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Hyphenated differential mobility spectrometry for rapid separation and detection

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Abstract: This paper reviews hyphenated differential mobility spectrometry (DMS) technology. DMS is a type of ion mobility spectrometry (IMS) also called high-field asymmetric waveform IMS. It is widely used in the detection of chemical warfare agents, explosives, drugs, and volatile organic compounds. Stand-alone DMS analysis of complex mixtures in real-field applications is challenging. Hyphenated DMS can improve resolution for rapid separation and detection. This review focuses on hyphenated DMS, including gas chromatography-DMS, DMS-mass spectrometry (MS), DMS-IMS, IMS-DMS, and DMS-DMS, as well as their associated principles, applications, and research procedures. Key problems in hyphenated DMS are considered.

Keywords: differential mobility spectrometry-ion mobility spectrometry; differential mobility spectrometry-mass spectrometer; gas chromatography-differential mobility spectrometry; hyphenated differential mobility spectrometry; sensors.

Introduction

Ion mobility spectrometry (IMS) is a commonly used sensor technology (Eiceman and Karpas 2013) for detecting chemical warfare agents (CWAs), explosives, and volatile organic compounds (VOCs). This technology is widely used in the field against terrorism and in environmental and health monitoring, because of its fast response, high sensitivity, good portability, and ease of operation. Differential mobility spectrometry (DMS), a variant of IMS, was reported to have originated in Russia in the 1980s. The literature on this technique was first published in 1993 by Buryakov and Krylov (Shvartsburg 2009, 2013). The method is also referred to as high-field asymmetric waveform ion mobility spectrometry, field ion spectrometry, ion mobility increment spectrometry, ion drift non-linearity spectrometry, and radiofrequency IMS. DMS can be effectively used to separate and characterize gas-phase ions.

The principle of DMS varies from that of conventional time-of-flight IMS. DMS identifies and detects ions at ambient pressure. Ions have nonlinear coefficients of mobility at high electric fields. At electric fields above 10,000 V/cm, they exhibit different mobility features. High-frequency asymmetric waveforms can generate alternating high and low electric fields in DMS. This method allows the separation of chemical substances by varying the gas-phase mobility of ions at alternating high and low electric fields.

As a detection technology, DMS shows many advantages, including low cost, simple design, high sensitivity, and selectivity. Ions can be separated in DMS to provide high-sensitivity detection and reduced complexity in field applications. However, stand-alone DMS detection is challenging in many real-world scenarios involving components in a complex mixture. DMS resolution (typical resolution 10) is limited, hindering detection and identification of complex mixtures. DMS is a stand-alone technology used to detect components in a complex mixture or complex biological matrix that may be challenging. Hyphenated DMS includes gas chromatography-DMS (GC-DMS), DMS-mass spectrometry (DMS-MS), DMS-IMS, IMS-DMS, and DMS-DMS. Hyphenated-DMS can improve resolution for rapid separation and detection. Hyphenated DMS, combined with single detection technology, can be used to eliminate different interferences and achieve orthogonal separation of information; thus, it can more quickly respond to complex mixtures. Hyphenated DMS techniques can provide powerful methods of detection and identification of chemicals, including CWAs, VOCs, pharmaceuticals, biomarkers and biological materials, CWA

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simulants, explosives, and environmental pollutants. This paper reviews the recent literature specific to the use of hyphenated DMS.

GC-DMS

GC-DMS typically integrates the characteristics of DMS as a detector after separation and elution by GC. The mixture is separated on a column in GC. DMS is applied to filter and measure ions in the analyzer at alternating high and low electric fields. DMS spectra are plots of ion current versus compensation voltage at a fixed separation condition. Compounds are identified by retention time and DMS spectra information in GC-DMS. GC-DMS combines the orthogonal principles of separation to produce second-dimension analytical information. One specific advantage of the DMS instrument as a chromatographic detector is that it can simultaneously monitor positive and negative ions from GC effluent. GC-DMS is widely used in various fields for detection. This section reviews relevant research related to GC-DMS applications in the detection of smoke alarms and fire debris, CWAs and explosives, VOCs, bacteria, water and wine, as well as health diagnosis.

Application of GC-DMS in smoke alarm and fire debris detection

Eiceman and Tarassov (2003) reported the application of GC-DMS methods in smart smoke alarms. In their study, the chemical composition of vapors from different fuel sources, such as cotton, paper, grass, and engine, was identified by GC-DMS. The orthogonal information provided by DMS, combined with the separation feature of GC, yielded spectra of retention time versus compensation voltage. Eiceman and Paz (2014) also reported the use of GC-DMS in airborne vapor monitoring in 2014. VOCs from resistors, capacitors, and insulation from wires at 200 C were collected and analyzed by GC-DMS. Plots of ion peak intensity, retention time, and compensation voltage were obtained. The experiment confirmed that GC-DMS can be used for air quality monitoring or smart smoke alarm detection.

Lu (Lu and Harrington 2007, Lu 2010) reported the application of GC-DMS coupled with chemometric analysis techniques for rapid classification and identification of compounds in forensic analysis. GC-DMS was used as a powerful device to detect ignitable liquids in fire debris. Each ignitable liquid sample obtained orthogonal second-dimension information by GC-DMS. The accuracy of the method was 99.07%±0.04%.

