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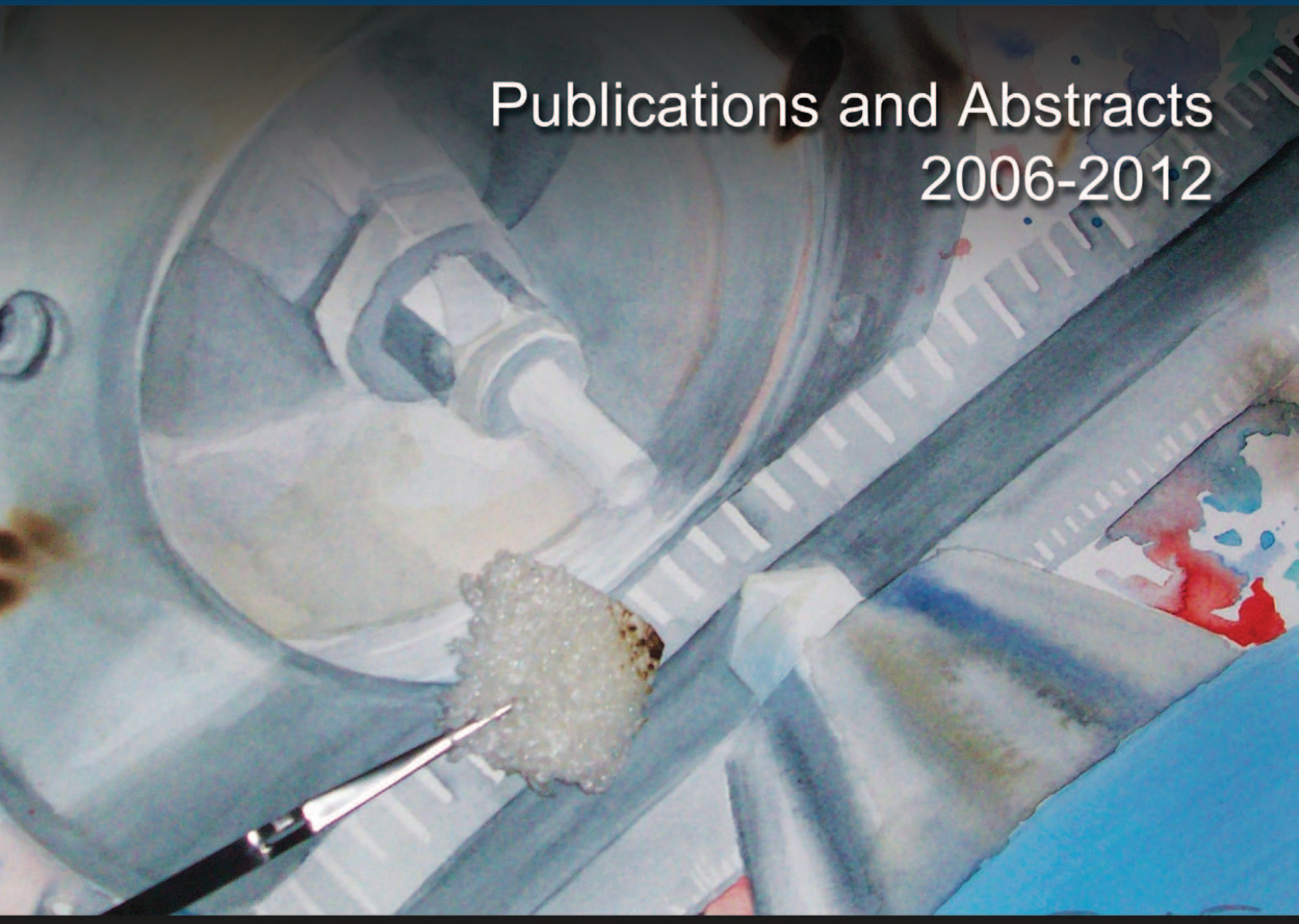

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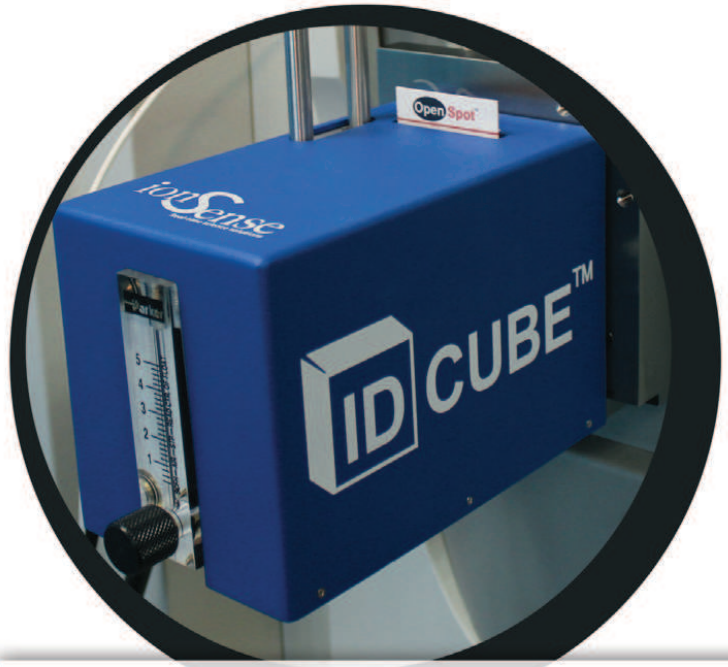

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Contents

Detection of nitro-organic and peroxide explosives in latent fingermarks by DART- and SALDI-TOF-mass spectrometry

F. Rowell, J. Seviour, A. Y. Lim, C. G. Elumbaring-Salazar, J. Loke, and J. Ma, Forensic Science International, no. 0, 2012.

The ability of two mass spectrometric methods, surface-assisted laser desorption/ionization-time of flight-mass spectrometry (SALDI-TOF-MS) and direct analysis in real time (DART-MS), to detect the presence of seven common explosives (six nitro-organic- and one peroxide-type) in spiked latent fingermarks has been examined. It was found that each explosive could be detected with nanogram sensitivity for marks resulting from direct finger contact with a glass probe by DART-MS or onto stainless steel target plates using SALDI-TOF-MS for marks pre-dusted with one type of commercial black magnetic powder. These explosives also could be detected in latent marks lifted from six common surfaces (paper, plastic bag, metal drinks can, wood laminate, adhesive tape and white ceramic tile) whereas no explosive could be detected in equivalent pre-dusted marks on the surface of a commercial lifting tape by the DART-MS method due to high background interference from the tape material. The presence of TNT and Tetryl could be detected in pre-dusted latent fingermarks on a commercial lifting tape for up to 29 days sealed and stored under ambient conditions.

