard in beer extract.

<table>
<thead>
<tr>
<th>Table 2 Comparison of exact and measured masses.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Deoxyxynivalenol</td>
</tr>
<tr>
<td>$^{13}$C$_6$-Deoxyxynivalenol</td>
</tr>
</tbody>
</table>

In conclusion, AccuTOF-DART has been demonstrated as a suitable to screen for deoxyxynivalenol in beer samples purified by simple procedure employing immunoaffinity columns.

**References**

Using Solid Phase Microextraction with AccuTOF-DART™ for Fragrance Analysis

Introduction
Solid phase microextraction (SPME) is a well established sampling technique that is often used to isolate volatile organic components in gaseous mixtures. Once the compounds have been collected, the SPME fibers are typically placed into a heated GC inlet which thermally desorbs these components into a GC-MS system for analysis. Normally, this analysis can take between 10 and 30 minutes to complete depending on the complexity of the samples. In this work, the Direct Analysis in Real Time (DART™) heated gas stream is used to desorb and directly introduce a SPME sample into a high-resolution mass spectrometer. This methodology produces comparable information to the traditional GC-MS technique but streamlines the results into only a few seconds of analysis time.

Experimental
A Supelco DVB/Carboxen/PDMS StableFlex SPME fiber was placed in an enclosed plastic bag with a banana for 10 minutes during each analysis. For direct analysis of the SPME fiber, the JEOL AccuTOF-DART™ system was set to the following parameters: needle voltage 3500V, discharge electrode 150V, grid electrode 250V, helium temperature 200 degrees C, and helium flowrate 2.3 L/min. A JEOL GC-Mate II high resolution sector bench top system equipped with a DB5-HT (0.25mm × 30m) was used for the GC-MS portion of the analysis. The GC-Mate II was set to the following parameters: inlet temperature 250 degrees C, split ratio 30, and helium flowrate 1.2 mL/min. The GC oven was set for the following temperature profile: 40 degrees C held for 2 min, ramp from 40 to 260 degrees C at 20 degrees C/min, 260 degrees C held for 2 min.

Results and Conditions
Figure 1 shows a typical AccuTOF-DART™ mass spectrum obtained for a banana headspace sample. At first glance, this spectrum might appear complex, but using the JEOL-provided ChemSW Search from List Software, all of the [M+H]+, [M+NH4]+, and [2M+H]+ for each alcohol, acetate, and butyrate were identified, summed together, and normalized in a matter of seconds. Additionally, these results were directly comparable to the data obtained for the traditional GC-MS analysis done using the GC-Mate II. Figure 2 shows a side-by-side comparison of these data sets. This work clearly demonstrates that the AccuTOF-DART™ can be used with SPME to quickly produce results that are comparable to traditional analysis techniques.

Figure 1. AccuTOF-DART mass spectrum for banana fragrance from SPME fiber.

Figure 2. Comparison of relative abundances observed for compound using GC-MS and DART-MS analysis.
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Fingerprints contain a great deal of chemical information that is not often exploited for forensic analysis. DART can detect and identify the chemical components of fingerprints, often providing information about what substances a subject has been handling.

An example is shown here for DART analysis of a single fingerprint made on a glass vial after touching an aspirin/oxycodone tablet. The aspirin and oxycodone are readily detected, along with minoxidil (hair-loss treatment), fatty acids, urea, lactic acid, squalene, cholestadiene, and the common plasticizer BEHP bis(ethylhexylphthalate). The amino acids A, F, G, I/L, S, P, T, and V are also detected with relative abundances between 0.5% and 18%. Other lipids can be detected at higher masses (not shown). Oxycodone is readily separated at the AccuTOF’s high resolving power from an unassigned interference at m/z 316.

Figure 1. Fingerprint on a glass vial after touching Oxycodone tablet.

Figure 2. Enlarged view of region near m/z 316, showing that oxycodone is resolved from interference at the same integer m/z.
Conclusion

DART can identify compounds in fingerprints, often making it possible to determine what substances a subject has been handling.

Table 1. Compounds detected within 0.002 u of compounds in a list of common drugs and components in human sweat.

<table>
<thead>
<tr>
<th>Name</th>
<th>Meas.</th>
<th>Calc.</th>
<th>Diff(u)</th>
<th>Abund.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>316.1554</td>
<td>316.1549</td>
<td>0.0005</td>
<td>2.3573</td>
</tr>
<tr>
<td>Aspirin-H₂O</td>
<td>163.0398</td>
<td>163.0395</td>
<td>0.0003</td>
<td>8.9676</td>
</tr>
<tr>
<td>Aspirin-fragment_1</td>
<td>139.0401</td>
<td>139.0395</td>
<td>0.0006</td>
<td>11.9823</td>
</tr>
<tr>
<td>Aspirin-fragment_2</td>
<td>121.0286</td>
<td>121.0290</td>
<td>0.0004</td>
<td>42.4559</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>210.1355</td>
<td>210.1355</td>
<td>0.0000</td>
<td>61.6484</td>
</tr>
<tr>
<td>Urea</td>
<td>61.0413</td>
<td>61.0402</td>
<td>0.0011</td>
<td>74.7234</td>
</tr>
<tr>
<td>Palmitic_acid</td>
<td>257.2477</td>
<td>257.2480</td>
<td>-0.0003</td>
<td>46.4336</td>
</tr>
<tr>
<td>C₁₆H₃₁O₂</td>
<td>255.2324</td>
<td>255.2324</td>
<td>0.0000</td>
<td>84.2178</td>
</tr>
<tr>
<td>Squalene</td>
<td>411.3996</td>
<td>411.3991</td>
<td>0.0005</td>
<td>100.0000</td>
</tr>
<tr>
<td>Cholestadiene</td>
<td>369.3525</td>
<td>369.3521</td>
<td>0.0004</td>
<td>19.7204</td>
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<tr>
<td>Lactic_acid</td>
<td>91.0400</td>
<td>91.0395</td>
<td>0.0005</td>
<td>21.1630</td>
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<tr>
<td>BEHP</td>
<td>391.2854</td>
<td>391.2849</td>
<td>0.0005</td>
<td>15.6784</td>
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<tr>
<td>Oleic_acid</td>
<td>283.2637</td>
<td>283.2637</td>
<td>0.0000</td>
<td>54.9441</td>
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<tr>
<td>Myristic_acid</td>
<td>229.2162</td>
<td>229.2168</td>
<td>-0.0006</td>
<td>18.8792</td>
</tr>
</tbody>
</table>

Figure 3. Amino acids A, F, G, I/L, S, P, T, and V detected with relative abundances between 0.5% and 18%
AccuTOF™ with DART™

Instantaneous Detection of Illicit Drugs on Currency

The widespread presence of illicit drugs on currency is an indication of the extent of the worldwide substance abuse problem. Remarkably, cocaine can be found on virtually all one-dollar bills in the United States — the upper limit for the general background level of cocaine is estimated to be 13 ng per bill.

The Direct Analysis in Real Time (DART™) ion source, combined with the AccuTOF™ mass spectrometer can be used to sample drugs on currency within seconds. No sample preparation (extraction, wipes, etc.) or chromatography is required. The bill is placed in front of the DART and the presence of drugs can be detected immediately. Only a small portion of the bill is sampled at any given time. This allows the analyst to view the distribution of drugs on the surface of a bill, and allows the bill to be retained for reexamination at a later time.