Application of GC-DMS in CWA and explosive detection

DMS combined with multicapillary column (MCC) GC was used to detect explosives, as reported in the study by Buryakov (2004). GC-DMS was used to detect three kinds of explosives, six kinds of CWAs, and drugs. The response time of detection with MCC-DMS was 0.7 s. Other similar studies discussed the different effects of mono-nitrotoluenes and nitrobenzenes, as well as other factors, such as temperature, ionization efficiency, and humidity of explosives (Buryakov 2003).

One type of GC-DMS device is Defender™ (Thermo Fisher, Corporation Inc., Franklin, MA, USA). Defender™ is a commercial DMS analyzer with gas separation capability by adjusting the peak positions and compensation voltage. The combination of high-speed GC and DMS technologies in this instrument enables rapid identification of plastic, explosives, triacetone triperoxide, nitrates, and other marker compounds, with the highest degree of sensitivity.

Application of GC-DMS for the detection of VOCs in air and aqueous phase

In 2005, Lambertus and Fix designed a microfabricated DMS coupled with a silicon microfabricated GC column for VOC detection. The instrument has 5500 theoretical plates. DMS can further perform separation and detection of VOCs that cannot be resolved by GC.

The other GC-DMS instrument is MicroAnalyzer™ (Sionex Corporation Inc., Waltham, MA, USA) which was introduced in 2006 (Figure 1). MicroAnalyzer™ uses a gas

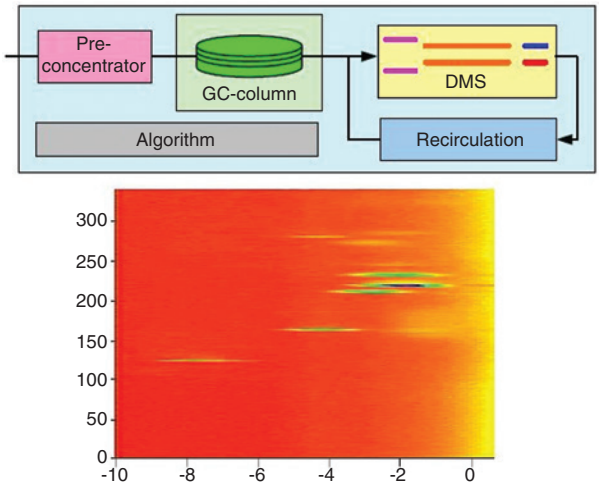

Figure 1: Instrumental implementation of GC-DMS MicroAnalyzer™.

sample preconcentrator as the inlet in GC. The instrument consists of a gas preconcentrator inlet, a fast separation chromatography column, and a DMS detector. GC-DMS can precisely identify and analyze ions in complex background environments.

Limero and Reese (2008, 2011, 2012) and James and Limero (2010) reported that Air Quality Monitor, formerly called Sionex MicroAnalyzer™, has been used to analyze common trace VOCs in the International Space Station. The instrument exhibited superior potential for ground testing and preflight preparations to substitute the aging volatile organic analyzer on the International Space Station. The atmosphere in the International Space Station is mostly scrubbed and recirculated, rendering VOC measurement in its atmosphere important to protect the health and safety of the crew.

Luong and Gras (2013) introduced a portable, fast GC combined with DMS for the detection of alkyl mercaptans and alkyl sulfides. Rapid resistively heated micromachined chromatography columns were used in the GC section. Total analysis time was <70 s over a range of 0.5–5 ppm.

Knau and Thomas (2003) reported the application of GC-DMS in 1,2,4-trichlorobenzene detection in surface water. DMS was used as a detector in the analysis of important pollutants in surface waters around the UK. Solid phase microextraction (SPME)-GC-DMS was compared with SPME-DMS. The use of SPME in the experiment resulted in many variations. GC-DMS was demonstrated as a suitable technique to detect trace contaminants on surface water. It is more affordable, easier to use, and exhibits greater portability compared with GC-MS. The former can be feasibly used to detect field-water contaminants.

Telgheder and Malinowski (2009) analyzed the compounds benzene, toluene, ethylbenzene, and xylene (BTEX) from surface waters by GC-DMS combined with SPME. Their method allows the sensitive detection of benzene, toluene, ethylbenzene, m-xylenes, o-xylenes, and p-xylenes. The detection limits of the six compounds were 0, 0.1–1, and 19 μg/l. GC-DMS was shown to be a suitable approach for BTEX analysis in real surface water. Liang (Liang and Kerpen 2012, 2013, Liang 2014) published a paper on a fast method, developed in 2014 and based on GC-DMS, to detect gasoline-related compounds in groundwater. The gasoline-related compounds BTEX were selected as fingerprint substances. A short column MXT-5 was used to separate the target BTEX compounds in groundwater. The analysis time was <2 min.

Camara and Gharbi (2013) reported the use of GC-DMS in headspace screening for odoriferous VOCs in fresh grapes and wines. GC-DMS is an effective method for on-site analysis of contaminants in foodstuffs, because of its direct and rapid characterization, as well as portability.

Hyphenated GC-DMS combined with a single detection technique can solve difficulties in determining species in mixtures. Orthogonal separation information was obtained using the hyphenated technique for accurate mixture detection.