Rapid identification of synthetic cannabinoids in herbal samples via direct analysis in real time mass spectrometry

R. A. Musah, M. A. Domin, M. A. Walling, and J. R. E. Shepard, Rapid Commun. Mass Spectrom., vol. 26, no. 9, pp. 1109–1114, 2012.

Dozens of synthetic cannabinoid analogs purposefully meant to circumvent legal restrictions associated with controlled substances continue to be manufactured and promoted as producing 'legal highs'. These designer drugs are difficult to identify in conventional drug screens not only because routine protocols have not been developed for their detection, but also because their association with complex plant matrices during manufacture generally requires labor-intensive extraction and sample preparation for analysis. To address this new and important challenge in forensic chemistry, Direct Analysis in Real Time Mass Spectrometry (DART-MS) is applied to the analysis of these designer drugs. METHODS DART-MS was employed to sample synthetic cannabinoids directly on botanical matrices. The ambient ionization method associated with DART-MS permitted the analysis of solid herbal samples directly, without the need for extraction or sample preparation. The high mass resolution time-of-flight analyzer allowed identification of these substances despite their presence within a complex matrix and enabled differentiation of closely related analogs. RESULTS DART-MS was performed to rapidly identify the synthetic cannabinoids AM-251 and JWH-015. For each cannabinoid, three hundred micrograms (300 μg) of material was easily detected within an excess of background matrix by mass. CONCLUSIONS New variations of herbal blends containing a wide range of base components and laced with synthetic cannabinoids are being produced, making their presence difficult to track by conventional methods. DART-MS permits rapid identification of trace synthetic cannabinoids within complex biological matrices, with excellent sensitivity and specificity compared with standard methods.

Direct analysis in real time mass spectrometry with collision-induced dissociation for structural analysis of synthetic cannabinoids

R. A. Musah, M. A. Domin, R. B. Cody, A. D. Lesiak, A. John Dane, and J. R. E. Shepard, Rapid Commun. Mass Spectrom., vol. 26, no. 19, pp. 2335–2342, 2012.

The emergence of numerous cannabinoid designer drugs has been tied to large spikes in emergency room visits and overdoses. Identifying these substances is difficult for the following reasons: (1) the compounds are novel, closely structurally related, and do not usually test positive in drug screens; (2) novel analogs rapidly appear on the market; (3) no standard protocols exist for their identification; and (4) customized and extensive sample preparation/extraction and analysis procedures are required to demonstrate their presence. METHODS: Direct analysis in real time mass spectrometry (DART-MS) employing collision-induced dissociation (CID) provided confirmatory structural information that was useful in characterizing the various cannabinoid analogs, including those contained in mixtures. CID analysis illustrated that, although closely related compounds fragment in a similar fashion, their structural differences still resulted in multiple diagnostic peaks that provided additional confidence towards structural identification. RESULTS: DART-MS spectra were acquired under CID conditions to rapidly differentiate among five synthetic cannabinoids contained within 'herbal' products purchased locally in New York State (USA). The spectra exhibited [M+H]+ ions and product ions unique to each cannabinoid that corresponded to major structural features. Five different cannabinoid analogs, alone and as mixtures of at least two cannabinoids, were identified in six herbal products and differentiated by their CID product ion patterns. CONCLUSION: Illicit synthetic cannabinoid products continue to be readily available despite national and international restrictions. These products contain a wide range of active components, and, in many cases, multiple active ingredients. DART-MS allows rapid analyses of these synthetic cannabinoids based on the exact masses of their [M+H]+ ions and product ion peaks generated using CID.

Analysis of select Dalbergia and trade timber using direct analysis in real time and time-of-flight mass spectrometry for CITES enforcement

C. Lancaster and E. Espinoza, Rapid Commun. Mass Spectrom., vol. 26, no. 9, pp. 1147–1156, 2012.

International trade of several Dalbergia wood species is regulated by The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). In order to supplement morphological identification of these species, a rapid chemical method of analysis was developed. METHOD Using Direct Analysis in Real Time (DART) ionization coupled with Time-of-Flight (TOF) Mass Spectrometry (MS), selected Dalbergia and common trade species were analyzed. Each of the 13 wood species was classified using principal component analysis and linear discriminant analysis (LDA). These statistical data clusters served as reliable anchors for species identification of unknowns. RESULTS Analysis of 20 or more samples from the 13 species studied in this research indicates that the DART-TOFMS results are reproducible. Statistical analysis of the most abundant ions gave good classifications that were useful for identifying unknown wood samples. CONCLUSIONS DART-TOFMS and LDA analysis of 13 species of selected timber samples and the statistical classification allowed for the correct assignment of unknown wood samples. This method is rapid and can be useful when anatomical identification is difficult but needed in order to support CITES enforcement.

Direct Analysis in Real Time (DART) Mass Spectrometry of Adulterants in Herbal Slimming Products using a Tandem Quadrupole MS and Data Directed Analysis

M. Jones, M. Twohig, K. Yu, M. Balogh, J. Tice, and B. Musselman, Planta Med, vol. 78, no. 05, p. P_127, 2012.

Several troubling studies show the adulteration of herbal slimming products with sibutramine is a common occurrence. Recent reports suggesting an increased risk of serious cardiovascular events (such as heart attack or stroke) in patients with known cardiovascular disease taking sibutramine have prompted the European Medicines Agency (EMA) to recommend that the use of sibutramine be suspended. The aim of this study is to develop specific methods for the rapid screening of herbal medicines for illicit adulteration with pharmaceutical drugs.

Herbal slimming aids were purchased over the internet from store websites and auction sites. Samples were analysed using a direct analysis in real time (DART) interface and a tandem quadrupole mass spectrometer. Samples purchased over the internet were found to contain undeclared pharmaceutical substances with the main component being sibutramine, an appetite suppressant used in the treatment of obesity. In addition to sibutramine, phenolphthalein and sildenafil were also identified none of which were declared on the box or enclosed information.

During our study we were able to identify nine samples that had been contaminated by sibutramine. DART with data directed analysis of the sample using a data directed high low collision energy experiment provides simultaneous intact molecular ion and fragmentation information, while allowing samples to be analysed very rapidly and without the need for complex sample preparation or chromatography. The testing of unlicensed herbal medicines and herbal dietary supplements are vital functions due to the possibility of illegal adulteration and/or contamination and the potential that exists for adverse health effects to unsuspecting consumers.