Over the past few years, we have used DART to examine paper currency from the United States and other countries. Cocaine was found at various levels on almost all US one-dollar bills. Cocaine was detected in significant amounts on a Venezuelan 50 Bolivares bill and in large amounts on a Spanish 2000 peseta bill. New currency and larger-denomination US bills were much less likely to show the presence of cocaine and other drugs.

Figure 1 shows the presence of cocaine on a US one-dollar bill. Cocaine is detected as C\textsubscript{17}H\textsubscript{22}NO\textsubscript{4} ([M+H]+) at m/z 304.15488. The assignment of this peak as cocaine was confirmed by raising the orifice potential to induce fragmentation (not shown). The cocaine fragment ion C\textsubscript{10}H\textsubscript{16}NO\textsubscript{2} is observed at m/z 182.1182. Mass measurements for both C\textsubscript{17}H\textsubscript{22}NO\textsubscript{4} and C\textsubscript{10}H\textsubscript{16}NO\textsubscript{2} were within one millimass unit.

Other drugs detected on dollar bills include methylphenidate (Ritalin, figure 2) and procaine. Procaine is a local anesthetic used by drug dealers as a cocaine adulterant.

Substances commonly detected on US bills include nicotine, diethyltoluamide (DEET bug repellent), sunscreen, dioctylphthalate (plasticizer), triethanolamine (from cosmetics) and glycerol and other polyols. Triethanolamine ([M+H]⁺, m/z 150.1130) is easily distinguished from the illicit drug methamphetamine ([M+H]⁺, m/z 150.1283) by its exact mass.

Figure 1. Cocaine on a US $1 bill.

Figure 2. Ritalin and cocaine on a US $1 bill. All compounds shown were detected as the [M+H]⁺ and composition assignments were verified by exact mass measurements.


MS-0501H

www.jeol.com
Instantaneous Detection of the “Date-Rape” Drug -- GHB

Gamma hydroxybutyrate (GHB) is a fast-acting central nervous system depressant\(^1\). Prior to its ban by the FDA in 1990, GHB was sold in bodybuilding formulas. It has been abused as a euphoriant. Because it is colorless and odorless, it can be added to alcoholic drinks of unsuspecting victims. An overdose can result in serious consequences, including respiratory depression and coma. GHB was classified as a Schedule I Controlled Substance in March, 2000.

Detection of GHB is problematic. GC/MS and LC/MS methods are time consuming. A rapid colorimetric assay for GHB has been developed\(^2\), but this assay suffers from some limitations. For example, ethanol produces the same colorimetric response as GHB.

The AccuTOF\textsuperscript{TM} mass spectrometer equipped with Direct Analysis in Real Time (DART\textsuperscript{TM}) can rapidly detect GHB anion (C\(_3\)H\(_7\)O\(_3\)\textsuperscript{-}, \(m/z\) 103.0395) on surfaces, in urine, and in ethanol. No solvent extraction, wipes, or chromatography are required. Examples are shown in the figures below.

---

The AccuTOF-DART™ was recently applied to an unusual analytical problem: finding the cause of oily stains on freshly laundered shirts (Figure 1). No cutting or extraction was required. Stained and unstained regions of the shirt were placed in the DART gas stream and the mass spectra were acquired.

The DART parameters were: helium gas, flow 3-4 LPM, gas heater set to 175 degrees C, positive-ion mode, PEG 600 exact mass reference standard. These conditions did not damage the shirt.

The mass spectrum of the stained region (Figure 2, top) showed a distinctive pattern of saturated fatty acids and their proton-bound dimers, monoglycerides, and triethanolamine. The same components were found in the dryer sheet (Figure 2, bottom). Elemental composition assignments were confirmed by exact mass measurements and computer-aided isotope pattern matching. The assignment of the fatty acids was confirmed by the presence of [M-H]^+ peaks in the negative-ion DART spectrum (not shown). Fatty acid esters will not produce [M-H]^+ peaks in negative-ion mode. After considering several possible sources of contamination, a matching pattern was found for the bargain-price fabric softener sheet that was placed in the clothes dryer with the shirts. The components causing the stains were released when the dryer sheet was exposed to high temperatures.

**Conclusion**

AccuTOF-DART was able to determine the nature and cause of oily stains on a shirt without causing any damage to the fabric. Solutions to the problem include lowering the dryer temperature, changing to a different brand of fabric softener, and re-washing the shirts.

---

**Figure 1.** Oily stain on a freshly laundered shirt placed in between DART ion source and AccuTOF mass spectrometer inlet. Inset: stain on shirt circled next to used dryer sheet.

**Figure 2.** (Top) AccuTOF-DART mass spectrum of stain on shirt. (Bottom) AccuTOF-DART mass spectrum of fabric softener sheet placed in the dryer with the shirts.
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Analysis of Biological Fluids

The AccuTOF-DART can detect a variety of substances in biological fluids such as urine, blood, and saliva with little or no sample preparation. These substances include drugs, amino acids, lipids, and metabolites.

Urine samples were analyzed by dipping a melting point tube in urine and placing the sample in front of the DART ion source. Figure 1 shows positive-ion DART mass spectra of a urine sample from a subject taking ranitidine to reduce stomach acid production. The enlarged view in the inset shows the ranitidine metabolites desmethyl ranitidine and ranitidine N-oxide.

Figure 2 shows a negative-ion DART mass spectrum of urine from the same subject. Compounds detected that fall within 0.002 u within the theoretical masses for compounds in a target list include nucleotide bases, caffeine metabolites, uric acid and related compounds, and organic acids.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>GBL</td>
<td>85.0295</td>
<td>85.0290</td>
<td>0.0005</td>
<td>11.0317</td>
</tr>
<tr>
<td>Pyruvic acid</td>
<td>87.0084</td>
<td>87.0082</td>
<td>0.0002</td>
<td>7.1380</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>89.0236</td>
<td>89.0239</td>
<td>-0.0003</td>
<td>8.3058</td>
</tr>
<tr>
<td>Creatine</td>
<td>112.0513</td>
<td>112.0511</td>
<td>0.0002</td>
<td>61.4851</td>
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<td>Purine</td>
<td>119.0354</td>
<td>119.0358</td>
<td>-0.0004</td>
<td>21.4610</td>
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<td>Diphydromethylnoradrenaline</td>
<td>127.0486</td>
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<td>131.0164</td>
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<td>Dihydropyrimidine</td>
<td>133.0469</td>
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<td>Hypoxanthine</td>
<td>135.0306</td>
<td>135.0307</td>
<td>0.0001</td>
<td>100.0000</td>
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<td>Methylhypoxanthine</td>
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<td>0.0001</td>
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<td>155.0487</td>
<td>0.0006</td>
<td>28.6232</td>
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<td>0.0011</td>
<td>22.9722</td>
</tr>
<tr>
<td>1,3-Dihydropurine</td>
<td>165.0489</td>
<td>165.0492</td>
<td>-0.0003</td>
<td>22.5018</td>
</tr>
<tr>
<td>Hypoxanthine</td>
<td>170.0513</td>
<td>170.0554</td>
<td>0.0041</td>
<td>39.7499</td>
</tr>
<tr>
<td>Dimethylhypoxanthine</td>
<td>179.0527</td>
<td>179.0518</td>
<td>0.0009</td>
<td>25.7977</td>
</tr>
<tr>
<td>AAMU (caffeine met.)</td>
<td>187.0467</td>
<td>187.0465</td>
<td>0.0002</td>
<td>76.4617</td>
</tr>
<tr>
<td>Cinnamalminomethyloxalic acid</td>
<td>217.0483</td>
<td>217.0501</td>
<td>-0.0017</td>
<td>67.3389</td>
</tr>
<tr>
<td>AAMU (caffeine met.)</td>
<td>225.0463</td>
<td>225.0524</td>
<td>0.0061</td>
<td>21.9092</td>
</tr>
<tr>
<td>Cytidine</td>
<td>242.0831</td>
<td>242.0777</td>
<td>0.0054</td>
<td>3.4345</td>
</tr>
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<td>Uric acid</td>
<td>243.0461</td>
<td>243.0417</td>
<td>0.0044</td>
<td>21.1156</td>
</tr>
<tr>
<td>Phenylacetylethylmalonic acid</td>
<td>263.1033</td>
<td>263.1032</td>
<td>0.0001</td>
<td>48.8665</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>313.1321</td>
<td>313.1334</td>
<td>-0.0013</td>
<td>8.7459</td>
</tr>
<tr>
<td>Ranitidine+Cl</td>
<td>349.1113</td>
<td>348.1105</td>
<td>0.0008</td>
<td>11.7296</td>
</tr>
</tbody>
</table>