Application of GC-DMS in bacterial detection and health diagnosis

A series of studies on pyrolysis of bacteria with GC-DMS analysis was reported. Schmidt and Tadjimukhamedov (2004) reported the identification of bacteria by the detection of bacterial pyrolysis with vapor characterizations by GC-DMS. Three-dimensional data were obtained from the spectra, including the chromatography retention time, compensation voltage, and ion intensity. The results showed that pyrolysis-GC/DMS (Py-GC/DMS) methods can identify *Escherichia coli* from *Micrococcus luteus*.

Prasad et al. (Prasad et al. 2006, Prasad and Pierce 2007, 2008, Prasad 2008) published a series of articles related to the analysis of various species of bacteria by Py-GC-DMS. They identified more than 70 chemicals in the headspace vapor of bacterial colonies. Identification of spores depended on the detection of crotonic acid released from different bacteria. Other chemicals, such as lipid A and lipoteichoic acid, allowed the particular distinction between Gram-negative (*Escherichia coli*) bacteria and Gram-positive (*Micrococcus luteus*) bacteria. Researchers improved the method to characterize eight viable bacterial strains and two spores in a further investigation. A Py-GC/DMS analyzer can analyze bacterial species on eight types of bacteria and obtain detailed biochemical information, such as topographical representations (3D) of retention time, compensation voltage, and ion intensity, by simultaneous detection of both modes of operation.

Cheung and Xu (2009) investigated two species of *Bacillus subtilis* and one species of *Bacillus megaterium* by Py-GC-DMS. William and Xu (2009) successfully differentiated bacterial species under the same genus by data processing based on multiple statistical approaches. Basanta and Jarvis (2010) examined the rapid, accurate, and non-invasive diagnosis of respiratory lung diseases in clinicians by GC-DMS. The breath exhaled by a patient with lung disease includes many VOC biomarkers that can be used for detection. Basanta and Jarvis also reported the two-stage thermal adsorption GC-DMS analysis of exhaled air from participants. Their method can identify people with severe chronic obstructive pulmonary disease

by analysis of exhaled air. Breath gas samples of patients and healthy volunteers were collected onto traps and desorbed for detection by GC-DMS. Purkhart and Koehler (2011) described a method of assessing the presence of severe intestinal infection by detection of mycobacterial VOCs. Significant differences were noted between chronically infected and non-infected animals by detection of exhaled breath. All research results showed that GC-DMS is a powerful tool for detecting exhaled breath vapor for the identification of certain diseases or infections.

Aksenov et al. (2014) published an article related to the use of GC-DMS to identify species that are healthy or infected with a disease by VOC feature (Figure 2). The accuracy of the method exceeded 90%. Early detection of diseases by GC-DMS exhibits advantages, including lower cost and rapid field deployment, compared with visual symptoms and DNA-based techniques.

DMS-MS

The current trend in analytical measurements moves toward a new generation of MS systems with enhanced sensitivity and high-throughput measurement. Increasing the sensitivity of MS can augment potential problems with isobaric interferences, which can reveal the undesirable effect of chemical noise on the quality of analysis, particularly for quantitative measurements. Therefore, fast and effective methods of sample pretreatment, which help reduce sample complexity, are needed. Over the past decade, DMS has been employed as a powerful pre-separation method coupled with atmospheric pressure ionization MS. DMS instruments (Schneider and Covey 2013) as ion filters can be integrated with MS (Figure 3). DMS can enhance the quality of analysis by pre-separating interfering ions to reduce chemical noise. Hyphenated MS techniques coupled with MS can enhance the quality of analysis of MS detection because the principles of DMS operation are orthogonal with MS.

Brief history of DMS-MS

Covey and Schneider (Covey and Schneider 2012, Schneider and Covey 2013) reported the brief history of DMS and its coupling with MS. Soviet MS and DMS researchers were the first to develop coupling DMS with electrospray ionization MS in 1991. Significant progress in DMS-MS technology was reported in several laboratories in North America.

Significant efforts by some research groups included laboratory work by Pacific Northwest National Laboratories, University of Florida, University of North Carolina, and Northeastern University. Owlstone Company launched a micromachine-based DMS direct coupling to MS. Groups from Loughborough University and PNNL also studied DMS coupled with MS. AB SCIEX collaborated with Sionex Company to develop a type of DMS-MS instrument called SelexION™. The most significant development in field asymmetric waveform ion