Sensitivity ‘Hot Spots’ in the Direct Analysis in Real Time Mass Spectrometry of Nerve Agent Simulants

G. A. Harris, C. E. Falcone, and F. M. Fernández, Journal of the American Society for Mass Spectrometry, vol. 23, no. 1, pp. 153–161, 2012.

Presented here are findings describing the spatial-dependence of sensitivity and ion suppression effects observed with direct analysis in real time (DART). Continuous liquid infusion of dimethyl methyl phosphonate (DMMP) revealed that ion yield “hot spots” did not always correspond with the highest temperature regions within the ionization space. For instance, at lower concentrations (50 and 100 μM), the highest sensitivities were in the middle of the ionization region at 200 °C where there was a shorter ion transport distance, and the heat available to thermally desorb neutrals was moderate. Conversely, at higher DMMP concentrations (500 μM), the highest ion yield was directly in front of the DART source at 200 °C where it was exposed to the highest temperature for thermal desorption. In matching experiments, differential analyte volatility was observed to play a smaller role in relative ion suppression than differences in proton affinity and the relative sampling positions of analytes. At equimolar concentrations sampled at the same position, suppression was as high as 26× between isoquinoline (proton affinity 952 kJ mol–1, boiling point 242 °C) and p-anisidine (proton affinity 900 kJ mol–1, boiling point 243 °C). This effect was exacerbated when sampling positions of the two analytes differed, reaching levels of relative suppression as high as 4543.0× ± 1406.0. To mitigate this level of relative ion suppression, sampling positions and molar ratios of the analytes were modified to create conditions in which ion suppression was negligible.

Rapid screening for synthetic antidiabetic drug adulteration in herbal dietary supplements using direct analysis in real time mass spectrometry

Z. Zhou, J. Zhang, W. Zhang, Y. Bai, and H. Liu, Analyst, vol. 136, no. 12, pp. 2613–2618, 2011.

Adulteration of herbal supplements with synthetic drugs is illegal. A rapid and reliable method which utilizes direct analysis in real time mass spectrometry (DART-MS) was developed for the identification of seven synthetic antidiabetic drugs used as adulterants in herbal dietary supplements. The supplement sample was simply extracted with methanol/water by manually shaking several times and directly analyzed using DART-MS. The presence of synthetic drug adulterants was confirmed through the accurate m/z values and MS/MS data obtained via quadruple time of flight mass spectrometry (QTOF MS). Parameters for the DART source were systematically optimized, and the limits of detection (LODs) in herbal supplement matrices were measured. This method was successfully applied to examine five commercial herbal dietary supplements, and two of them proved to be adulterated with metformin without labeling.

Analysis of Alprazolam by DART-TOF Mass Spectrometry in Counterfeit and Routine Drug Identification Cases

W. C. Samms, Y. J. Jiang, M. D. Dixon, S. S. Houck, and A. Mozayani, Journal of Forensic Sciences, vol. 56, no. 4, pp. 993–998, 2011.

The high prevalence of alprazolam abuse translates to an increased workload for crime laboratories in characterizing seized tablets. These tablets may originate as diverted pharmaceuticals or counterfeited mimics, so efficient analytical techniques should provide confirmatory data while minimizing destruction of evidence. We offer the first report of a validated forensic method for confirming alprazolam tablets by direct analysis in real time–time of flight (DART-TOF) mass spectrometric analysis. This technique provides rapid identification of target analytes with minimal sample preparation, allowing direct analysis in the atmospheric sample gap. Selectivity is achieved through high resolution and mass accuracy, unique ion fragments, and chlorine isotopic ratios. This method utilizes fragmentation in two separate voltage functions to observe the alprazolam pseudo molecular ion at 309.09070 using 40 V and major ion fragments of 281.07197 and 205.07657 at 120 V. These parameters allow our laboratory to confirm alprazolam tablets efficiently, without compromising quality forensic standards.

Structural Elucidation of Direct Analysis in Real Time Ionized Nerve Agent Simulants with Infrared Multiple Photon Dissociation Spectroscopy

J. L. Rummel, J. D. Steill, J. Oomens, C. S. Contreras, W. L. Pearson, J. Szczepanski, D. H. Powell, and J. R. Eyler, Analytical Chemistry, vol. 83, no. 11, pp. 4045–4052, 2011.

The high prevalence of alprazolam abuse translates to an increased workload for crime laboratories in characterizing seized tablets. These tablets may originate as diverted pharmaceuticals or counterfeited mimics, so efficient analytical techniques should provide confirmatory data while minimizing destruction of evidence. We offer the first report of a validated forensic method for confirming alprazolam tablets by direct analysis in real time–time of flight (DART-TOF) mass spectrometric analysis. This technique provides rapid identification of target analytes with minimal sample preparation, allowing direct analysis in the atmospheric sample gap. Selectivity is achieved through high resolution and mass accuracy, unique ion fragments, and chlorine isotopic ratios. This method utilizes fragmentation in two separate voltage functions to observe the alprazolam pseudo molecular ion at 309.09070 using 40 V and major ion fragments of 281.07197 and 205.07657 at 120 V. These parameters allow our laboratory to confirm alprazolam tablets efficiently, without compromising quality forensic standards.

Development and validation of AccuTOF-DART™ as a screening method for analysis of bank security device and pepper spray components

A. M. Pfaff and R. R. Steiner, Forensic Science International, vol. 206, no. 1–3, pp. 62–70, 2011.

Analysis of bank security devices, containing 1-methylaminoanthraquinone (MAAQ) and o-chlorobenzylidenemalononitrile (CS), and pepper sprays, containing capsaicin, is a lengthy process with no specific screening technique to aid in identifying samples of interest. Direct Analysis in Real Time (DART™) ionization coupled with an Accurate Time of Flight (AccuTOF) mass detector is a fast, ambient ionization source that could significantly reduce time spent on these cases and increase the specificity of the screening process. A new method for screening clothing for bank dye and pepper spray, using AccuTOF-DART™ analysis, has been developed. Detection of MAAQ, CS, and capsaicin was achieved via extraction of each compound onto cardstock paper, which was then sampled in the AccuTOF-DART™. All results were verified using gas chromatography coupled with electron impact mass spectrometry.