Figure 1. Ranitidine metabolites in human urine.

Table I. Compounds identified by exact mass.

Figure 2. Negative-ion DART mass spectrum of urine from the same subject.
Quantitative analysis is possible. DART response is proportional to sample quantity. However, the absolute response is dependent on the position of the sample in the DART gas stream and on position of the sample relative to the mass spectrometer sampling orifice.

Addition of an internal standard can compensate for variations in ion abundance due to differences in placement of the sample tube in the DART ion source. Figure 3 shows the working curve obtained for urine samples that have been spiked with gamma hydroxy butyrate (GHB) at concentrations ranging from 0 ppm to 800 ppm. Samples were spiked with 50 ppm of a deuterated internal standard (d6-GHB). A melting point tube was dipped into the urine samples and then placed in front of the DART source. Results were obtained within seconds. Five replicates were measured for each concentration over a period of five days. Excellent linearity was observed.

Although some compounds can be detected in whole blood, whole blood is not well suited for analysis with no sample preparation. Minimal sample preparation can reveal compounds that are not readily detected in whole blood. Figure 4 shows amino acids detected in whole blood. Centrifuging the blood sample to remove blood cells makes it possible to detect triglycerides (Figure 5). The addition of acetonitrile to remove blood proteins makes it possible to detect other compounds, such as ranitidine (Figure 6).

Figure 3. GHB in urine.

Figure 4. Amino acids in whole human blood.

Figure 5. Triglycerides in human blood plasma.
Analysis of other body fluids has been investigated briefly. Figure 7 shows the detection of amino acids and caffeine in a saliva sample from a coffee drinker.

**Conclusion**

DART can be used to analyze biological fluids. Only a few drops of fluid are required for the analysis.

Detection limits for many compounds with no sample preparation or preconcentration are in the high ppb to low ppm range.
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AccuTOF-DART™
Clandestine Methamphetamine Labs: Rapid Impurity Profiling by AccuTOF-DART™

Introduction
Methamphetamine is a Schedule II Controlled Substance that is illegally manufactured in clandestine labs. There are several common synthetic pathways in use. For this study, methamphetamine was synthesized from phenyl-2-propanone by the (1) Leukart synthesis or (2) Reductive Amination, or from ephedrine or pseudoephedrine by the (3) Nagai, (4) Birch, and (5) Edme syntheses. Each of these reaction sequences resulted in unique impurity profiles1-3 that can be used by law enforcement to track the activities of clan labs, distribution networks, and trafficking patterns. The AccuTOF-DART was used to examine the starting materials, reaction mixtures, and final products from each reaction scheme.

Experimental
A JEOL AccuTOF-DART mass spectrometer was used for all measurements. Samples were deposited on the sealed end of melting point tubes and measured in positive-ion mode with helium DART gas and a gas heater setting of 350°C. Polyethylene glycol (average MW 600) was used as a reference standard for exact mass measurements.

Results
Examples are given of the DART mass spectra measured for methamphetamine synthesized by the Birch (Figure 2) and Nagai (Figure 3) synthetic methods.

Meth Synthetic Pathways

- Phenyl-2-propanone (P2P)
  1. Leukart
     P2P + methylformamide
  2. Reductive Amination
     P2P + methylamine

- Ephedrine/Pseudoephedrine
  3. Nagai (HJ + red P)
  4. Birch (Li + NH3)
  5. Edme (SOCl2)
     H2/Pd-BaSO4
     many other permutations exist!

Figure 1. Common synthetic pathways for the illicit manufacture of methamphetamine.
Conclusion
The AccuTOF-DART can provide rapid impurity profiling that can be used by law enforcement to characterize the starting products, reaction mixtures, and semi-purified final products for methamphetamine manufactured in clandestine laboratories. The results support and complement the alternative GC/MS methods.

Acknowledgement
These data were provided by Prof. Jason Shepard. A more complete discussion of these results for all five reaction methods will be found in a forthcoming publication (reference 4).

References
X-Ray Fluorescence Helps Identify Peaks in DART Mass Spectrum of Electrical Tape - ElementEye JSX-1000S and AccuTOF-DART

**Introduction**

The identification of electrical tapes is important for forensic investigation of improvised explosive devices [1]. Pyrolysis mass spectrometry [2] and X-Ray Fluorescence (XRF) [3] are among the methods that are used for the forensic analysis of electrical tapes.

Direct Analysis in Real Time (DART) can be operated with a high gas temperature as an alternative to conventional pyrolysis GC/MS methods [4,5]. A sample of electrical tape analyzed with the AccuTOF-DART™ showed distinctive peaks in the negative-ion DART mass spectrum. No reasonable elemental compositions could be determined by assuming the presence of only the common organic elements: C, H, O, P, S, Cl, Si, and Br. X-ray fluorescence (XRF) data obtained with the ElementEye™ indicated the presence of Zn and Sb, allowing us to correctly assign the elemental compositions for the peaks observed in the DART mass spectrum.

**Experimental**

A piece of electrical tape was placed in the DART gas stream with the DART gas heater set to 500°C (pyrolytic DART conditions). A sample of poly(perfluoropropyl ether) was measured in the same data file as a mass reference standard for exact mass measurements. Elemental compositions with isotope matching were determined by using Mass Mountaineer™ software. The XRF spectrum of the sample was measured with the Element Eye by using the Quick and Easy Organic Analysis method and the ElementEye reporting program. The collimator was set to 2 mm and the total analysis time was 60 seconds.

**Results and Discussion**

The negative-ion DART mass spectrum in Figure 1 shows distinctive peaks with isotope patterns that suggest the presence of multiple halogens (chlorine and/or bromine). This is not unexpected considering that electrical tape can be made of polyvinyl chloride (PVC). However, no reasonable elemental composition assignments could be made by assuming only elements present in common organic polymers. To assign the elemental compositions, we needed additional information about which other elements might be present.

