Analyst

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/d6an00028b

Dielectric barrier discharge ionization (DBDI) enables rapid analysis of new psychoactive substances with ion mobility-mass spectrometry

Bradley B. Garrison, Copeland R. Johnson, Ralph Aderorho and Christopher D. Chouinard *

Received 8th January 2026,
Accepted 9th March 2026

DOI: 10.1039/d6an00028b

rsc.li/analyst

New psychoactive substances (NPS) present a major public health crisis across the world due to their variable potency, constant evolution within the recreational drug community, and ability to skirt legal/policy regulations. Because of the frequency with which new substances are introduced, it is increasingly difficult for clinical, toxicological, and forensic laboratories to keep up with the newest drug threats, presenting a critical need for development of rapid analytical methods capable of confident structural characterization. In the present work, we demonstrate successful coupling of a commercial dielectric barrier discharge ionization (DBDI) source to two ion mobility-mass spectrometry (IM-MS) instruments, including high-resolution Structures for Lossless Ion Manipulations (SLIM). The DBDI source enables rapid introduction of NPS which can subsequently be characterized by IM-MS. Specifically, we show that IM can be used to differentiate structural isomers of synthetic cannabinoids, benzodiazepines, nitazenes, and fentanyl analogues with very minor differences in their collision cross sections (CCS). We also note that the mobility spectra for those compounds presenting protonation site isomers ("protomers") differed from previous work on electrospray ionization (ESI)-generated species from our group and others; this observation is not unsurprising given the different fundamental mechanism of DBD ionization and warrants future interrogation. Finally, we demonstrate the combination of ion mobility with tandem mass spectrometry (MS/MS) for mobility-aligned fragmentation that provided additional structural information for confident characterization. The coupling of DBDI with IM-MS/MS (especially high-resolution IM) constitutes a powerful approach for rapid analysis of several classes of NPS that could be used to improve throughput in the future.

Introduction

New psychoactive substances (NPS) are a broad group of drugs illicitly manufactured to mimic the effects of controlled substances. These include four major classes: stimulants (*e.g.*, cathinones, "bath salts", *etc.*), hallucinogens, cannabinoids, and depressants (*e.g.*, fentanyl analogues, benzodiazepines, *etc.*).[1–3] NPS can skirt federal regulations and avoid illegal classifications, while also evading policy restrictions by utilizing different synthetic pathways and/or chemical precursors.[2] But with >1300 unique NPS identified by the United Nations Office on Drugs and Crime (UNODC), far less is understood about their potency and unintended side effects than their traditional counterparts.[2] All of these factors have led to NPS being recognized as a major public health concern.[1–3] The constantly evolving NPS landscape, with estimates as high as one new substance being introduced into the illicit drug market each week, has generated an impetus for analytical techniques capable of structurally characterizing new species as well as their metabolites. Gold-standard methods include mass spectrometry-based techniques, typically coupled with gas or liquid chromatography (GC/LC-MS).[4–11] However, these methods often require considerable sample preparation and lengthy (chromatographic) analysis times, significantly limiting throughput.

Ambient ionization is "the ionization of unprocessed or minimally modified samples in their native environment".[12] The first ambient ionization mass spectrometry (AIMS) techniques, reported in the early 2000s, included desorption electrospray ionization (DESI), a solvent-based technique reported by Takats *et al.*,[13] and direct analysis in real time (DART), a plasma-based technique developed by Cody *et al.*[14] In the two decades since, AIMS has seen significant development in both technology (>45 ambient techniques reported in literature)

---

*Clemson University, Department of Chemistry; Clemson, SC 29634, USA.
E-mail: cchouin@clemson.edu*

and its applications;[12,15,16] one notable example is the low-temperature plasma (LTP) ionization source which has seen application to drugs of abuse.[17–20] Another promising ionization technique is dielectric barrier discharge ionization (DBDI), a plasma-based technique first reported in 2007 by Na *et al.*[21,22] DBDI involves generation of a low temperature plasma yielding reactive species (*e.g.*, H_3O^+ from ambient water vapor) for soft atmospheric pressure ionization *via* processes including proton transfer. This technique enables analysis of solid, liquid, or gaseous samples without the need for chromatography or sample preparation,[23] allowing for high throughput analysis; several recent reviews of DBDI in mass spectrometry cover its fundamentals and applications.[23,24] The technology has also recently been commercialized as "soft ionization by chemical reaction in transfer" (SICRIT) by Plasmion GmbH, and demonstrated for forensics applications including illicit drugs and explosives.[23,25–28]

Despite the promise of high throughput AIMS techniques like DBDI in fast screening of illicit drugs in biological fluids,[29] differentiation of isobaric/isomeric species (especially in potentially complex matrixes) can be a challenge in lieu of prior separations (*i.e.*, chromatography). One emerging solution is the coupling of ambient ionization with ion mobility spectrometry (IMS), a post-ionization gas-phase technique capable of rapid separation of ions based on differences in their size, shape, and charge. In addition to separation capabilities, IMS can also measure an ion's mobility constant (K) which can be used to derive its collision cross section (CCS), a representative parameter that improves confidence of identification.[30–32] Coupling mobility with MS (IM-MS) provides a hybrid technique capable of simultaneously measuring both CCS and m/z of a given analyte, an approach that has been widely used to distinguish NPS isomers.[33–46]