Simple and Rapid Screening for Methamphetamine and 3,4-Methylene-dioxymethamphetamine (MDMA) and Their Metabolites in Urine Using Direct Analysis in Real Time (DART)-TOFMS

M. Kawamura, R. Kikura-Hanajiri, and Y. Goda, Yakugaku Zasshi, vol. 131, no. 5, pp. 827–833, 2011.

An ionization technique, direct analysis in real time (DART) has recently been developed for the ambient ionization of a variety samples. The DART coupled with time-of-flight mass spectrometry (TOFMS) would be useful as a simple and rapid screening for the targeted compounds in various samples, because it provides the molecular information of these compounds without time-consuming extraction. In this study, we investigated rapid screening methods of illicit drugs and their metabolites, such as methamphetamine (MA), 3,4-methylenedioxymethamphetamine (MDMA), amphetamine (AP) and 3,4-methylenedioxyamphetamine (MDA) in human urine using DART-TOFMS. As serious matrix effects caused by urea in urine samples and ionizations of the targeted compounds were greatly suppressed in the DART-TOFMS analyses, simple pretreatment methods to remove the urea from the samples were investigated. When a pipette tip-type solid-phase extraction with a dichloromethane and isopropanol mixed solution as an eluent was used for the pretreatment, the limits of detection (LODs) of 4 compounds added to control urine samples were 0.25 μg/ml. On the other hand, the LODs of these compounds were 0.5 μg/ml by a liquid-liquid extraction using a dichloromethane and hexane mixed solution. In both extractions, the recoveries of 4 compounds from urine samples were over 70% and these extraction methods showed good linearity in the range of 0.5-5 μg/ml by GC-MS analyses. In conclusion, our proposed method using DART-TOFMS could simultaneously detect MA, MDMA and their metabolites in urine at 0.5 μg/ml without time-consuming pretreatment steps. Therefore it would be useful for screening drugs in urine with the molecular information.

Validation of Thin Layer Chromatography with AccuTOF-DART™ Detection for Forensic Drug Analysis

S. E. Howlett and R. R. Steiner, Journal of Forensic Sciences, vol. 56, no. 5, pp. 1261–1267, 2011.

Thin layer chromatography (TLC) is a technique that is commonly employed in the forensic drug analysis of pharmaceutical preparations. Detection is typically accomplished using various visualization spray reagents. Conventional gas chromatography–mass spectrometry (GC-MS) analysis is typically performed to confirm the TLC results. Depending on the drugs tested and the instrument conditions required, this confirmation can take up to an hour to complete. Direct analysis in real time (DART™) is an ionization source, coupled to an accurate-mass time-of-flight mass spectrometer that has the capability to ionize materials under ambient conditions. To streamline analysis, the combination of TLC with DART™ detection is proposed to screen and subsequently identify drug compounds, all from the same TLC plate. DART™ confirmations of TLC analyses take <10 min to complete and compare favorably to GC-MS in sensitivity and selectivity. This study validates the use of TLC-DART in the forensic identification of the components of several pharmaceutical preparations.

Direct Analysis in Real Time Coupled to Multiplexed Drift Tube Ion Mobility Spectrometry for Detecting Toxic Chemicals

G. A. arris, M. wasni , and . M . er n n dez, Anal. Chem., vol. 83, no. 6, pp. 1908–1915, 2011.

Current and future chemical threats to homeland security motivate the need for new chemical detection systems to provide border, transportation, and workplace security. We present the first successful coupling of a commercial direct analysis in real time (DART) ion source to a resistive glass monolithic drift tube ion mobility spectrometer (DTIMS) as the basis for a low maintenance, versatile, and robust chemical monitoring system. in situ ionization within the electric field gradient of the instrument enhances sensitivity and provides a safe sampling strategy. The instrument uses nitrogen as both the DART discharge and DTIMS drift gases, allowing for a high electric field to be used for ion separation while keeping cost-of-use low. With the use of a traditional signal averaging acquisition mode, the 95% probability of detection (POD) for analytes sampled from melting point capillary tubes was 11.81% v/v for DMMP, 1.13% v/v for 2-CEES, and 10.61 mM for methamidophos. Sensitivity was improved via a prototype transmission-mode geometry interface, resulting in an almost 2 orders of magnitude decrease in the POD level for DMMP (0.28% v/v). As an alternative to transmission mode operation, digital multiplexing of the DTIMS ion injection step was also implemented, finding a 3-fold improvement in signal-to-noise ratios for 200 ?s gate injections and a 4.5-fold for 400 ?s gate injections.

Current and future chemical threats to homeland security motivate the need for new chemical detection systems to provide border, transportation, and workplace security. We present the first successful coupling of a commercial direct analysis in real time (DART) ion source to a resistive glass monolithic drift tube ion mobility spectrometer (DTIMS) as the basis for a low maintenance, versatile, and robust chemical monitoring system. in situ ionization within the electric field gradient of the instrument enhances sensitivity and provides a safe sampling strategy. The instrument uses nitrogen as both the DART discharge and DTIMS drift gases, allowing for a high electric field to be used for ion separation while keeping cost-of-use low. With the use of a traditional signal averaging acquisition mode, the 95% probability of detection (POD) for analytes sampled from melting point capillary tubes was 11.81% v/v for DMMP, 1.13% v/v for 2-CEES, and 10.61 mM for methamidophos. Sensitivity was improved via a prototype transmission-mode geometry interface, resulting in an almost 2 orders of magnitude decrease in the POD level for DMMP (0.28% v/v). As an alternative to transmission mode operation, digital multiplexing of the DTIMS ion injection step was also implemented, finding a 3-fold improvement in signal-to-noise ratios for 200 ?s gate injections and a 4.5-fold for 400 ?s gate injections.

Determination of drugs and drug-like compounds in different samples with direct analysis in real time mass spectrometry

E. S. Chernetsova and G. E. Morlock, Mass Spectrom. Rev., vol. 30, no. 5, pp. 875–883, 2011.

Direct analysis in real time (DART), a relatively new ionization source for mass spectrometry, ionizes small-molecule components from different kinds of samples without any sample preparation and chromatographic separation. The current paper reviews the published data available on the determination of drugs and drug-like compounds in different matrices with DART-MS, including identification and quantitation issues. Parameters that affect ionization efficiency and mass spectra composition are also discussed.