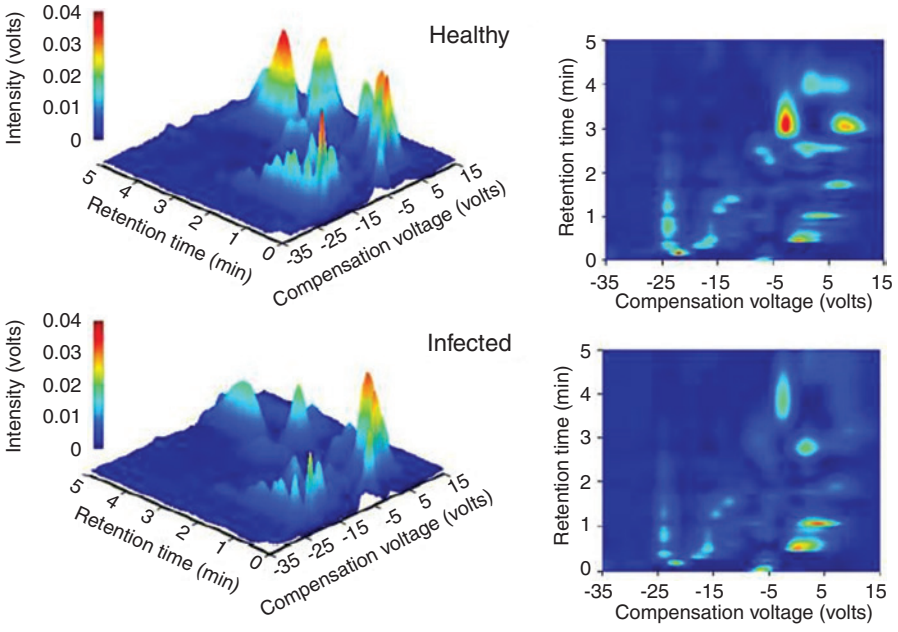

Figure 2: GC-DMS spectral identification of the VOC feature between healthy and infected animals.

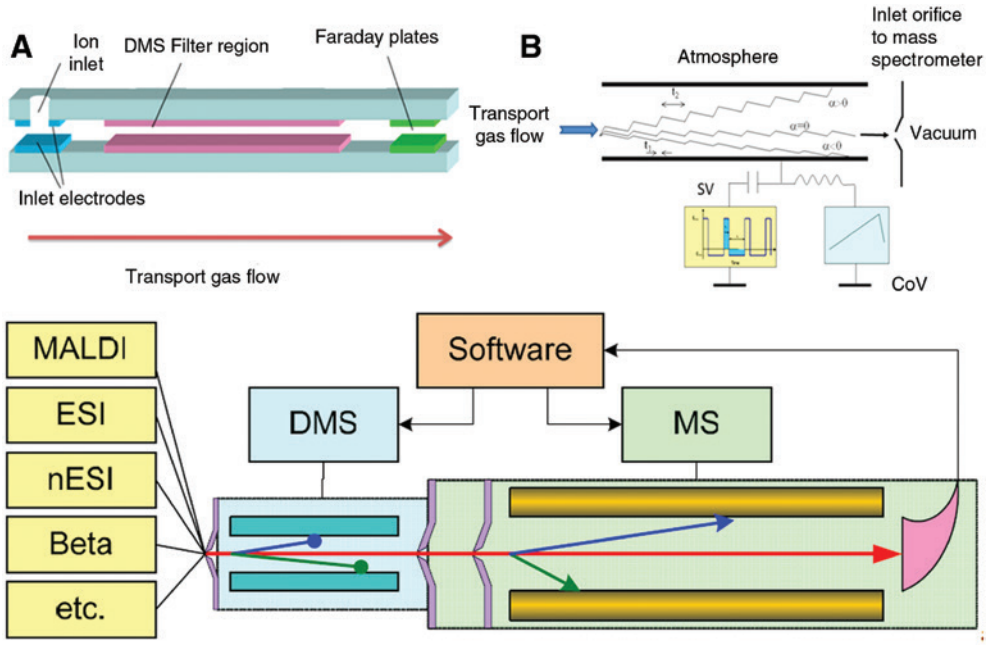

Figure 3: Schematic of DMS-MS principles and interface operation.

mobility spectrometry (FAIMS) instrumentation was its combination with MS and subsequent commercialization by the group of Roger Guevremont at the National Research Council of Canada. Under their guidance, the FAIMS waveform generator was developed into a safe commercial device that required minimal to no maintenance after setup.

Schneider and Covey provided an overview of DMS-MS principles, characteristics of gas-phase separation and detection, as well as progress in instrumentation. Schneider (Schneider and Covey 2010, Menlyadiev and Stone 2012, Schneider and Nazarov 2015a,b) was the first to report on a series of papers about the optimization of DMS-MS instruments (Figure 4). Important factors, including DMS parameters, interface geometry, and optimization of transport gas flow control, are discussed in this paper.

Application of DMS-MS for fast separation in forensic and drug detection

Tadjimukhamedov and Jackson (2010) reported on planar DMS coupled with a mini-handheld rectilinear ion trap MS (weight=10 kg) and application of DMS-MS in illicit drug detection. DMS can separate drugs of similar molecular weights, such as morphine (MW=285.34) and diazepam (MW=284.7). DMS-MS can more efficiently separate and identify fragmentations of diazepam at lower limits of detection (50 ng/ml) in urine extract samples compared with stand-alone MS detection (200 ng/ml).

Hall et al. (2012a,b) reported the use of DMS-MS as a high-throughput analytical method for forensic drug analysis. The interface of DMS-MS measured a few centimeters, and ion movement across interface occurred only in seconds. Thus, DMS can be suitably coupled to all types of MS while

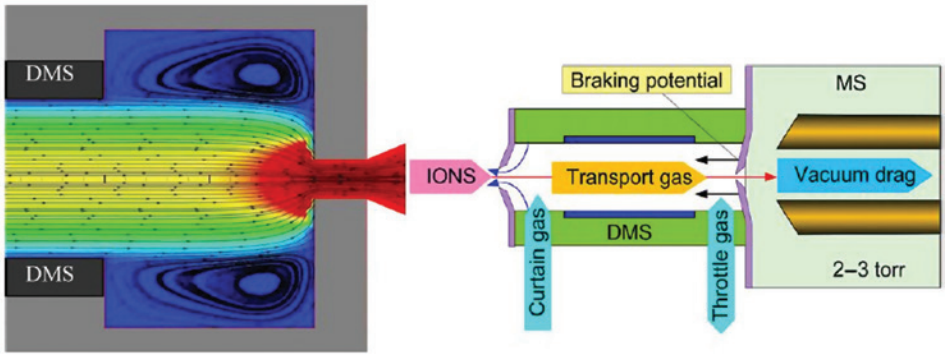

Figure 4: Simulation of optimization of DMS-MS instrumentation.