Due to the post-ionization separation capabilities of IMS, it was logically coupled with DBDI by several groups shortly after its development.[47–49] The approach has since been employed in numerous applications, including for direct testing of pharmaceuticals.[50] Other ambient ionization techniques including liquid extraction surface analysis (LESA), desorption electrospray ionization (DESI), liquid-microjunction surface sampling probe (LMJ-SSP), and paper spray (PS) have also been coupled with IM-MS for applications ranging from dried blood spot analysis to leaf spray (LS).[51–53] Amongst the IMS techniques demonstrated are commercial and homebuilt drift tubes (DTIMS), as well as high field asymmetric waveform (FAIMS) devices. In the present work, we demonstrate successful coupling of a commercial DBDI source with two IM-MS platforms, a drift tube-QTOF and a structures for lossless ion manipulations (SLIM) traveling wave ion mobility (TWIMS) instrument. SLIM utilizes serpentine paths to allow long-path separations (13+ meters) with resolving power of >200.[54,55] Our group has previously shown SLIM differentiation of several forensics-relevant isomer groups including fentanyl analogues, synthetic cannabinoids, xylazine metabolites, performance-enhancing drugs, and explosives albeit using more traditional electrospray ionization (ESI) and/or atmospheric pressure chemical ionization (APCI) techniques.[36,38,39,56,57]

Experimental methods

Chemicals and reagents

Standards of JWH 018 4-hydroxyindole, JWH 018 *N*-(5-hydroxypentyl), JWH 018 6-hydroxyindole, JWH 250 *N*-(4-hydroxypentyl), JWH 250 *N*-(5-hydroxypentyl), JWH 250 5-hydroxyindole, MDA-19 *N*-(4-hydroxyhexyl), MDA-19 *N*-(5-hydroxyhexyl), 4-cyano CUMYL-BUTINACA, APP-BUTINACA phenylpropanoic acid, oxazepam, demoxepam, *N*-desmethylclobazam, nimetazepam, (±)-3-methyl nitrazepam, 4′-chloro deschloroalprazolam, meclonazepam, (±)-meclonazepam, nitazene, 4′-hydroxy nitazene, *N*-desethyl etonitazene, *N*-piperidinyl 4′-hydroxy nitazene, *N*-pyrrolidino metonitazene, isotonitazene, *N*-desethyl protonitazene, metonitazene, methylenedioxynitazene, ethyleneoxynitazene, *N*-pyrrolidino etonitazene, *N*-piperidinyl metonitazene, protonitazene, isotonitazene, ethylene etonitazene, protodesnitazene, isotodesnitazene, 5-methyl etodesnitazene, despropionyl *ortho*-methylfentanyl, despropionyl *meta*-methylfentanyl, despropionyl *para*-methylfentanyl, (±)*cis*-isofentanyl, α-methyl acetylfentanyl, *N*-(1-benzyl-4-piperidyl)-*N*-benzylpropanamide, β-methyl fentanyl, (±)-*trans*-3-methyl fentanyl, β-hydroxythiofentanyl, 4-ANPP, alfentanil, sufentanil, and despropionyl 2′-fluoro-*ortho* fentanyl were purchased from Cayman Chemical (Ann Arbor, MI) as 1 mg mL^{-1} solutions in methanol. Standards of *para*-methyl acetylfentanyl, cyclopropyl fentanyl, crotonyl fentanyl, butyryl fentanyl, *ortho*-fluorofentanyl, cyclohexyl fentanyl, carfentanil, acetyl norfentanyl, cyclopentyl fentanyl, *ortho*-methyl acetyl fentanyl, fentanyl, isobutyryl fentanyl, *para*-fluorofentanyl, ocfentanil, and norfentanyl were purchased from Cerilliant Corporation (Round Rock, TX) as 1 mg mL^{-1} solutions in methanol. Chemical structures for all surveyed NPS are provided in Fig. S1–S4. All controlled substances were purchased as appropriate DEA-exempt preparations. All samples were prepared at 1 μg mL^{-1} of analyte in 50/50 (v/v) water (0.1% formic acid)/methanol. All solvents were Fisher Scientific Optima LC-MS grade.

Instrumentation

All analyses were performed using a SICRIT© DBDI source (Plasmion GmbH, Augsburg, Germany) coupled to either (a) an Agilent 6560 drift tube (DT) IM-QTOF (Santa Clara, CA), or (b) a MOBIE HRIM SLIM (MOBILion Systems, Inc., Chadds Ford, PA, USA) with Agilent 6546 QTOF. Images of the coupling to both instruments are shown in Fig. S5 and S6. Both systems had an accompanying Agilent 1290 Infinity II UHPLC used as an autosampler. Samples (10 μL) were introduced *via* flow injection analysis (FIA) with a flow rate of 0.500 mL min^{-1} of 50 : 50 (v/v) water (0.1% formic acid)/methanol. The DBDI source was operated in positive mode with amplitude of 2200 V, frequency of 45 kHz, and set temperature of 200 °C. Where electrospray ionization (ESI) results are presented, they were acquired using an Agilent dual Jetstream source (AJS) operated with conditions as reported on previously.[37] Instrumental conditions for the Agilent 6560 and MOBILion MOBIE/Agilent 6546 QTOF are contained in the SI; briefly, the drift tube was maintained at approximately 3.95 Torr nitrogen gas and approximately 25 °C, with electric field strength of 18.5 V cm^{-1}. The MOBIE was maintained at 2.50 Torr nitrogen gas and ambient temperature, with SLIM IM separations performed using a sine traveling wave (TW) operating at 25 kHz and 30 V_{pp}; based on the electrode geometry, this frequency equates to a TW speed of 225 m s^{-1}.