![Fig. 1 Negative-ion AccuTOF-DART mass spectrum of a piece of electrical tape.](image-url)
Among the elements detected in the XRF spectrum (Figure 2, Table 1) are antimony, zinc, chlorine and bromine. Adding these elements to the constraints for the elemental composition calculation for the AccuTOF-DART data allows us to correctly assign the elemental compositions for these peaks (Figure 3). The measured isotope peaks show excellent agreement with the calculated isotope patterns (Figure 4).

<table>
<thead>
<tr>
<th>Analysis Target</th>
<th>Result</th>
<th>Unit</th>
<th>3sigma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminium</td>
<td>1.01</td>
<td>%</td>
<td>0.30</td>
</tr>
<tr>
<td>Iron</td>
<td>0.18</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Manganese</td>
<td>0.00</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Nickel</td>
<td>0.00</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.43</td>
<td>%</td>
<td>0.01</td>
</tr>
<tr>
<td>Silicon</td>
<td>1.38</td>
<td>%</td>
<td>0.05</td>
</tr>
<tr>
<td>Strontium</td>
<td>0.00</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Titanium</td>
<td>0.19</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Antimony</td>
<td>1.87</td>
<td>%</td>
<td>0.02</td>
</tr>
<tr>
<td>Copper</td>
<td>0.03</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.27</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Calcium</td>
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<td>%</td>
<td>0.02</td>
</tr>
<tr>
<td>Sulfur</td>
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<td>%</td>
<td>0.01</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0.09</td>
<td>%</td>
<td>0.01</td>
</tr>
<tr>
<td>Bromine</td>
<td>0.03</td>
<td>%</td>
<td>0.00</td>
</tr>
<tr>
<td>Chlorine</td>
<td>19.21</td>
<td>%</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 1. Elements detected by the ElementEye

Fig. 3. Elemental composition assignments for the peaks in the mass spectrum from Figure 1 calculated after determining the presence of Zn, Sb, Cl, and Br from the XRF data.
Conclusion

Elemental composition assignments based on accurate mass and isotope measurements by mass spectrometry require the operator to provide a list of elements that may be present and their limits. If an element is omitted from the list, the correct assignment will not be reported. If too many elements are added to the list, the number of possible compositions becomes uninterpretable. The ElementEye is a rapid and convenient tool that provides complementary elemental information allowing us to assign the unknown peaks in the AccuTOF-DART data for the electrical tape sample.

References


Detection of the Peroxide Explosives TATP and HMTD

Introduction
The explosive peroxide compounds triacetone triperoxide (TATP) and hexamethylenetriperoxide diamine (HMTD) are difficult to detect by conventional mass spectrometry methods. These compounds can be easily detected by the Direct Analysis in Real Time (DART™) ion source.

Experimental
Measurements were made with the AccuTOF-DART mass spectrometer operated in positive-ion mode under standard conditions. Little or no heat was required to observe these compounds. Dilute solutions of standard samples of TATP and HMTD were analyzed by dipping melting point tubes into the liquid and dangling the melting point tubes in the DART ion source. Dilute aqueous ammonium hydroxide on a cotton swab was held in the DART gas stream to enhance detection of TATP as the ammoniated molecule.

Results
TATP is readily detected as [M+NH₄]⁺ at m/z 240.1447 (Figure 1). A trace fragment at m/z 91.0399 is assigned as the C₃H₇O₃⁺ fragment. Exact mass measurements allow the assignment of the peak at m/z 223.0968 as C₁₂H₁₅O₄⁺, which is assigned as monobutyl phthalate [M+H]⁺. Exact mass measurements avoid a mistaken assignment of this peak as protonated TATP (m/z 223.1182), which is not observed.

HMTD is observed as the protonated molecule at m/z 209.0776. This is major species observed. A few small characteristic fragment ions may also be observed in the HMTD mass spectrum.

Conclusion
Peroxide explosives TATP and HMTD were easily detected by the AccuTOF-DART with no sample preparation. Both compounds were detected at trace levels on a variety of surfaces including fingertips, boarding passes, and cloth. Exact mass measurements confirmed the compositions and avoided mistaken assignment of a contaminant as a target analyte peak.

Figure 1. AccuTOF-DART mass spectrum of TATP

Figure 2. AccuTOF-DART mass spectrum of HMTD
Instantaneous Detection of Explosives on Clothing

The detection of explosives is of vital importance in forensic applications and in preventing criminal or terrorist activity. The analytical detection of explosives on surfaces is normally done by using solvent extractions or wipes and chromatography or chromatography combined with mass spectrometry. This is inefficient because solvent extractions and wipes only result in a partial transfer of material from the surface into the sampling material. Furthermore, the chromatographic analysis can be time-consuming and requires the use of disposable solvents (an environmental concern).

The JEOL AccuTOF™ with Direct Analysis in Real Time (DART™) has demonstrated the capability to detect both volatile and involatile explosives on surfaces such as plastic, cloth, concrete, glass, cardboard, metal, and more. No wipes or solvent extractions are required. The method is instantaneous, environmentally friendly, and does not require solvents. An example is shown in this application note.

A construction company has been recently conducting blasting to remove boulders near our offices. One of our employees happened to walk through the edge of the plume from the blasting when he arrived for work in the morning. At the end of the day, more than eight hours later, we tested him for exposure to explosives. By placing the employee’s necktie in front of the DART we could easily detect nitroglycerin, as shown in Figure 1 (below). It was not necessary to take the tie off to perform the analysis.

![Image of necktie under DART](image)

**Figure 1.** Nitroglycerin detected on an employee’s tie after exposure to a plume from blasting. Methylene chloride vapor was placed beneath the DART to enhance the formation of [M+Cl]−. All elemental compositions were easily confirmed by exact mass measurements.
Detection of Explosives in Muddy Water

The AccuTOF time-of-flight mass spectrometer equipped with Direct Analysis in Real Time (DART™) has been used to detect a wide variety of explosives in or on a variety of materials ranging from solutions to samples deposited on surfaces ranging from ABS plastic to metal, clothing and cardboard. Detection is rapid, specific, and sensitive. To demonstrate DART’s ability to detect explosives in a “messy” sample, we took a sample of muddy water from a frog pond in the woods near our laboratory. The water was spiked with 3 ppm of an explosives mixture, mixed and allowed to stand. A glass rod was dipped into the spiked water solution and then placed between the DART and the first orifice of the AccuTOF atmospheric pressure interface. An aqueous solution of 0.1% trifluoroacetic acid was placed under the glass rod to permit the formation of trifluoroacetate adducts for HMS and RDX. The results are shown in the figure below. The total time for analysis was 20 to 30 seconds.

Explosives detected in muddy water:

Some Explosives Analyzed by DART
- Sodium perchlorate
- Nitroglycerin (NG)
- Ethylene glycol dinitrate (EGDN)
- Dinitrotoluene (DNT)
- Amino-dinitrotoluene (DNT)
- Trinitrobenzene
- Hexamethylenetriperoxidediamine (HTMD)
- Triacetone triperoxide (TATP)
- Trimethylenetetranitramine (RDX)
- Tetramethylenetetra nitramine (HMX)
- Picrylmethylnitramine (Tetryl)
- Pentaerythritol tetranitrate (PETN)
**AccuTOF™ with DART™**

**Rapid Detection and Exact Mass Measurements of Trace Components in an Herbicide**

Analytical chemists are often asked to identify trace components in manufactured compounds such as drugs, consumer products, and agricultural chemicals. A common approach to the identification of minor components is to use gas or liquid chromatography coupled with high-resolution mass spectrometry. Although this approach is effective, it may be time-consuming and difficult to set up.