using atmospheric pressure ionization. DMS-MS can be used to detect cocaine and drug metabolites by DMS ion filter rapid pre-separation. For forensic analysis, DMS-MS exhibited potential for replacing the time-consuming GC or LC separation technology for drug analysis. For example, the analysis time required by DMS-MS separation of cocaine (Figure 5) and four different additives is only 5 s, whereas that required by chromatography is 10 min.

Galhena and Harris (2010) reported on a technique in which DMS-MS was coupled with surface sampling to detect counterfeit antimalarial drug tablets. Desorption electrospray ionization generated ions from samples, and ions underwent pre-separation by DMS and detection in MS. DMS section improved the signal-to-noise ratios (70%–190%) of the entire system. Three kinds of chemicals were included, namely, sodiated lactose (m/z ¼365.106), sodiated artesunic acid (m/z ¼407.108), and R6G (m/z ¼443.233), for testing by DMS-MS.

Bennett and Gamage (2014) reported on desorption electrospray ionization (DESI)-DMS-MS used to image sea algae samples. DMS improved the image quality by pre-filtering targeted ions. Biological tissue samples, including sea algae and mouse brain tissues, were used for the DESI-DMS-MS test. The results showed that the signal-to-noise ratio increased by 10-fold at fixed optimization compensation voltages in DMS.

Picard and Lacoursiere (2012) reported on high-throughput laser diode thermal desorption (LDTD)-DMS-MS technology for testosterone detection. Testosterone detection is used in clinic the clinical field. LDTD achieved sample introduction into a system. DMS improved the signal-to-noise ratio for testosterone quantification. Testosterone analysis for LDTD-DMS-MS lasted for only 7 s, whereas that for LC-MS lasted for 3–5 min. The technology can generate effective quantitation data at ultra-high-throughput speed.

Porta and Varesio (2013) reported on integrated liquid extraction surface analysis (LESA)-DMS-MS for analysis of tissue extraction samples by gas-phase separation (Figure 6). The method can replace traditional LC-MS in analyzing drugs of abuse and detecting metabolites in postmortem tissues. Cocaine and its metabolite sample were tested by LESA-DMS-MS. The analysis time to detect 30 drugs was only 1.5 min. DMS increased the signal-to-noise ratios by pre-separation background interferences. DMS also improved the limit of detection (LODs) and limit of quantitation (LOQs) of the technique.

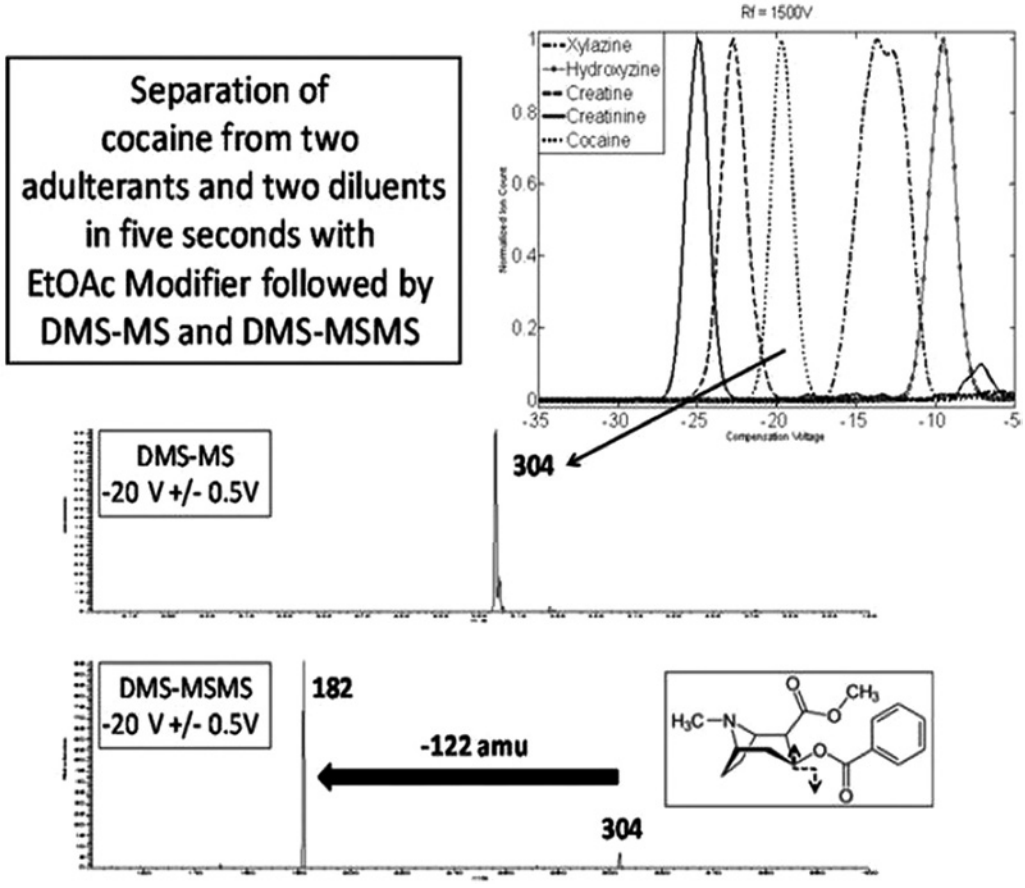

Figure 5: Detection of four additives and cocaine by DMS-MS.