Detection of illicit drugs on surfaces using direct analysis in real time (DART) time-of-flight mass spectrometry

A. H. Grange and G. W. Sovocool, Rapid Commun. Mass Spectrom., vol. 25, no. 9, pp. 1271–1281, 2011.

Methamphetamine (meth) from meth syntheses or habitual meth smoking deposited on household surfaces poses human health hazards. The U.S. State Departments of Health require decontamination of sites where meth was synthesized (meth labs) before they are sold. National Institute for Occupational Safety and Health (NIOSH) methods for meth analysis require wipe sampling, extraction, clean-up, solvent exchange, derivatization, and/or mass spectral analysis using selected ion monitoring. Rapid and inexpensive analyses could screen for drug-contamination within structures with greater spatial resolution, provide real-time analyses during decontamination, and provide thorough documentation of successful clean ups. Herein an autosampler/open-air ion source time-of-flight mass spectrometric technique is described that required only direct sampling using cotton-swab wipes. Each wipe sample collection required 2 min and data acquisition required only 13 s per sample. Optimum collision-induced dissociation voltages, desorption gas temperatures, and wipe sample solvents were determined for 11 drugs. Peaks were observed in analyte-ion traces for 0.025 μg/100 cm2 of meth and seven other drugs. This level is half the detection limit of NIOSH methods and one-fourth of the lowest U.S. state decontamination limit for meth. Dynamic ranges of 100 in concentration were demonstrated for eight drugs, which is sufficient for a screening technique. The volatilities of 11 drugs deposited on glass were determined. The pick up of the drugs by solvent-soaked cotton-swab wipes from glass relative to acrylic latex paint was also compared.

New approach to detecting counterfeit drugs in tablets by DART mass spectrometry

E. Chernetsova, P. Bochkov, G. Zatonskii, and R. Abramovich, Pharmaceutical Chemistry Journal, vol. 45, no. 5, pp. 306–308, 2011.

The possibility of using DART mass spectrometry for the identification of active ingredients in tableted drugs has been studied. Analytical results for some drugs such as glycin, nootropyl, anaprilin, mexidol, and biseptol are presented. The benefits and limitations of DART mass spectrometry as applied to fast screening of tableted pharmaceuticals for detecting counterfeits are discussed.

Study on rapid and direct analysis of illegally added six PDE5 inhibitors in health food by DART-MS/MS method

CHENG, Xian-lon, LI ,Wen-jie, LI, Wei-jian, XIAO, Xin-yue, LIN, Rui-chao, and WEI, Feng, Chinese Journal of Pharmaceutical Analysis, vol. 31, pp. 438–442, 2011.

To develop a directed analysis of 6 phosphodiesterase 5(PDE5)inhibitors: sildenafil, tadalafil,acetildenafil, hydroxyhomosildenafil, aminotadalafil, pseudo-vardenfil in health food. Methods:Triple quadrupol MS with DART ion souce was used to perform the direct analysis.The DART sampler delivery rate was 0.2 mm·s-1.The temperature of carry gas of DART was 450 ℃.The capillary voltage was kept at 4 kV.The temperature of the drying gas of triple quadrupol MS was set at 350 ℃.The flow rate of the drying gas of triple quadrupol MS was set at 10 L·min-1,respectively.Product ion scan mode was used with scan range from 50-550 amu.The precursor ions were set as m/z 475.1(sildenafil),m/z 467.2(acetildenafil),m/z 505.1(hydroxyhomosildenafil),m/z 390.1(tadalafil),m/z 391.2(aminotadalafil),m/z 460.3(pseudo-vardenfil).The identification was performed by comparing the mass spectrum of detected peak in samples with the mass spectrum of peak in reference substance.Results:The limit of detection for each of 6 PDE5 inhibitors was under 1 μg·g-1.Sildenafil was detected in 6 samples,and tadalafil was detected in 1 sample.Conclusion:The method is employed to simultaneous detection of 6 PDE5 inhibitors in health food.

Analysis of printing and writing papers by using direct analysis in real time mass spectrometry

J. Adams, International Journal of Mass Spectrometry, vol. 301, no. 1–3, pp. 109–126, 2011.

A quick and direct method for identifying organic components of papers in library and archival collections with minimal destructive sampling is needed for preservation, forensic, and general purposes. Direct analysis in real time mass spectrometry (DART-MS) is used for characterizing 16 reference papers of known manufacture in terms of their pulp composition and pitch contaminants. Unique mass spectra are obtained from bleached kraft, chemithermomechanical, and stone groundwood pulp papers in real time without extractions, derivatizations, chromatographic separations, and other time- and chemical-consuming sample preparations. Phytosteroids are volatilized from bleached hardwood kraft but not from bleached softwood kraft papers, which differentiates the two of them. The kraft papers are in turn differentiated from chemithermomechanical pulp papers by lignin-derived thermolyis products: syringyl products arise from hardwood, but guaiacyl and coumaryl products arise from softwood, chemithermomechanical pulp papers. Stone groundwood papers contain a number of extractives that are volatilized, which serve to differentiate them from all the other papers. Papers that contain rosin vs. alkyl ketene dimer (AKD) sizings are immediately differentiated. The DART-MS methodology is fast and simple, and the spectra are repeatable. Microsamples as small as ∼10 μg tweezed from the paper surface may be analyzed. These benchmark spectra are the prelude to further applications of DART-MS in paper research and the beginning of the development of a searchable library of DART-MS spectra of printing and writing papers by the Library of Congress.

A Rapid Technique for the Confirmation of Iodine and Red Phosphorus Using Direct Analysis in Real Time and Accurate Mass Spectrometry

R. R. Steiner, Microgram J, vol. 7, no. 1, pp. 3–6, 2010.

Iodine and red phosphorus are chemicals commonly seen in clandestine methamphetamine laboratories. Current analytical methods used for the confirmation of these chemicals include FTIR and GC/MS, usually after a derivatization or reaction with other compounds. X-ray diffraction and scanning electron microscope-energy dispersive x-ray analysis are also used to confirm these chemicals, but all of these techniques tend to be time-consuming or produce poisonous products. A novel technique, using the JEOL-IonSense AccuTOF-DART system, has been developed which yields accurate mass spectra usually in less than ten minutes of analysis time, with no sample preparation.

Explosives Detection Using Direct Analysis in Real Time (DART) Mass Spectrometry

J. M. Nilles, T. R. Connell, S. T. Stokes, and H. Dupont Durst, Propellants, Explosives, Pyrotechnics, vol. 35, no. 5, pp. 446–451, 2010.