Data acquisition and processing

Acquisition of the IM-QTOF data was performed using Agilent MassHunter B.09.00 (Build 9.0.9044.0). Acquisition of the MOBIE SLIM data was performed using Agilent MassHunter Acquisition Version 11.0 (Build 11.0.221.1) and MOBILion EyeOn 2.3 software (0.0.2.4201-release-2.3.0.0). All SLIM data were first converted from the MOBILion .mbi file format into Agilent .d file format using MOBILion EyeOn software and then preprocessed using the PNNL PreProcessor 4.0 (2022.02.18) (Richland, WA) with a drift bin compression of 3 : 1 and spike removal of 2.[58] All data files were visualized/processed in Agilent IM-MS Browser 10.0.1 (Build 10.0.1.10039). Raw data extracted from Agilent IM-MS Browser were processed in Microsoft Excel.

Results and discussion

Ion mobility separations of DBDI-generated NPS species

The objective of this research was to demonstrate the coupling of an ambient ionization technique (DBDI) with ion mobility-mass spectrometry (IM-MS) for rapid separation of isobaric/isomeric novel psychoactive substances (NPS) in lieu of preceding chromatographic separations. NPS samples (powders or solutions) were dissolved or diluted, respectively, prior to flow injection analysis (FIA) using the two IM-MS instruments. Because there was no preceding chromatographic step, total analysis time was ~1 minute per sample, discounting the minimal preparation (dissolution/dilution) required; this enabled a throughput of roughly 60 samples/hour. We first investigated the mobility resolution of representative isomers within the classes of benzodiazepines, nitazenes, synthetic cannabinoids, and fentanyl analogues using low-resolution (R_p ~50–60) DTIMS. Benzodiazepine isomers oxazepam, demoxepam, and *N*-desmethylclobazam, each detected as their protonated ion at *m*/*z* 287.062, demonstrated near baseline separation with measured $^{DT}CCS_{N2}$ of 164.6, 170.6, and 178.0 Å^2, respectively (Fig. 1A). These compounds differ only in the position of nitrogen/oxygen substituents in their seven-member ring. Similarly, nitazenes *N*-desethyl protonitazene and metonitazene differ only in the position of a single ethyl substituent, yet were well resolved with measured $^{DT}CCS_{N2}$ of 204.9 and 198.6 Å^2, respectively (Fig. 1B). Notably, metonitazene exhibits two significant mobility features, presumably due to the presence of protonation site isomers ("protomers"); this is not surprising based on previous work by Hollerbach *et al.* demonstrating observation of protomers for many similar nitazenes due to the presence of multiple protonatable basic sites.[40] Most interestingly, the relative ratio of these features (where the lower mobility species is more abundant) differs from similar compounds in that previous work and indicates a fundamental difference in protomer formation between solution-phase *vs.* gas-phase ionization techniques (*i.e.*, electrospray *vs.* DBDI) for these compounds; this is also not surprising based on previous works that demonstrated how changing ionization source conditions can influence the formation of protomers in similar drugs.[35,37,38,41,42] Other examples of successful separations included synthetic cannabinoids MDA-19 *N*-(4-hydroxyhexyl)/APP-BUTINACA phenylpropanoic acid (Fig. 1C) and fentanyl analogues *ortho*-/*para*-fluorofentanyl (Fig. 1D). $^{DT}CCS_{N2}$ were measured for all compounds using the single-field method with Agilent Tune Mix ions as calibrants[59] and all values are found in Table S3. It should be noted that baseline resolution was not demonstrated for all isomeric pairs/groups; this was especially true in cases where multiple isomers existed and/or ΔCCS ≤ 2.0%.

For those more challenging separations, we turned to high-resolution ion mobility (HRIM) with SLIM, which has previously been used to interrogate NPS isomers with resolving power of ~200. The separation benefits are clearly demonstrated by comparing low-resolution DTIMS with high-resolution SLIM for nitazenes 4′-hydroxy nitazene and *N*-desethyl etonitazene (Fig. 2A and B). These isomers differ in the position of an ethyl substituent, yielding a ΔCCS of only 2.2%. While moderate separation is observed with DTIMS, they are well resolved with SLIM. It should be noted that 4′-hydroxy nitazene displays different relative intensities for its multiple observed mobility features, and this is presumably due to differences in the experimental conditions in the two measurements (*e.g.*, energy imparted by differences in static *vs.* dynamic electric fields, *etc.*); this and similar classes of illicit substances have previously demonstrated such behavior (resulting from protomers) and will be discussed later in this manuscript. Several fentanyl analogues were also challenging to differentiate by DTIMS, such as cyclopropyl fentanyl and crotonyl fentanyl which differ by only ΔCCS 1.4% (Fig. 2C and D). As observed in the resulting DTIMS and SLIM mobility spectra, separation is improved both between major peaks and, to a much lesser extent, secondary (protomer) peaks; the difference in relative mobility separation improvements between protomer isomers has not been observed previously, and will be discussed later in this manuscript. Lastly, separation of isomers *cis*-isofentanyl, *para*-methyl acetylfentanyl, and *N*-(1-benzyl-4-piperidyl)-*N*-benzylpropanamide constituted a significant challenge as they differ only in the position of a methyl/methylene group. Specifically, the latter two have ΔCCS of only ~0.3% (Fig. 2E and F), and are completely overlapping in the DTIMS spectrum, while SLIM yields moderate resolution between the two.