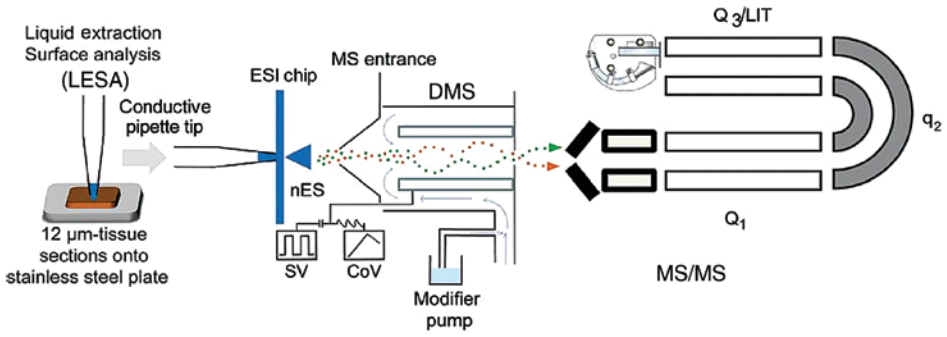

Figure 6: Detection platforms for LESA-DMS-MS/MS analyses.

Application of DMS-MS in isotope and structural isomer separation

Torre and Piper reported the use of DMS-MS (de la Torre and Gonzales 2001, Piper and Emery 2013) in carbon isotope ratio measurement. Accurate detection of isotopes was the key factor in many applications. For example, accurate testosterone detection can identify whether testosterone in sport-testing samples is from synthetic or endogenous sources.

Schneider et al. (Coy and Krylov 2010, Schneider and Covey 2010, Varesio and Le Blanc 2011, Brown and Smith 2012) reported the application of DMS-MS in isobaric species detection by monitoring different element compositions for biomarker evaluation. DMS-MS devices were also reported to perform separation and detection of structural isomers, including leucine and isoleucine. Schneider and Covey (2010) reported the separation and detection of diastereomers by DMS-MS. Their results showed that increased resolution was achieved by DMS pre-separation by increasing the residence time in ephedrine and pseudoephedrine detection. Schneider also separated (Schneider et al. 2012) diphenhydramine and phenyltoloxamine using DMS-MS.

Kailemia and Park (2014) reported the detection of glycosaminoglycan diastereomers by DMS-MS in 2014. DMS separated two sets of epimeric glycosaminoglycan tetramers. DMS also resolved epimer pairs; thus, hyphenated MS can identify the two epimers from each other.

DMS can be used in the separation and detection of structural isomers. DMS can separate the same structural isomer product ions that cannot be separated using hyphenated MS spectra. St-Jacques and Anichina (2010) reported the separation of structural isomers thymine and thymine dideoxynucleotide by DMS-MS, as well as UV-induced bond modifications and separation of structural isomers in DMS. The results also showed that DMS-MS can be used in isomer separation.

Rorrer and Yost (2011) reported the detection of phthalic acid isomers by DMS-MS. Parson and Schneider (2011) also reported the detection of small-molecule structural isomers by DMS-MS. Propranolol and isomeric glucuronide metabolites were also separated in DMS. Therefore, DMS-MS is a suitable high-throughput analytical method used to separate isomeric exogenous metabolites from complex tissues.

Lipid isomers were detected by DMS-MS in the study by Maccarone and Duldig (2014). Phosphatidylcholines were detected by DMS-MS after electrospray ionization with silver adduction. Phospholipid isomers with silver adduction ionization were transmitted through the DMS device at fixed optimization compensation voltages. The method rapidly quantified lipid isomers within a short time (<3 min).

Blagojevic and Chramow (2011) detected isomeric protonated dipeptides by DMS-MS. Two pairs of protonated peptides (glycine-alanine and alanine-glycine, glycine-serine and serine-glycine), as well as eight different modifiers, were separated and detected by DMS-MS. In the study by Shvartsburg and Smith (2011), DMS-MS detected isomers of peptides with mixtures consisting of two types of transport gas. They reported that isomeric phosphopeptides were separated by DMS-MS after phosphorylation. Shvartsburg and Smith (2013) also reported that more than 10 peptide isomers and conformers of proteins can be detected by DMS-MS. Klaassen and Szwandt (2009) reported the application of C-DMS-MS/MS in peptide analysis. The selectivity-enhancing technique of hyphenated DMS could filter out matrix interferences during peptide drug detection in rat serum. Kapron and Jemal (2005) reported the detection of amine drug in a metabolite sample by LC-DMS-MS/MS. DMS removed the metabolite interference before entry to MS. In the study by Beach and Kerrin (2015), neurotoxin β-*N*-methylamino-L-alanine was detected by LC-DMS-MS/MS. This method was found to remove interference from isomers and other

sample components. Prasad and Belford (2014) reported the use of LC-FAIMS-MS to improve the limits of quantitation compared with LC-MS in six-peptide detection. Guevremont and Kloakowski (2005) reported that DMS hyphenated technology can increase selectivity for LC-MS analysis. Thus, the DMS-MS method can be further applied in biological fields in the future.