The growing use of explosives by terrorists and criminals creates a need for instrumentation which can rapidly analyze these energetic compounds, preferably on site. Direct analysis in real time (DART) is a promising technology for surface analysis with little or no sample preparation. Therefore, DART ionization is evaluated for use in detecting explosives on solid substrates and in liquid matrices. Fifteen explosives were chosen as a consequence of their common usage. Five surfaces were chosen to represent a wide range of physical properties such as composition, porosity, surface morphology, and thermal and electrical conductivity. Additionally these surfaces are commonly found in everyday surroundings. All 75 compound-surface combinations produced a clear, easily identifiable, mass spectra characteristic of the targeted analyte. Simultaneous detection of five explosives is demonstrated on these same surfaces. Lastly, rapid detection of trace contamination in common fluids is also explored.

Ricin Activity Assay by Direct Analysis in Real Time Mass Spectrometry Detection of Adenine Release

V. L. H. Bevilacqua, J. M. Nilles, J. S. Rice, T. R. Connell, A. M. Schenning, L. M. Reilly, and H. D. Durst, Analytical Chemistry, vol. 82, no. 3, pp. 798–800, 2010.

Biotoxin activity assays typically involve multistep sample preparation, multicomponent reactions, multistep analysis, or a combination thereof. We report a single-step, real-time ricin activity assay that requires little or no sample preparation and employs direct analysis in real time mass spectrometry. The release of adenine from the inhomogeneous substrate herring sperm DNA by ricin was determined to be 53 ± 2 pmol adenine per picomole of ricin per hour. This procedure can be readily adapted to any enzyme for which a reactant or product of low molecular weight (up to ~600) can be identified.

Validation of the Direct Analysis in Real Time Source for Use in Forensic Drug Screening

R. R. Steiner and R. L. Larson, Journal of Forensic Sciences, vol. 54, no. 3, pp. 617–622, 2009.

Thin layer chromatography (TLC) is a technique that is commonly employed in the forensic drug analysis of pharmaceutical preparations. Detection is typically accomplished using various visualization spray reagents. Conventional gas chromatography–mass spectrometry (GC-MS) analysis is typically performed to confirm the TLC results. Depending on the drugs tested and the instrument conditions required, this confirmation can take up to an hour to complete. Direct analysis in real time (DART™) is an ionization source, coupled to an accurate-mass time-of-flight mass spectrometer that has the capability to ionize materials under ambient conditions. To streamline analysis, the combination of TLC with DART™ detection is proposed to screen and subsequently identify drug compounds, all from the same TLC plate. DART™ confirmations of TLC analyses take <10 min to complete and compare favorably to GC-MS in sensitivity and selectivity. This study validates the use of TLC-DART in the forensic identification of the components of several pharmaceutical preparations.

Quantitation of Chemical Warfare Agents Using the Direct Analysis in Real Time (DART) Technique

J. M. Nilles, T. R. Connell, and H. D. Durst, Analytical Chemistry, vol. 81, no. 16, pp. 6744–6749, 2009.

Direct analysis in real time (DART) is an ion source that permits rapid mass spectrometric detection of gases, liquids, and solids in open air under ambient conditions. It is a unique technology in the field of chemical weapons detectors in that it does not require a vapor pressure, does not require sample preparation, and is nondestructive to the original sample. While the DART technique has had success as a first line instrument of detection, there have been lingering doubts over the technique's quantitative reliability and reproducibility. Here, we demonstrate its capability to produce linear calibration curves (R2 = 0.99 or better) for the nerve agents GA, GB, and VX as well as the blister agent HD. Independently prepared check standards measured against these curves typically have recovery errors less than 3%. We show the DART instrument response to be linear over roughly 3 orders of magnitude. Furthermore, this study shows that averaging as few as three measurements for each data point is sufficient to produce high quality calibration curves, thus reducing data collection time and providing quicker results.

An Improved Protocol for the Analysis of Alcohols by Direct Analysis in Real Time Mass Spectrometry

J. A. Laramée, H. D. Durst, J. M. Nilles, and T. R. Connell, American Laboratory, vol. 41, no. 7, pp. 25–27, 2009.

It was previously reported1 that when Direct Analysis in Real Time (DART™) (JEOL USA, Inc., Peabody, MA) mass spectrometry was applied to the analysis of very pure alcohols, their mass spectra were unexpectedly complicated. The plethora of peaks was found to be a DART-induced artifact that resulted from the open-air nature of the technique. This problem was solved by converting the alcohol into its corresponding carbamate via an N-hydro-C-alkoxy-addition reaction (reaction 1) with phenyl isocyanate:

RO + C6 5N CO → RO−C(O)N C6 5 (1)

Although this reaction conveniently allows alcohols to be DART'ed, the reaction time ranges from 1 to 16 hr. This obviously led the authors to test the hypothesis that shorter reaction times can be achieved by using activated phenyl isocyanates with proper ring substitution. It is now timely to report these results.

Alcohols Can Now Be Analyzed by a Direct Analysis in Real-Time Method: Applications for Chemical Warfare Agent Synthesis

J. A. Laramée, H. D. Durst, J. M. Nilles, and T. R. Connell, American Laboratory, vol. 41, no. 4, pp. 24–27, 2009.

The cardinal principle for an operation involving chemical agents is to limit the potential exposure to a minimum number of personnel, for a minimum period of time, to a minimum amount of the chemical agent consistent with safe and efficient operations.1 This requires that the synthetic schemes be rapid and free from unnecessary by-products that would require otherwise further sample handling. Thus, acid/base chemistries with alcohols as intermediates are often used to synthesize phosphonofluoridates, phosphoramidocyanidate, and phosphonothioates.

Dovetailing into the cardinal principle is the need for a rapid chemical analysis method that can accurately confirm the identity and purity of the starting materials, intermediates, and final product(s). In order to accomplish these objectives, the U.S. Army's Edgewood Chemical Biological Center (ECBC) has been using the Direct Analysis in Real Time (DART™) method (JEOL USA, Inc., Peabody, MA) since 2002.2 Since that time, a flurry of other open-air methods based on the use of metastable species has been seen.

During the course of a large synthesis project comprising many organophosphorus compounds and their isotopically labeled analogs, it was observed that the DART datum for labeled alcohol intermediates neither corroborated the nuclear magnetic resonance (NMR) datum nor the GC-MS datum. Yet the data from these three analytical methods were in agreement when the final chemical agent product was analyzed. An investigation was initiated in order to discover the cause of this discrepancy, and a procedure was developed that allowed alcohols and organophosphorus intermediates to be analyzed by DART.