Effect of gas-phase ionization by DBD on protomer ratio

Several previous studies have investigated the presence of fentanyl/nitazene protomers formed during electrospray ioniza-

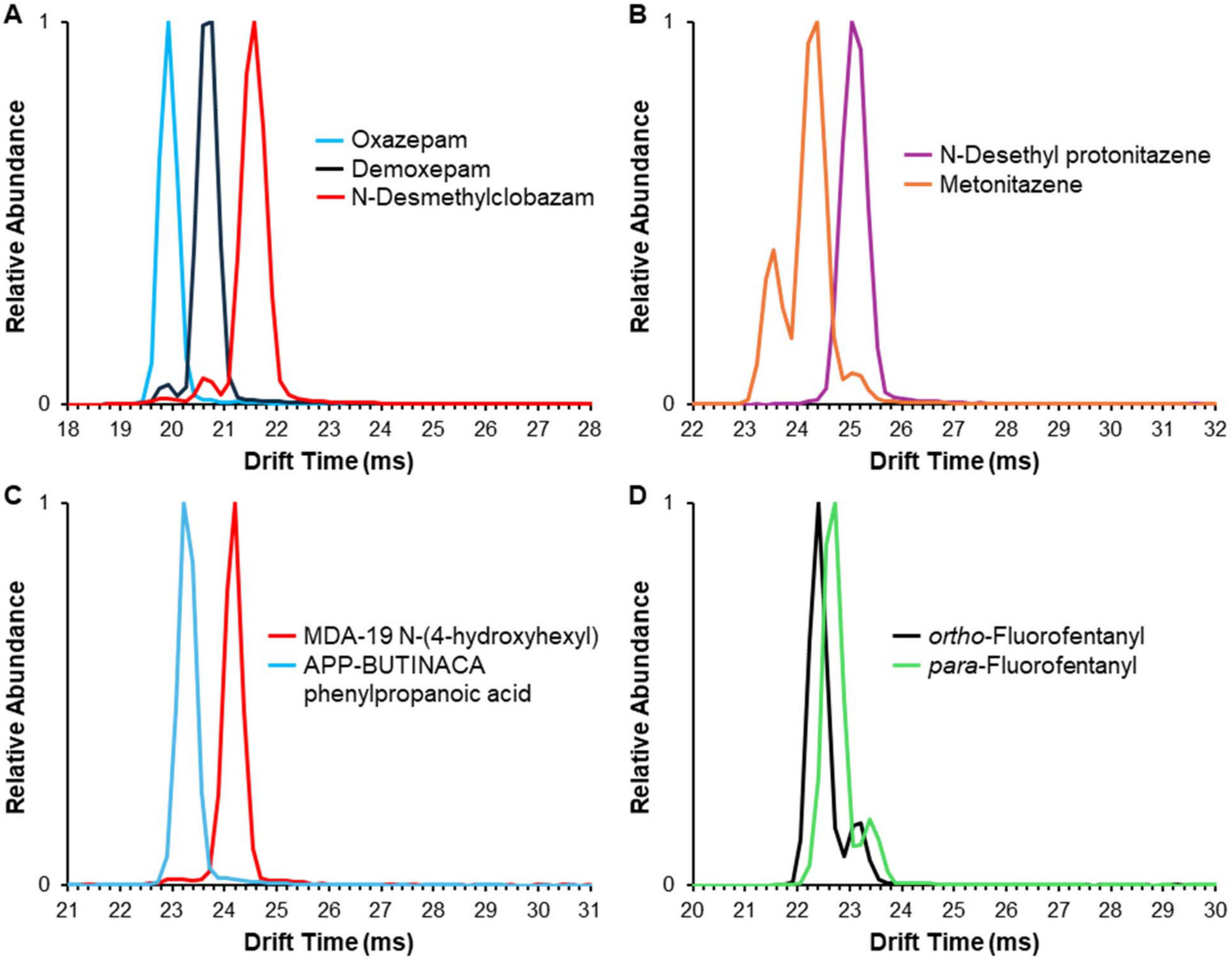

Fig. 1 DTIMS spectra showing separation of isomers: (A) benzodiazepines oxazepam, demoxepam, and *N*-desmethylclobazam; (B) nitazenes *N*-desethyl protonitazene and metonitazene; (C) synthetic cannabinoids MDA-19 *N*-(4-hydroxyhexyl)/APP-BUTINACA phenylpropanoic acid; and (D) fentanyl analogues *ortho*-/*para*-fluorofentanyl.