Liquid chromatography hyphenated with DMS-MS

Both DMS and chromatography have pre-separation functions when coupled with MS. DMS can add theoretical plates after chromatography separation without increasing the separation time. LC-DMS-MS exhibits superior separation capability and rapid detection of features. Orthogonal information provides accurate identification and quantitative analyses of complex mixtures.

Varesio and Le Blanc (2011) reported the two-dimensional (2D) LC-DMS-MS separation and detection of compounds in urine. HPLC-DMS-MS provides orthogonal information of both separation methods. Eight mixture compounds, namely, bromazepam, chlorprothixene, clonapzepam, fendiline, flusilazol, oxfendazole, oxycodone, and pamaquine, with the same mass (m/z 316) underwent separation and detection by LC-DMS-MS. A total of 36 compounds in complex urine sample were also separated and detected by 2D LC-DMS-MS (MS).

Ray and Kushnir (2015) reported the detection of steroids by LC-DMS-MS/MS in 2015. DMS provides further separation capability to improve MS/MS detection accuracy and enhance the selectivity of analyses.

The technique provides a selective and sensitive method for detecting corticosterone, 11-deoxycortisol, 11-deoxycorticosterone, 17-hydroxyprogesterone, and progesterone in human plasma and serum matrix. Covey and Schneider (2012) reported the detection of various steroid samples by LC-DMS-MS. DMS pre-filtering can reduce chemical noise for MS, improve LOD and LOQ for various analyses, and increase sample throughput by reducing or eliminating the necessary LC run time.

Jin and Jarvis (2013) reported a sensitive and selective approach, which was developed to quantitate allopregnanolone and its 5β isomer pregnanolone in human plasma by LC-MS with MS/MS detection. The additional DMS prevents the problems of LC co-elution in complex steroid detection. Plasma samples from normal, pregnant, and postpartum women were analyzed using this method.

Jasak and Blanc (2012) reported the detection of triazole metabolites in plant matrix by DMS to improve LC-MS/MS sensitivity. Triazole derivative metabolites exhibit similar physicochemical properties; thus, their analysis in complex matrixes proves to be extremely difficult. More than 10 representative plant materials can be separated using the new method, which is valid and reproducible, leading to accurate and reliable results.

Hyphenated DMS-MS improves the speed of separation at the front of MS more significantly than a traditional separation method. Hyphenated DMS-MS provides a new selectivity method for complex matrix detection.

DMS-IMS

The hyphenated DMS-IMS method provides complete information regarding ion movement in the gas phase, thereby enhancing selectivity and resolving the capability of instruments compared with stand-alone DMS or IMS detection.

Coupled DMS and IMS have many advantages, such as complementary information regarding ion species; these techniques also enhance selectivity and accuracy of identification. The hyphenated DMS-IMS device has orthogonal characteristics, particularly for rapid separation and detection of small organic ions.

DMS and IMS apply different ion separation principles. One kind of ion was separated in IMS depends on the coefficient of mobility (K_0) and drift times. Another kind of ion was separated in DMS depends on the electric field dependence of mobility (E parameter). Hyphenated DMS and IMS use different ion separation principles to enhance compound identification.

The portable hyphenated DMS-IMS device (Anderson 2008) developed by Sionex Corporation Inc. (Waltham, MA, USA) rapidly separates both positive and negative ions (Figure 7). Two IMS drift tubes were used for further separation and detection after DMS pre-filtration. In the hyphenated DMS device, the detection information included DMS compensation voltage and IMS drift-time data.

The advantages of DMS-IMS^2 include high sensitivity to most toxic industry compounds (TICs), VOCs, CWAs, and organophosphate compounds; high-speed detection; portability; and low power consumption.

Nazarov and Anderson (2007) reported the DMS-IMS 2D spectra for toluene ions. Keqi et al. (Eiceman and Schmidt 2005, Keqi 2006, Burchfield and Niu 2014) also reported the DMS-IMS detection of proteins and CWAs. Maziejuk and Ceremuga (2015) reported on IMS combined with a DMS detector named PRS-1W in 2015. The PRS-1W