Screening of Cocaine and Its Metabolites in Human Urine Samples by Direct Analysis in Real-Time Source Coupled to Time-of-Flight Mass Spectrometry After Online Preconcentration Utilizing Microextraction by Packed Sorbent

E. Jagerdeo and M. Abdel-Rehim, Journal of the American Society for Mass Spectrometry, vol. 20, no. 5, pp. 891–899, 2009.

Microextraction by packed sorbent (MEPS) has been evaluated for fast screening of drugs of abuse with mass spectrometric detection. In this study, C8 (octyl-silica, useful for nonpolar to moderately polar compounds), ENV+ (hydroxylated polystyrene-divinylbenzene copolymer, for extraction of aliphatic and aromatic polar compounds), Oasis MCX (sulfonic-poly(divinylbenzene-co-N-polyvinyl-pyrrolidone) copolymer), and Clean Screen DAU (mixed mode, ion exchanger for acidic and basic compounds) were used as sorbents for the MEPS. The focus was on fast extraction and preconcentration of the drugs with rapid analysis using a time-of-flight (TOF) mass spectrometer as the detector with direct analysis in a real-time (DART) source. The combination of an analysis time of less than 1 min and accurate mass of the first monoisotopic peak of the analyte and the relative abundances of the peaks in the isotopic clusters provided reliable information for identification. Furthermore, the study sought to demonstrate that it is possible to quantify the analyte of interest using a DART source when an internal standard is used. Of all the sorbents used in the study, Clean Screen DAU performed best for extraction of the analytes from urine. Using Clean Screen DAU to extract spiked samples containing the drugs, linearity was demonstrated for ecgonine methyl ester, benzoylecgonine, cocaine, and cocaethylene with average ranges of: 65–910, 75–1100, 95–1200, and 75–1100 ng/mL (n = 5), respectively. The limits of detection (LOD) for ecgonine methyl ester, benzoylecgonine, cocaine, and cocaethylene were 22.9 ng/mL, 23.7 ng/mL, 4.0 ng/mL, and 9.8 ng/mL respectively, using a signal-to-noise ratio of 3:1.

Rapid Semi-Quantitative Surface Mapping of Airborne-Dispersed Chemicals Using Mass Spectrometry

A. H. Grange, Environmental Forensics, vol. 10, no. 3, pp. 183–195, 2009.

Chemicals can be dispersed accidentally, deliberately, or by weather-related events. Rapid mapping of contaminant distributions is necessary to assess exposure risks and to plan remediation, when needed. Ten pulverized aspirin or NoDozTM tablets containing caffeine were dispersed across a concrete driveway using the exhaust port of a shop vacuum cleaner. Water-soaked, cotton swabs were used to collect wipe samples from 100 cm2 areas within a 7 x 12 grid pattern to map the caffeine distribution. An autosampler/Direct Analysis in Real Time (DARTTM)/time-of-flight mass spectrometer was used to acquire ion chromatograms for the [M+H]+ semi-quantitation ion (m/z 195). Prior to analysis, unheated, non-energized helium gas was blown across the swabs to remove debris that could plug the cone orifice. Carry over was mitigated by interspersing wipe sample swabs with water-soaked swabs to provide hot water vapor to clean the region around the cone orifice into the mass spectrometer between sample swabs. Carry over was further reduced relative to the ion abundances from analyte peaks by acquiring data a second time. Remaining carry over was seen as ion abundance plateaus in ion chromatograms before and after each analyte peak. The higher plateau was treated as the baseline for each analyte peak by a macro procedure written in Lotus 123TM. A second macro procedure plotted multi-color, semi-quantitation maps for high, moderate, low, and non-detect levels of caffeine.

Detection of Gamma-Hydroxybutyric Acid in Various Drink Matrices via AccuTOF-DART

M. J. Bennett and R. R. Steiner, Journal of Forensic Sciences, vol. 54, no. 2, pp. 370–375, 2009.

A new screening method for detecting gamma-hydroxybutyric acid (GHB) in drink matrices, using the IonSense, Inc. (Saugus, MA) direct analysis in real time (DART) ion source coupled to a JEOL exact mass time-of-flight mass spectrometer (AccuTOF), was validated and compared with the current screening methodology. The DART ion source allows for analysis of samples under ambient conditions with little to no sample preparation. Fifty drink specimens were spiked at levels of 1, 2, 3, and 4 mg/mL GHB, and analyzed on the AccuTOF-DART. Positive detection of GHB occurred for each of the samples at each concentration level, giving 100% accuracy for the samples tested. Twenty-five of the 50 drink specimens were spiked at 1 mg/mL GHB and tested using a color test known as the GHB Color Test #3. Only two of these 25 specimens tested positive for the presence of GHB, giving only 8% accuracy. Implementation of this new methodology as a screening tool for GHB analysis will quickly eliminate negative specimens allowing the examiner to focus analysis time on those that screened positive.

A Collaborative Epidemiological Investigation into the Criminal Fake Artesunate Trade in South East Asia

P. N. Newton, F. M. Fernandez, A. Plancon, D. C. Mildenhall, M. D. Green, L. Ziyong, E. M. Christophel, S. Phanouvong, S. Howells, E. McIntosh, P. Laurin, N. Blum, C. Y. Hampton, K. Faure, L. Nyadong, C. W. R. Soong, B. Santoso, W. Zhiguang, J. Newton, and K. Palmer, PLoS Medicine, vol. 5, no. 2, p. e32, 2008.

Since 1998 the serious public health problem in South East Asia of counterfeit artesunate, containing no or subtherapeutic amounts of the active antimalarial ingredient, has led to deaths from untreated malaria, reduced confidence in this vital drug, large economic losses for the legitimate manufacturers, and concerns that artemisinin resistance might be engendered. With evidence of a deteriorating situation, a group of police, criminal analysts, chemists, palynologists, and health workers collaborated to determine the source of these counterfeits under the auspices of the International Criminal Police Organization and the Western Pacific World Health Organization Regional Office. A total of 391 samples of genuine and counterfeit artesunate collected in Vietnam, Cambodia, Lao PDR, Myanmar (Burma) and the Thai/Myanmar border, were available for analysis. Sixteen different fake hologram types were identified. High-performance liquid chromatography and/or mass spectrometry confirmed that all specimens thought to be counterfeit (195/391, 49.9%) on the basis of packaging contained no or small quantities of artesunate (up to 12 mg per tablet as opposed to ~ 50 mg per genuine tablet). Chemical analysis demonstrated a wide diversity of wrong active ingredients, including banned pharmaceuticals, such as metamizole, and safrole, a carcinogen, and raw material for manufacture of methylenedioxymethamphetamine (‘ecstasy'). Evidence from chemical, mineralogical, biological, and packaging analysis suggested that at least some of the counterfeits were manufactured in southeast People's Republic of China. This evidence prompted the Chinese Government to act quickly against the criminal traders with arrests and seizures.