tion (ESI) using various IM-MS/MS platforms.[35,37,38,40–42] A few of these works demonstrated that changes to experimental variables including solvent composition, ion source parameters, and ion mobility method (*e.g.*, low-field drift tube IMS, trapped IMS, high-field differential mobility spectrometry, and even SLIM)[34,36–38,42] could easily affect the ratio of the protomers observed, presumably by shifting the energetic transition barrier between these various ionization states. In fact, we observed significant differences in relative abundance of protomer peaks in this study when measuring 4′-hydroxy nitazenes with either DTIMS or SLIM (Fig. 2A and B). As for ionization source/parameters, Ieritano *et al.* posited that, because ESI is a solution-based ionization technique, the observed ratio of those protomers may differ if generated by a gas-phase ionization technique (*e.g.*, atmospheric pressure chemical ionization, APCI; or DBDI), assuming there was a difference in the relative solution- and gas-phase basicity of the protonatable sites. Here we present an example of both a fentanyl and nitazene analogue which differ considerably in the ratio of protomers observed between ESI and DBDI. Fig. 3A shows a mobility overlay of ESI- and DBDI-generated *trans*-3-methylfentanyl, observed as its protonated species at *m*/*z* 351.244. As shown previously by our group,[37] when ionized *via* ESI this compound displays a major mobility peak at ~22.8 ms (CCS 187.4 Å^2) with a less abundant, lower mobility species at ~23.4 ms (CCS 193.1 Å^2). However, the DBDI-generated protonated species sees a shift in the relative abundances, with the two protomers being similar and the lower mobility species being slightly more abundant. Similarly, Fig. 3B shows a mobility overlay of ESI- and DBDI-generated protonitazene, observed as its protonated species at *m*/*z* 411.241, where again there is a major mobility feature at ~25.0 ms (CCS 211.4 Å^2) and a less abundant, lower mobility species at ~25.9 ms (CCS 219.0 Å^2). Similar to the fentanyl analogue example, ionization by DBDI causes a shift to a more abundant low mobility species. Fig. S7 show the mass spectra for protonitazene (ESI- *vs.* DBDI-generated) corresponding to the mobility data in Fig. 3B; this comparison shows no significant differences in the mass spectra

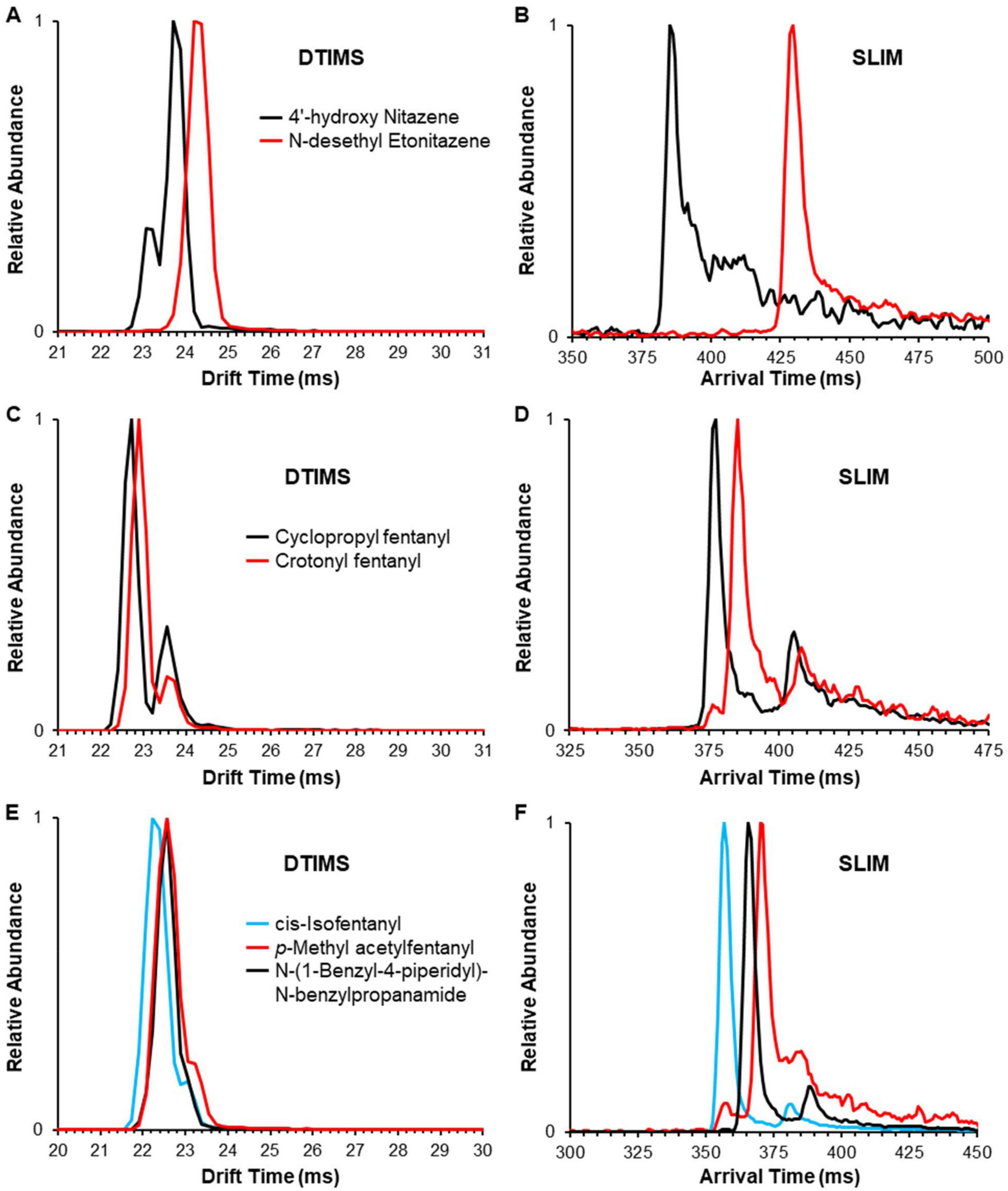

Fig. 2 Comparison of DTIMS and SLIM mobility spectra for isomer groups: (A and B) nitazenes 4′-hydroxy nitazene and *N*-desethyl etonitazene; (C and D) cyclopropyl fentanyl and crotonyl fentanyl; and (E and F) *cis*-isofentanyl, *para*-methyl acetylfentanyl, and *N*-(1-benzyl-4-piperidyl)-*N*-benzylpropanamide.