The AccuTOF with Direct Analysis in Real Time (DART™) provides a rapid solution. The high dynamic range of both source and detector permit the determination of minor components in the presence of a major component. The AccuTOF always provides high-resolution data with exact mass measurements and accurate isotope ratios that can provide elemental composition assignments for unknown compounds.

In this example, a few dust particles from a sample of atrazine herbicide containing 1% propazine and 0.2% simazine were deposited on a glass rod and placed in front of the DART. The mass spectrum shown below was measured in seconds. All three components were detected with good signal-to-noise and excellent mass accuracy and isotopic abundances.

**Exact Mass Measurements**

<table>
<thead>
<tr>
<th>Compound</th>
<th>[M+H]⁺</th>
<th>Measured</th>
<th>Calculated</th>
<th>Diff. (mmu)</th>
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<td>Atrazine</td>
<td>C₈H₁₅N₅Cl</td>
<td>216.10159</td>
<td>216.10160</td>
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<tr>
<td>Propazine</td>
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<tr>
<td>Simazine</td>
<td>C₇H₁₃N₅Cl</td>
<td>202.08440</td>
<td>202.08595</td>
<td>+1.60</td>
</tr>
</tbody>
</table>
Rapid Analysis of \( p \)-Phenylenediamine Antioxidants in Rubber

**Introduction**

\( p \)-Phenylenediamine (PPD) and derivative compounds are commonly used as antioxidants and antiozonants in black rubber. These compounds can cause sensitization leading to contact dermatitis in susceptible individuals. Detection of additives in polymers such as rubber can be important for clinical, forensic, and manufacturing applications. Here we show that DART can be used to identify the presence of these compounds within seconds without requiring any solvents or sample preparation.

**Experimental**

Analysis was carried out by using the AccuTOF-DART. A piece of rubber from a mountain bike tire was placed in front of the DART ion source, which was operated with helium in positive-ion mode and a gas heater temperature of 250 degrees C. Signals appeared within seconds after placing the rubber in front of the DART source.

**Results**

Exact mass measurements combined with accurate isotopic abundances provided elemental compositions (Table I) that were searched against the NIST mass spectral database. Three antiozonant compounds were recognized from their exact mass measurements (see Table I): N-Phenyl-\( p \)-phenylenediamine (PPD), N-Isopropyl-N’-phenyl-\( p \)-phenylenediamine (IPPD), and N-(1,3-Dimethyl butyl)-N’-phenyl-\( p \)-phenylene diamine (DMBPPD).

<table>
<thead>
<tr>
<th>Meas. mass u</th>
<th>Abund. %</th>
<th>Diff. mmu</th>
<th>Unsat.</th>
<th>Compositions</th>
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</thead>
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<td>226.147202</td>
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<td>0.20</td>
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<td>( \text{C}<em>{15}\text{H}</em>{18}\text{N}_2 ) IPPD ( \text{M}^+ )</td>
</tr>
<tr>
<td>227.154297</td>
<td>0.00</td>
<td>-0.53</td>
<td>7.5</td>
<td>( \text{C}<em>{15}\text{H}</em>{19}\text{N}_2 ) IPPD ( \text{[M+H]}^+ )</td>
</tr>
<tr>
<td>268.194214</td>
<td>0.00</td>
<td>0.27</td>
<td>8.0</td>
<td>( \text{C}<em>{18}\text{H}</em>{24}\text{N}_2 ) DMBPPD ( \text{M}^+ )</td>
</tr>
<tr>
<td>269.201385</td>
<td>0.00</td>
<td>-0.40</td>
<td>7.5</td>
<td>( \text{C}<em>{18}\text{H}</em>{26}\text{N}_2 ) DMBPPD ( \text{[M+H]}^+ )</td>
</tr>
</tbody>
</table>

Figure 1. DART mass spectrum of a rubber particle from a mountain bike tire.

Table 1. Elemental compositions for \( p \)-phenylenediamine antiozonants in a rubber tire.
Direct Analysis of Adhesives

DART can be used with a heated gas stream to rapidly pyrolyze and identify low-volatility materials such as adhesives and resins, directly on surfaces. Although these materials are not pure compounds, a library of DART mass spectra can be created and searched to identify materials, and exact mass measurements coupled with accurate isotopic abundances can be used to identify unknown components. Examples are shown here for cured and uncured epoxies and acrylate adhesives on metal and glass.

All samples were analyzed by acquiring positive-ion mass spectra with the DART source operated with helium and a gas heater setting of 450°C (helium temperature ~350°C). All mass spectra were measured over the m/z range 60-1000 at a resolving power of 6000. Following each analysis, a glass rod coated with PEG 600 was placed in front of the DART source to provide a calibration for exact mass measurements. A nominal-mass library of adhesive mass spectra was created by using the software link to the NIST version 2.0 mass spectra database search program. All figures shown here are copied from that library and only integer masses are shown although exact masses were recorded for all peaks.

Figure 1. Cyanoacrylate adhesive on metal (Product 1)

Figure 2. Cyanoacrylate adhesive on metal (Product 2)
**Figure 3.** Methacrylate ester adhesive on glass (Product 3)

**Figure 4.** Epoxy resin (black component, uncured)

**Figure 5.** Epoxy hardener (white component)
Both cyanoacrylate products show ethyl cyanoacrylate (m/z 126.0555) and fragment ions C$_4$H$_2$NO$^+$ (m/z 80.0136) and C$_4$H$_4$NO$_2^+$ (m/z 98.0242). Product 2 shows an additional peak at measured m/z 113.0602. This differs by only -0.05 u from the calculated m/z for C$_6$H$_9$O$_2$, tentatively assigned as [M+H]$^+$ for allyl methacrylate. Product 2 also shows a series of high-mass peaks that differ by 44.0262, indicative of ethylene oxide based polymer subunits. A product described as a “methacrylate ester” (Figure 3) was dominated by the same C$_6$H$_9$O$_2^+$ peak (assigned as allyl methacrylate), with methacrylic acid observed as C$_4$H$_7$O$_2^+$ at m/z 87.0447 (+0.1 mmu error).

Several binary epoxy formulations (separate resin and hardener) were examined. Figures 4 and 5 show the spectrum of two separate uncured components of a fast-curing epoxy and Figure 6 shows the cured epoxy.

The major compound in the uncured epoxy resin (black component) is identified by exact mass as the diglycidyl ether of bisphenol A or DGEBA. This has the composition C$_{21}$H$_{24}$O$_4$ with [M+NH$_4$]$^+$ observed at m/z 358.2018. Fragments are seen at m/z 191.1072 (C$_{12}$H$_{15}$O$_2^+$) and m/z 325.143982 (C$_{23}$H$_{32}$NO$_4^+$). The major component in the hardener is identified as tris (2,4,6-dimethylaminomethyl) phenol (“DMP”), a widely used epoxy accelerator, with abundant fragments at nominal m/z 164.1075 (C$_{10}$H$_{14}$NO$^+$) and 221.165388 (C$_{13}$H$_{21}$N$_2$O$^+$). Peaks corresponding to DGEBA and the accelerator are evident in the cured epoxy resin.

A variety of other glues, cements, and adhesives were examined. Each showed a characteristic pattern, permitting the identification of the material. Residual solvent, residual monomer, unreacted and partially reacted components were detected together with pyrolysis fragments.