Detection of Chemical Warfare Agents on Surfaces Relevant to Homeland Security by Direct Analysis in Real-Time Spectrometry

J. A. Laramée, H. . Durst, T. R. Connell, and J. M. Nilles, American Laboratory, vol. 40, pp. 16–20, 2008.

Unlike other analytical methods that necessitate that the surface be sprayed with electrically charged solvents, or that require solvent extraction, DART leaves the sample surface undisturbed.

Analysis of low-volatility, condensed-phase chemicals on surfaces has been an extremely difficult and long-standing objective in environmental monitoring. When target analytes possess picotorr vapor pressures, the problem of monitoring becomes formidable. As such, any noncontact sampling at atmospheric pressure that does not require solvents or wipes would be a technological breakthrough. In addition, the absence of sample preparation would allow extremely rapid analysis in time-critical situations. Today, such a technology is now available. It is known as Direct Analysis in Real Time1 or DART™ (JEOL USA, Inc., Peabody, MA).

The U.S. Army has been testing and developing DART since 2002 for the detection of chemical warfare agents on surfaces. Fast, safe, and accurate detection of chemical agents is critical for protection, security, and decision-making. Sample preparation is seldom a requirement with DART, since the contaminated surface is simply analyzed directly using a plume of gaseous Rydberg atoms. Unlike other analytical methods that necessitate that the surface be sprayed with electrically charged solvents,2 or that require solvent extraction, DART leaves the sample surface undisturbed. This is a forensically worthy advantage. Recent findings of chemical warfare agent detection on militarily relevant surfaces in Homeland Security is a new approach to Warfighter safety

Flammable Solvent Detection Directly from Common Household Materials Yields Differential Results: An Application of Direct Analysis in Real-Time Mass Spectrometry

C. M. Coates, S. Coticone, P. D. Barreto, A. E. Cobb, R. B. Cody, and J. C. Barreto, Journal of Forensic Identification, vol. 58, no. 6, pp. 624 –631, 2008.

In this study, we report the analysis of volatile flammable solvents present on common household materials by employing a mass spectrometric technique that incorporates a novel ion source: direct analysis in real time (DART). We used the new ionization method to directly volatilize and ionize a solvent sample, which was then sent to a high-resolution mass spectrometer. We analyzed two common flammable solvents, gasoline and paint thinner, directly from cotton, drywall, and nylon materials. DART sampling occurs directly from the chemical matrix of the common household materials, with no sample preparation needed. Cotton swabs containing solvents, gasoline, and paint thinner produced characteristic signature peaks. In addition, different substrates (cotton, nylon, and drywall) containing gasoline and paint thinner were tested to determine the possibility of detecting aromatic and aliphatic solvents from a complex chemical matrix using DART technology. Specifically, we discovered that nylon was a poor substrate for DART detection of gasoline, with the entire signal disappearing in only two hours. Surprisingly, DART easily detected paint thinner on nylon even after 16 hours. Notably, DART was effective in all other cases, detecting both paint thinner and gasoline over a 0- to 16-hour period on cotton and drywall substrates. We conclude that DART sample detection directly from household materials is not simply a matter of vapor pressure; instead, direct DART detection probably dependent on a complex interaction involving adsorption effects or matrix effects on the ionization mechanism of the flammable solvents. We demonstrate and report a potentially simple, powerful, and useful alternative to traditional mass spectrometric analysis.

Comparison of the Novel Direct Analysis in Real Time Time-of-Flight Mass Spectrometry (AccuTOF-DART™) and Signature Analysis for the Identification of Constituents of Refined Illicit Cocaine

J. D. S. Ropero-Miller, N. D. Bynum, and J. F. Casale., Microgram Journal, vol. 5, no. 1–4, p. 5, 2007.

The characterization of 25 illicit cocaine samples by a novel application of direct analysis in real time (DART) sample introduction coupled with time-of-flight mass spectrometry (TOF-MS) and cocaine signature analyses is provided. The AccuTOF-DART™ analysis of the cocaine samples resulted in the detection of most analytes, although some compounds were not detected. This new technique is easy, rapid, requires very little sample, and can be used to screen even complex mixtures. Potential applications, including use for signature analyses of controlled substances, are discussed.

Differentiating Writing Inks Using Direct Analysis in Real Time Mass Spectrometry

R. W. Jones, R. B. Cody, and J. F. McClelland, Journal of Forensic Sciences, vol. 51, no. 4, pp. 915–918, 2006.

Writing ink analysis is used in establishing document authenticity and the sources and relative ages of written entries. Most analytical methods require removing samples or visibly altering the document. Nondestructive, in situ analysis of writing inks on paper without visible alteration is possible using mass spectrometry with a new ion source called Direct Analysis in Real Time. Forty-three different black and blue ballpoint, black fluid, and black gel inks were examined. Both dyes and persistent but thermally labile components of the inks contribute to the mass spectra, principally as protonated molecules [M+H]+. Numerous ink components were identified from the spectra. The spectra were placed in a searchable library, which was then challenged with two spectra from each of the 43 inks. The best match for each of the challenge spectra was correct for all but one ink, which matched with a very similar ink by the same manufacturer.

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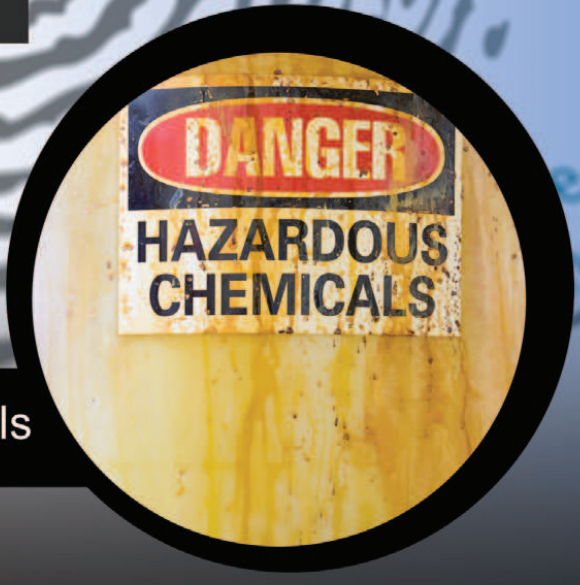

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