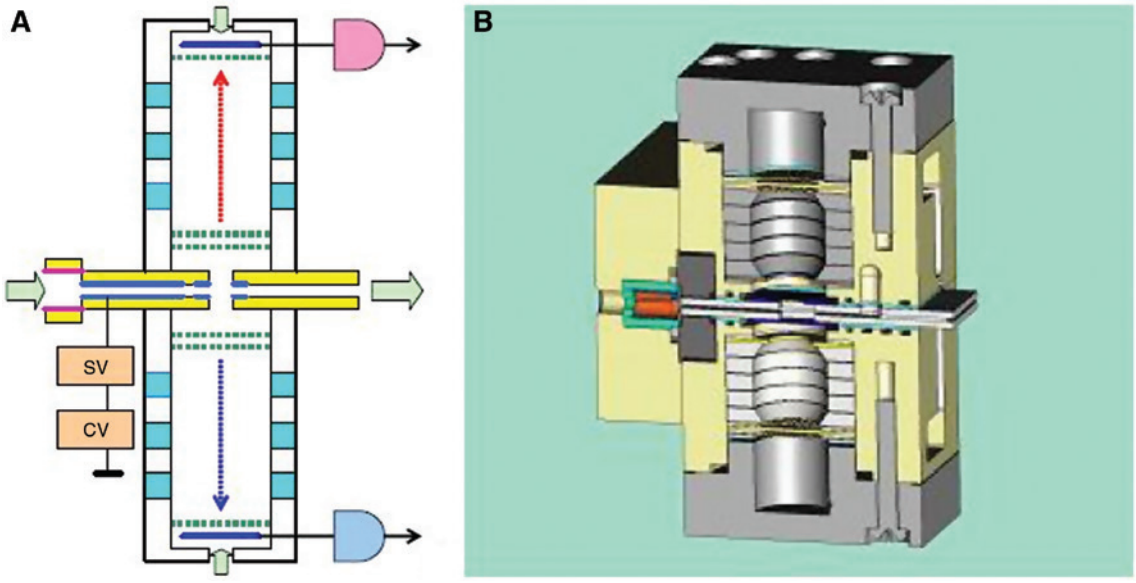

Figure 7: Schematic of DMS-IMS[2].

detector can detect CWAs, including sarin, soman, tabun, and VX, at very low concentrations within a short detection time and with few scans.

Pollard and Hilton (2011) reported on three isomeric tripeptides, namely, tyrosine-glycine-tryptophan (YGW), tryptophan-glycine-tyrosine (WGY), and tyrosine-tryptophan-glycine (YWG), which were separated and detected using an IMS-DMS-MS instrument. Three tripeptides were separated in the IMS section and generated one mobility peak for each tripeptide. YWG was used to identify two peaks through further separation by DMS. Cheng and Chen (2014) reported the IMS-DMS detection of the CWA simulant DMMP.

Hyphenated DMS-IMS enhances separation capabilities. This technique can overcome the shortcomings in complex interference mixture detection via single-separation technology.

DMS-DMS

Menlyadiev and Stone (2012) reported on hyphenated DMS. A DMS instrument was constructed from a DMS/DMS drift tube (Figure 8) for separating electronic components to generate and separate voltages and compensation voltages in each DMS analyzer, an amplifier for Faraday plate detectors, flow controllers for the delivery of sample and dopant gases, and two computers to control the electronic components of each DMS analyzer and for data acquisition. Unlike orthogonality separation methods, to

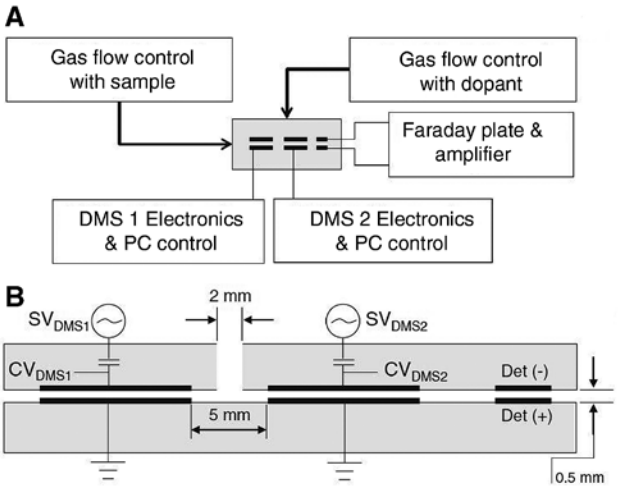

Figure 8: Schematic of a DMS/DMS system with enlarged graphics of the DMS/DMS analyzer.

simplify the interpretation of data from DMS/DMS studies and avoid such complications, a hyphenated instrument with Faraday plate detectors was developed to explore the merits of DMS/DMS methods. Dimethyl methyl phosphonate (DMMP) and triethyl phosphate (TEP) (simulant of CWAs) were tested by DMS/DMS.

Conclusions and outlook

We presented in this review a brief summary of hyphenated DMS. Recent progress in the field of hyphenated DMS

(including GC-DMS, DMS-MS, DMS-IMS, and DMS-DMS) for fast separation and detection was reported. The advantages of hyphenated DMS technology in detecting CWAs, VOCs, drugs and pharmaceuticals, structural isomers, and proteins were discussed. Advances in hyphenated GC-DMS systems may be applied in new application areas, including clinical diagnosis and rapid analysis of gas and toxic substances. Progress in hyphenated DMS-MS systems may be applied in biological analysis and detection for high-throughput separation and analysis of drug abuse. DMS plays a small pre-separation part as a hyphenated system at the front of micro mass spectrometry suitable for mini-instruments. DMS-MS can be combined with various ionization techniques to develop a free sample processing approach for rapid detection. Advances in DMS-IMS may be applied in field applications, as well as miniaturization and portable instrument technology. Hyphenated DMS plays a significant role in the rapid separation, selective separation, and high-throughput rapid analysis of gas and drugs in complex matrices.

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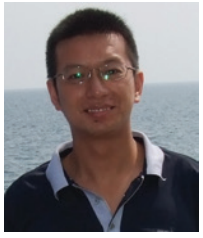
Bionote



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