**Conclusion**

DART can be applied to the direct identification of adhesives and resins on surfaces. Exact mass measurements coupled with accurate isotopic abundances aid in the assignment of components in the adhesive formulations.
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DART can be used to analyze polymers, cements, resins, and glues by increasing the gas temperature to 450-550°C to induce pyrolysis. This has been applied to a variety of polymers including Nylons, polypropylene and polyethylene, polyethylene terephthalate (PET), polystyries, poly(methyl methacrylate) (PMMA), polycarbonate, phenoxy resin, polystyrene, and cellulose. Examples are shown here for standard samples of Nylon, polystyrene, and cellulose.

The DART source was operated with helium in positive-ion mode. The gas heater was set to 475°C. Resins were cured in an oven for several hours before analysis; some resin samples had been cured for longer periods of time (months or years). Exact masses and accurate isotopic abundances were used to assign elemental compositions for peaks in the mass spectra. Nominal-mass spectra were exported into a library database in NIST format to facilitate identification of unknowns.

---

**Figure 1.** Nylon 12: Poly(lauryl lactam).

![Graph showing mass spectra for nylon 12](image)

**Figure 2.** Polystyrene bead, average molecular weight ~ 240,000

![Graph showing mass spectra for polystyrene](image)
It should be noted that mass spectra of commercial polymers may be dominated by plasticizers and other additives which can complicate the analysis. Nevertheless, it was possible to identify polyethylene in a milk bottle, poly(ethylene terephthalate) in a soda bottle, and polystyrene in a CD case and a mass spectrometer filament box.

**Conclusion**

Polymers can be analyzed by DART. Fingerprint mass spectra are produced, and common formulation components can often be identified and confirmed by exact mass measurements.
Rapid Analysis of Glues, Cements, and Resins

DART™ can be used to analyze polymers, cements, resins, and glues by increasing the gas temperature to 450-550°C to induce pyrolysis. This has been applied to a variety of glues and resins, including epoxies, polyimide resins, PVD cement, and cyanoacrylates. Examples are shown here for cured and uncured epoxy resin and cyanoacrylate glues.

The DART was operated with helium in positive-ion mode. The gas heater was set to 475°C. Resins were cured in an oven for several hours before analysis; some resin samples had been cured for longer periods of time (months or years). Exact masses and accurate isotopic abundances were used to assign elemental compositions for peaks in the mass spectra. Nominal-mass spectra were exported into a library database in NIST format to facilitate identification of unknowns.

The black component (Figure 1) of a common binary quick-curing epoxy is found to be bisphenol A diglycidyl ether (DGEPA) and the white component (Figure 2) is the hardener DMP 30. The cured epoxy (Figure 3) shows some peaks common to both of these components, but new peaks are also observed from the polymerized resin.

Two different cyanoacrylate glues were examined. Both showed ethyl cyanoacrylate [M+H]^+ (m/z 126) and its fragments C_H_2NO^+ (m/z 80) and C_H_4NO_2^+ . Product 1 also contained allyl methacrylate and a polymer component with ethylene oxide (EO) subunits. Product 2 contained the common plasticizers tributyl citrate and tributyl acetylcitrate.

Conclusion

Glues, cements, and resins can be analyzed by DART. Fingerprint mass spectra are produced, and common formulation components can be identified and confirmed by exact mass measurements.
Figure 3. Cured epoxy resin on metal surface

Figure 4. Cured cyanoacrylate glue product 1

Figure 5. Cured cyanoacrylate glue product 2
~ Application Note for DART ~

**Analysis of Organic Contaminant on Metal Surface**

DART can ionize organic substance on solid surface in atmospheric pressure. By utilizing this feature, we analyzed organic contaminant adhered to a metal part (Fig. 1).

We wiped of the organic contamination on the metal surface by using ceramic fiber paper and analyzed it by holding up the ceramic fiber paper directly into the DART ion source. Peaks with 74 interval at m/z 371, m/z 445, and m/z 519 are observed (Fig. 2; upper). The elemental compositions of these ions were deduced from their respective accurate masses (Table 1) and they were found to be poly(dimethylsiloxane) series.

One of the candidates for the contamination was silicone vacuum grease. The grease was analyzed separately by DART and the mass spectrum (Fig. 2; lower) was found to contain the same peaks. We concluded that the contamination was from the vacuum grease.

**Conditions**

- **Ionization:** DART (+)
- **Helium gas temperature:** 250°C

![Fig. 1 Organic contamination on metal surface](image)

![Fig. 2 DART (+) mass spectra](image)

**Table 1** Estimated elemental compositions of major ions from the sample

<table>
<thead>
<tr>
<th>Observed m/z</th>
<th>Calculated m/z</th>
<th>Error (ppm)</th>
<th>Estimated composition</th>
<th>Unsaturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>371.10133</td>
<td>371.10178</td>
<td>-1.20</td>
<td>12C10 1H31 16O5 28Si5</td>
<td>0.5</td>
</tr>
<tr>
<td>445.12036</td>
<td>445.12057</td>
<td>-0.48</td>
<td>12C12 1H37 16O6 28Si6</td>
<td>0.5</td>
</tr>
<tr>
<td>519.13959</td>
<td>519.13936</td>
<td>0.44</td>
<td>12C14 1H43 16O7 28Si7</td>
<td>0.5</td>
</tr>
</tbody>
</table>

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Analysis of low polar compound by DART
~ analysis of organic electroluminescence materials ~

Introduction
In MS Tips No. D031 we introduced the example of high polar compound analysis with DART. This application note introduces the example of the analysis of low polar compounds.

For the mass spectrometric analysis of organic electroluminescence (EL) materials, which have been one of the typical luminescent materials in LC/MS (APCI, APPI), GC/MS (refer to MS Tips 78 and 87), MALDI-TOFMS, and TOFSIMS have been used.

This time, we have analyzed organic EL materials using DART as follows.

Methods
The samples were adhered to the tip of a glass rod and presented directly to the DART™ ion source.

Sample
- 4,4’-Bis(carbazol-9-yl)biphenyl (CBP)
- 4,4’-Bis(2,2-diphenyl-ethen-1-yl)biphenyl (DPVBi) (made by Luminescence Technology Corp., Taiwan)

Mass spectrometer
JMS-T100TD time-of-flight mass spectrometer

Ionization
DART (+)

Helium gas temperature
250 °C

Results and discussion

In both samples, [M+H]⁺ was detected as base peak. In addition, [M+NH4]⁺ and [M]⁺ were also detected.

DART has been proven effective in the analysis of low polar compounds such as organic EL.
Chemical Reaction Monitoring with the AccuTOF-DART™ Mass Spectrometer

Introduction
DART provides a convenient means for monitoring the progress of chemical reactions. Reactants, intermediates, products and byproducts can be detected by simply dipping a glass rod into the reaction pot and then placing the rod in front of the DART ion source. The AccuTOF’s ability to measure accurate masses and isotopic abundances makes it possible to confirm or identify the elemental compositions of peaks in the mass spectra. Here we show the use of AccuTOF-DART to monitor the acetylation of 1,2-hexanediol as a function of time.