and no considerable fragmentation that could have potentially contributed to the difference in protomer ratio observed. More interestingly, the previous work from Hollerbach *et al.* showed a relatively higher abundance of the more mobile species;[40] in that case, it should be noted that their ion source contained only a simple fused silica nanoelectrospray (nESI) emitter,

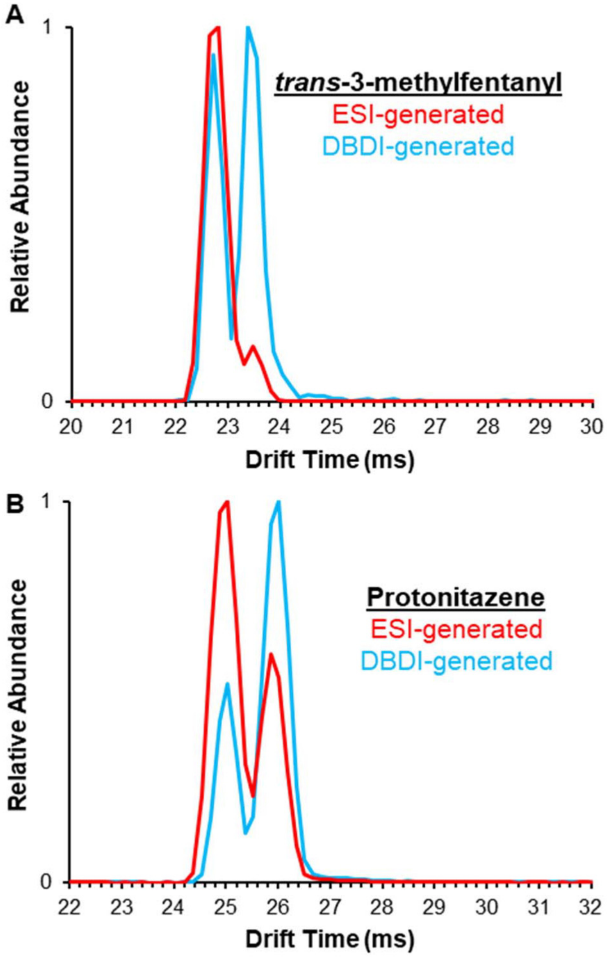

Fig. 3 Comparison of ESI-generated and DBDI-generated protomers, as observed in their mobility spectra, for (A) *trans*-3-methylfentanyl and (B) protonitazene.

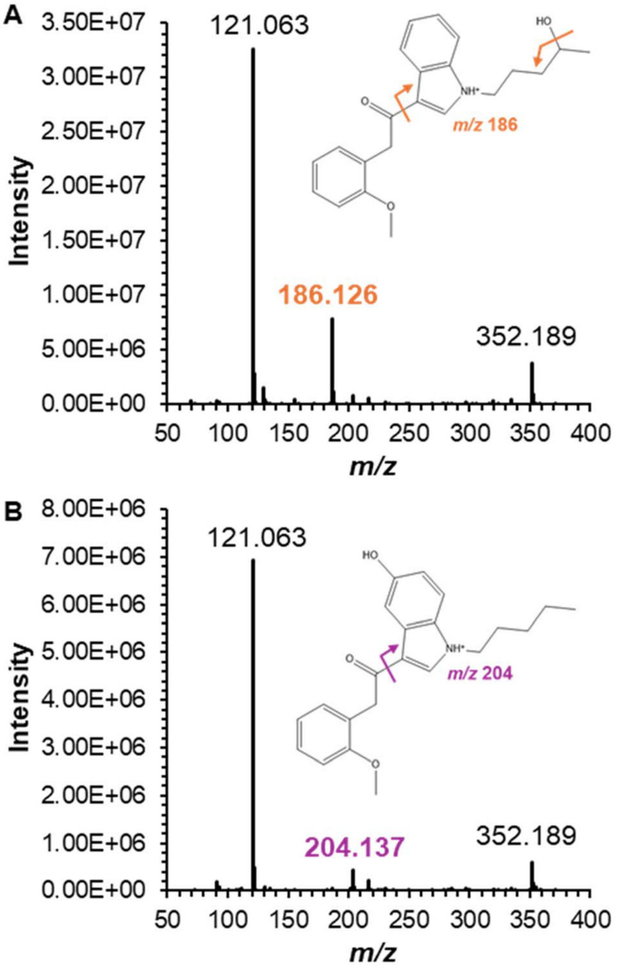

Fig. 4 Mobility-aligned tandem mass spectrometry (MS/MS) fragmentation patterns reveal characteristic product ions for isomers (A) JWH 250 *N*-(4-hydroxypentyl) and (B) JWH 250 5-hydroxyindole.

without applied nebulizing gas and/or heat (presumably a more gentle environment than the commercial Agilent Jetstream source presented here), which was possibly the cause of the difference. These observations underscore the importance of maintaining experimental conditions and also prompt a broader, more in-depth fundamental study of the difference in solution- and gas-phase generated drug protomers; the results of the proposed study will be the topic of a future publication. Lastly, it is interesting to note that while SLIM generally improved mobility separations, it was not always uniform even within the spectrum for a given substance. Specifically, we observed that the peak-to-peak resolution of higher mobility (likely *N*-protomer) features for cyclopropyl and crotonyl fentanyl was improved, but the lower mobility (likely *O*-protomer) species experienced only minimal change. The identities of these mobility features (*N*- *vs.* *O*-protomer) were confirmed for cyclopropyl and crotonyl fentanyl by performing mobility-aligned MS/MS on each feature, which yielded characteristic fragmentation patterns that matched those previously reported by our group[35,38] and others;[41,42] the lower mobility features especially displayed characteristic fragments at *m*/*z* 228, 132, and 132, representative of *O*-protonation. This phenomenon has not been previously observed, but we hypothesize that it results from effects of the different amide substituents (*i.e.*, cyclopropane *versus* propylene) on *O*-protomer structure.