Experimental
600 µl of 1,5-hexanediol (4.9 mmol) was mixed with 700 µl (12.3 mmol) of glacial acetic acid and one drop of concentrated sulfuric acid in a loosely capped scintillation vial. The reaction was slowly warmed with a heat gun and a fume vent was positioned over the reaction vial and the DART source. Samples were taken periodically for analysis with the AccuTOF-DART by dipping a melting point tube into the reaction mixture and placing the tube in front of the DART ion source for a few seconds. The reaction progress was monitored by plotting the fractional abundances of the protonated molecules (MH⁺) as measured for each component in the mass spectra.

Results
Figure 1 shows the time dependence of the fractional abundances of unreacted 1,5-hexanediol (MH⁺ at m/z 119.1072), the reaction intermediate 1,5-hexanediol monoacetate (MH⁺ at m/z 161.1178) and the product 1,5-hexanediol diacetate (MH⁺ at m/z 203.1283). At 20 minutes, roughly equal amounts of the intermediate monoacetate and the diacetate are present. At 90 minutes, the reaction was incomplete and unchanging because an insufficient excess of acetic acid was present. Adding another 100 µl of acetic acid allowed the reaction to go to completion in 120 minutes.

Conclusion
AccuTOF-DART provides a convenient and rapid means for monitoring the progress of chemical reactions. Reactants, intermediates, and products are readily detected.

Figure 1. Synthesis of 1,5-hexanediol diacetate monitored by AccuTOF-DART.
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**Summary**

Organometallic compounds play an important role in chemistry, as recently recognized by the awarding of the 2005 Nobel Prize in Chemistry to Chauvin, Schrock and Grubbs. Characterization of organometallic compounds by mass spectrometry can sometimes be complicated by problems with solubility and reactivity. Electron ionization can be used for some volatile organometallics. Fast atom bombardment (FAB) and electrospray ionization (ESI) are useful provided suitable solvents can be used. Field desorption (FD) is often effective, but FD emitters can be fragile and the analysis should be carried out by an experienced operator.

DART (Direct Analysis in Real Time) complements these methods and provides an alternative; it is fast and does not require solvents. The sampling area is purged with an inert gas, reducing the likelihood of undesirable reactions. Further, AccuTOF-DART permits exact mass measurements without requiring the presence of a reference standard during the sample measurement. DART is extremely robust and does not require special operator training.

Mass spectra of several organometallic compounds were obtained by using DART. A few dry particles of each compound were placed in front of the DART source on a melting point tube and mass spectra were obtained within seconds. The best results were obtained by using small quantities of sample; very large quantities can result in ion-molecule reactions between sample ions and sample neutrals, resulting in isotopic patterns characterized by both \( M^+ \) and \([M+H]^+\). All labeled assignments were confirmed by exact mass measurements and isotope pattern matching.

**Ferrocene: \( \text{Fe(C}_5\text{H}_5)_2 \)**

Ferrocene produces a molecular ion \( M^+ \) for low sample quantities (micrograms or less). If a larger quantity is analyzed, ion-molecule reactions result in protonation of the molecule to produce \([M+H]^+\).

---

**Figure 1.** Top: Theoretical isotope pattern for \( \text{Fe(C}_5\text{H}_5)_2 \)^+. Middle: Mass spectrum obtained by using a very small quantity of ferrocene. Bottom: Mass spectrum obtained by analyzing a large quantity of ferrocene on the melting point tube.
Tungsten hexacarbonyl: W(CO)₆
Like ferrocene, tungsten hexacarbonyl produces mass spectra characterized by a molecular ion for low sample concentrations. A protonated molecule is observed if large sample quantities are presented to the DART source.

![Image of W(CO)₆ isotope pattern and mass spectrum]

*Figure 2. Top: theoretical isotope pattern for W(CO)₆⁺. Bottom: measured mass spectrum for tungsten carbonyl.*

Acetylacetonato rhodium dicarbonyl: C₅H₈O₂Rh(CO)₂
This compound readily produces a molecular ion.

![Image of C₅H₈O₂Rh(CO)₂ isotope pattern and mass spectrum]

*Figure 3. Top: theoretical isotope pattern for C₅H₈O₂Rh(CO)₂⁺. Bottom: measured mass spectrum.*
(1,5-cyclooctadiene) platinum (II) chloride (C₈H₁₂PtCl₂)
This compound does not readily protonate. However, it produces an ammonium adduct if vapor from a dilute solution of ammonium hydroxide is present. Chloride loss and a related water adduct are also observed. A dimer ((C₈H₁₂)Pt₂Cl₃)²⁺ is also observed at higher mass (not shown).

---

Bis(diphenylphosphoethane) platinum dichloride: Pt(DPPE)Cl₂
This compound behaves in a similar manner to (1,5-cyclooctadiene) platinum (II) chloride. An ammonium adduct can be observed, together with a chloride loss and a dimer [2M-Cl]⁺.

---

Figure 4. Top inset: theoretical isotope pattern for [C₈H₁₂PtCl₂+NH₄]⁺.
Bottom: measured mass spectrum.

---

Figure 5. DART mass spectrum of Pt(DPPE)Cl₂. Top: mass spectrum for m/z 350 to m/z 1500. Bottom: enlarged view of region near [M-Cl]⁺.

---

Conclusion
AccuTOF-DART provides a convenient means for characterizing many organometallic compounds. No solvents are required and excellent agreement between theoretical and observed masses and isotopic abundances are obtained.
~ Application Note for DART ~

Analysis of highly polar compound by DART
~ analysis of ionic liquid ~

Introduction
Direct analysis in real time (DART™) is applicable to a wide variety of samples; from low polar to highly polar compounds. Ionic liquids have drawn much attention from various engineering fields, such as tribology, because of their unique properties of electrical conductivity, extremely low vapor pressure, low viscosity, low combustibility, etc. The sample was analyzed by dipping a glass rod to the sample and presented it directly to the DART™ ion source.

Methods
Sample 1-ethyl-3-methylimidazolium-bis(trifluoromethylsulfonyl)imide (EMI-TFSI)
Mass spectrometer JMS-T100TD time-of-flight mass spectrometer
Ionization DART (+), DART (-)
Helium gas temperature 200 °C

Results and discussion

As shown in Fig. 2, base peaks were observed at m/z 111 and m/z 280 for DART(+) and DART(-) respectively. The elemental compositions of the cation and anion were confirmed by accurate mass measurements as shown in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Measured</th>
<th>Theoretical</th>
<th>Error (10^-3 u)</th>
<th>Elucidated formula</th>
<th>Unsaturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cation</td>
<td>111.09226</td>
<td>111.09222</td>
<td>0.04</td>
<td>C6H11N2</td>
<td>2.5</td>
</tr>
<tr>
<td>Anaion</td>
<td>279.91569</td>
<td>279.91729</td>
<td>-1.60</td>
<td>C2F6NO3S2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Fig. 1 Structural formulae of EMI-TFSI

Fig. 2 DART mass spectra (top: DART(+) bottom: DART(-)
AccuTOF™ Mass Spectrometers

Elemental Compositions from Exact Mass Measurements and Accurate Isotopic Abundances

Introduction

Exact masses have been used for decades to calculate elemental compositions for known and unknown molecules. The traditional approach calculates all possible combinations of user-specified atoms that fall within a given error tolerance of a measured mass. The number of possible combinations increases dramatically with increasing mass and as more atoms are included in the search set. In many cases, it is not possible to determine a unique composition based on mass alone.