Coupling ion mobility separations with structural characterization by tandem mass spectrometry

In each instrument demonstrated herein, the mobility separations precede a quadrupole time-of-flight (QTOF) mass spectrometer, enabling acquisition of fragmentation spectra *via* tandem mass spectrometry (MS/MS) of previously mobility separated species (*e.g.*, isomers, protomers, *etc.*) in a method referred to as mobility-aligned fragmentation (MAF); our group has previously demonstrated this for several classes of NPS.[35,39] While IMS is beneficial for *separating* species in a complex mixture, this approach is critical for confident identification because it supplements acquisition of mobility/CCS and accurate mass with structurally informative fragmentation patterns. Fig. 4 presents mobility-aligned fragmentation patterns for JWH 250 synthetic cannabinoid isomers, *N*-(4-hydroxypentyl) and 5-hydroxyindole, which differ only in the position of single hydroxyl group. These species are mobility separated, with measured CCS of 188.7 and 193.0 Å^2, respectively, but in lieu of pure chemical standards for mobility-matching it would be exceedingly difficult to assign the position of the hydroxyl group. MS/MS here shows different fragmentation behavior, namely in the loss of the terminal hydroxyl group (as neutral water) from JWH 250 *N*-(4-hydroxypentyl) yielding a characteristic fragment ion at *m*/*z* 186 (Fig. 4A), a mass difference of 18 from the diagnostic fragment observed at *m*/*z* 204 for JWH 250 5-hydroxyindole (Fig. 4B); the difference arises from the stability of the hydroxyl group in the latter, due to its position on the conjugated ring. This IM-MS/MS approach provides a powerful structural characterization technique by combining IM separation of potential isobars/isomers, measurement of CCS (which is helpful for improving confidence of identification in both knowns and unknowns), and fragmentation pattern for structure elucidation.

Conclusions

Dielectric barrier discharge ionization (DBDI) allowed for rapid introduction of several classes of novel psychoactive substances (NPS) into two different ion mobility-mass spectrometry (IM-MS) platforms. We demonstrated several examples of isomer separations by ion mobility, including for benzodiazepine isomers oxazepam, demoxepam, and *N*-desmethylclobazam, which differ only in the position of nitrogen/oxygen substituents in their seven-member ring and have measured $^{DT}CCS_{N2}$ of 164.6, 170.6, and 178.0 Å^2, respectively. More challenging isomer pairs, such as cyclopropyl and crotonyl fentanyl (ΔCCS 1.4%), required high-resolution Structures for Lossless Ion Manipulations (SLIM) ion mobility to be adequately resolved. In several instances, such as for *trans*-3-methylfentanyl and protonitazene, we observed mobility spectra that differed significantly from those generated with electrospray ionization (ESI), potentially due to the differing mechanism (gas- *vs.* solution-phase) for the two techniques. This highlights both the significant need to standardize protomer measurements in NPS analysis, and to perform future fundamental studies on these molecular classes. In the final experiments, we performed mobility-aligned fragmentation which provided the final structural characterization point, in this case by determining the location of a single hydroxyl group in two synthetic cannabinoid isomers; the species (following mobility separation) could be individually dissociated and yielded diagnostic product ions characteristic of precursor structure. Aside from the throughput advantage offered by this approach, the combination of high-resolution mobility separations (enabling differentiation of isobars/isomers with subtle structural differences), CCS measurement (which can also be aided by computational modeling for theoretical structure identification), and MS/MS for structure elucidation indicates that DBDI-IM-MS/MS has a promising future for applications in rapid NPS analyses.

Author contributions

BBG: investigation, formal analysis, methodology, writing – original draft; CRJ: formal analysis, writing – original draft; RA: investigation; CDC: conceptualization, funding acquisition, supervision, writing – review and editing.

Conflicts of interest

The authors receive research funding from MOBILion Systems, Inc. and Agilent Technologies.

Data availability

Data available on request from the authors.

The data that support the findings of this study are available from the corresponding author, CDC, upon reasonable request.

Supplementary information (SI) is available. Supplementary information includes instrumental parameters, collision cross sections (CCS), molecular structures of NPS, images of the source coupling, and comparative MS and MS/MS spectra. See DOI: https://doi.org/10.1039/d6an00028b.

Acknowledgements

The authors would like to thank Plasmion GmbH for the opportunity to demo the SICRIT© source, especially for technical support from Taylor Hayward and assistance from Kyle Pfohl. Financial support for this work was provided by Agilent Technologies (Global Academic Research Support Program #2624930), MOBILion Systems, and Clemson University startup funds.

Portions of the TOC graphic were generated using AI (Google Gemini).