A common source of error in measuring isotopic abundances with scanning mass spectrometers is related to fluctuations in ion current during measurement. The AccuTOF family of mass spectrometers overcomes this problem by analyzing all of the isotopes formed at the same instant. Combined with a high-dynamic-range detector, this provides highly accurate isotopic abundances. It has been shown that accurately measured isotopic abundances can be combined with measured exact masses to dramatically reduce the number of possible elemental compositions for an unknown. It is often possible to deduce a unique elemental composition, facilitating the identification of unknown substances.

Figure 1. Elemental composition calculation for thioridazine from combined exact mass measurement with isotope matching.
Experimental

Samples in this report were measured with the AccuTOF-DART™ mass spectrometer. Similar procedures can be used with other members of the AccuTOF mass spectrometer family. Calibrated mass spectra were centroided and saved as JEOL-DX (JCAMP) text files. These text files were processed with the Elemental Composition Workshop from the Mass Spec Tools™ software suite distributed with AccuTOF mass spectrometers. The program permits automated isotope matching for measured mass spectra and provides a visual comparison between the measured and theoretical isotopic abundances for each hit (Figure 1).

Eleven small drug samples were deposited on melting point tubes and mounted on a support. Samples were passed sequentially in front of the DART source with a measurement time of about 3 seconds per sample. Neat PEG 600 on a melting point tube was also measured to provide an external mass calibration standard. Elemental compositions were calculated by assuming even-electron ions, a mass measurement error tolerance of 0.003 u, and default tolerances for isotope matching. Elemental limits were set to:

\[ C^{0/70} H^{0/80} O^{0/20} N^{0/10} S^{0/2} Cl^{0/1}. \]

The correct elemental composition was successfully determined for each sample as shown in Table 1. The total number of compositions calculated without isotope matching is shown in column 4 of the table. The correct composition was the number 1 ranked composition from the automated isotope match for all compounds measured. The most dramatic example was reserpine [M+H]+ (C_{33}H_{41}N_{2}O_{9}) which gave 30 compositions without isotope matching. Isotope matching reduced the number of possible compositions to 11 of which the best match corresponded to the correct composition.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Composition</th>
<th>Calculated m/z</th>
<th>#Compositions</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenolphthalein</td>
<td>C_{20}H_{15}O_{4}</td>
<td>319.097035</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Promazine</td>
<td>C_{17}H_{21}N_{2}S</td>
<td>285.142544</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Quinine</td>
<td>C_{20}H_{25}N_{2}O_{2}</td>
<td>325.191603</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Nortriptylene</td>
<td>C_{19}H_{22}N</td>
<td>264.175224</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>C_{21}H_{27}N_{2}S_{2}</td>
<td>371.161565</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>C_{17}H_{20}N_{2}S_{2}Cl</td>
<td>319.103572</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Doxepin</td>
<td>C_{19}H_{22}NO</td>
<td>280.170139</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>C_{21}H_{31}O_{5}</td>
<td>363.21715</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Reserpine</td>
<td>C_{33}H_{41}N_{2}O_{9}</td>
<td>609.281208</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Caffeine</td>
<td>C_{6}H_{11}N_{4}O_{2}</td>
<td>195.088201</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>C_{37}H_{68}NO_{13}</td>
<td>734.469069</td>
<td>22</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. [M+H]+ elemental compositions determined for 11 drugs measured in 0.58 minutes with the AccuTOF-DART. All compositions were correctly identified. The rms mass measurement error was 2.2 ppm.

References
3. JEOL USA, Inc. customers only.

MS-0510D-2
Identifying “Buried” Information in LC/MS Data

It is not always easy to identify minor unknown components in complex LC/MS datasets. The new DART™ ion source screened for components that were not immediately recognized in LC/MS analysis of tea samples.

LC/TOFMS datasets can contain high-resolution, exact-mass data for all ionized components of a complex mixture. Even with concurrent UV detection and chromatographic enhancement software, it is not always easy to identify all of the components that are present in the dataset. Furthermore, suppression effects may mask important information. Here, a new technique known as Direct Analysis in Real Time (DART™) was used to screen tea samples and provide elemental compositions for minor components that were “buried” in LC/MS data collected for tea analysis. DART is a powerful new ionization method that permits direct analysis of solid, liquid, or gas samples at atmospheric pressure and ground potential. DART has been applied to rapid in-situ analysis of a very wide range of materials ranging from drugs to explosives, foods, and beverages.

Experimental Conditions
Drinking-quality green tea was analyzed directly by dipping a glass rod into the liquid and placing the rod between the DART source and the mass spectrometer orifice. Analysis was complete within 30 seconds. Following the tea analysis, a piece of filter paper dipped in PEG 600 was placed in front of the DART to provide reference masses for exact mass measurements. LC/MS conditions were described in a previous application note. (http://www.jeolusa.com/DesktopModules/Bring2mind/DMX/Download.aspx?EntryId=29&PortalId=2&DownloadMethod=attachment).

Results and Conclusions
Elemental compositions for several components are given in Table 1 for several compounds identified by DART. Compositions were identified by combined exact-mass measurements and isotope pattern matching for the observed [M+H]⁺ species. Candidate compositions were proposed by searching the mass spectral database for suitable compounds having the correct elemental composition. Following DART analysis, reconstructed ion mass chromatograms were generated from the LC/MS data for the exact mass of each component.

DART is ideal for screening because the analysis is rapid, suppression is minimal, solvent adducts are not observed, and exact mass measurements are simple and accurate. The presence of several isomers having these candidate compositions was confirmed by the RIC’s. The LC/MS data shows well-separated isomers and provides quantitative information about each component.

| 1. C₆H₄O₂: Benzoquininone |
| 2. C₄H₄O₂: Furanone |
| 3. C₅H₄O₂: Furfural, pyranone |
| 4. C₆H₆O₃: Maltol |
| 5. C₇H₆O₃: Sesamol, dihydroxybenzaldehydes, salicylic acid |
| 6. C₆H₈O₄: Quercetin |
| 7. C₇H₈O₅: Myricetin |

Table 1. Elemental compositions and some candidate compounds identified by DART in green tea.

Figure 1. Portion of positive-ion DART mass spectrum for green tea sampled with a glass rod. Larger components such as #6-8, caffeine and catechin were detected but are not shown here.

Figure 2. Reconstructed mass chromatogram for m/z 139.0395 (C₇H₇O₃⁺).
**DART Contamination Resistance: Analysis of Compounds in Saturated Salt and Buffer Solutions**

DART provides very simple mass spectra that are free of multiple charging and alkali metal cation adducts such as \([M+Na]^+\) and \([M+K]^+\). This facilitates identification of target compounds in mixtures and simplifies assignment of elemental compositions for unknowns. 50 ppm solutions of chlorpromazine were prepared in ultrapure deionized (DI) water, aqueous solutions of saturated sodium chloride and saturated potassium phosphate buffer, and raw urine. Two microliters of each solution were applied to glass melting point tubes and analyzed by DART. The mass spectra are shown below. All spectra are characterized by \([M+H]^+\) and there is no evidence of \([M+Na]^+\) or \([M+K]^+\). Sample suppression is not observed at this concentration.

DART analysis of chlorpromazine in various solutions.

*Note: Ranitidine (m/z 315) is also present in the urine background.*

**Conclusion**

DART provides simple mass spectra, free of alkali metal cation adducts, even when analytes are present in concentrated salt or buffer solutions.
AccuTOF LC series with DART Bibliography

Updated: May 2016


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