References

1 A. Shafi, A. J. Berry, H. Sumnall, D. M. Wood and D. K. Tracy, New Psychoactive Substances: A Review and Updates, *Ther. Adv. Psychopharmacol.*, 2020, **10**, DOI: 10.1177/2045125320967197.

2 M. J. Y. Neoh, A. Carollo, M. Lim, O. Corazza, A. Coppola and G. Esposito, The Novel Psychoactive Substances Epidemic: A Scientometric Perspective, *Addict. Neurosci.*, 2023, **5**, 100060, DOI: 10.1016/j.addicn.2022.100060.

3 I. C. Santos, D. Maia, R. J. Dinis-Oliveira and D. J. Barbosa, New Psychoactive Substances: Health and Legal

Challenges, *Psychoactives*, 2024, **3**(2), 285–302, DOI: 10.3390/psychoactives3020018.

4 E. K. Hardwick and J. T. Davidson, Structural Characterization of Nitazene Analogs Using Electrospray Ionization–Tandem Mass Spectrometry (ESI–MS/MS), *Drug Test. Anal.*, 2025, **17**(11), 2127–2140, DOI: 10.1002/dta.3921.

5 L. M. Huppertz, S. Kneisel, V. Auwärter and J. Kempf, A Comprehensive Library–based, Automated Screening Procedure for 46 Synthetic Cannabinoids in Serum Employing Liquid Chromatography–quadrupole Ion Trap Mass Spectrometry with High–temperature Electrospray Ionization, *J. Mass Spectrom.*, 2014, **49**(2), 117–127, DOI: 10.1002/jms.3328.

6 M. Villain, M. Concheiro, V. Cirimele and P. Kintz, Screening Method for Benzodiazepines and Hypnotics in Hair at Pg/Mg Level by Liquid Chromatography–Mass Spectrometry/Mass Spectrometry, *J. Chrom. B*, 2005, **825**(1), 72–78, DOI: 10.1016/j.jchromb.2004.12.036.

7 C. A. Valdez, Gas Chromatography-Mass Spectrometry Analysis of Synthetic Opioids Belonging to the Fentanyl Class: A Review, *Crit. Rev. Anal. Chem.*, 2022, **52**(8), 1938–1968, DOI: 10.1080/10408347.2021.1927668.

8 I. I. Papoutsis, S. A. Athanaselis, P. D. Nikolaou, C. M. Pistos, C. A. Spiliopoulou and C. P. Maravelias, Development and Validation of an EI–GC–MS Method for the Determination of Benzodiazepine Drugs and Their Metabolites in Blood: Applications in Clinical and Forensic Toxicology, *J. Pharm. Biomed. Anal.*, 2010, **52**(4), 609–614, DOI: 10.1016/j.jpba.2010.01.027.

9 H. Choi, S. Heo, S. Choe, W. Yang, Y. Park, E. Kim, H. Chung and J. Lee, Simultaneous Analysis of Synthetic Cannabinoids in the Materials Seized during Drug Trafficking Using GC-MS, *Anal. Bioanal. Chem.*, 2013, **405**(12), 3937–3944, DOI: 10.1007/s00216-012-6560-z.

10 J. L. Vicente, H. Chassaigne, M. V. Holland, F. Reniero, K. Kolář, S. Tirendi, I. Vandecasteele, I. Vinckier and C. Guillou, Systematic Analytical Characterization of New Psychoactive Substances: A Case Study, *Forensic Sci. Int.*, 2016, **265**, 107–115, DOI: 10.1016/j.forsciint.2016.01.024.

11 S. Hooshfar, S. Tchu, C. Yun and K. L. Lynch, Development of a High-Throughput Differential Mobility Separation–Tandem Mass Spectrometry (DMS-MS/MS) Method for Clinical Urine Drug Testing, *J. Mass Spectrom. Adv. Clin. Lab*, 2022, **23**, 50–57, DOI: 10.1016/j.jmsacl.2021.12.008.

12 C. L. Feider, A. Krieger, R. J. DeHoog and L. S. Eberlin, Ambient Ionization Mass Spectrometry: Recent Developments and Applications, *Anal. Chem.*, 2019, **91**(7), 4266–4290, DOI: 10.1021/acs.analchem.9b00807.

13 Z. Takats, J. M. Wiseman, B. Gologan and R. G. Cooks, Mass Spectrometry Sampling Under Ambient Conditions with Desorption Electrospray Ionization, *Science*, 2004, **306**(5695), 471–473, DOI: 10.1126/science.1104404.

14 R. B. Cody, J. A. Laramée and H. D. Durst, Versatile New Ion Source for the Analysis of Materials in Open Air under Ambient Conditions, *Anal. Chem.*, 2005, **77**(8), 2297–2302, DOI: 10.1021/ac050162j.

15 A. Henderson, L. M. Heaney and S. Rankin–Turner, Advancements in Ambient Ionisation Mass Spectrometry in 2024: An Annual Review, *Anal. Sci. Adv.*, 2025, **6**(1), e70007, DOI: 10.1002/ansa.70007.

16 H. S. Shepard, J. C. May and J. A. McLean, Ambient Ionization Strategies for the Characterization of Microbial Systems *via* Mass Spectrometry, *Analyst*, 2026, **151**, 939–948, DOI: 10.1039/D5AN01214G.

17 A. U. Jackson, J. F. Garcia-Reyes, J. D. Harper, J. S. Wiley, A. Molina-Díaz, Z. Ouyang and R. G. Cooks, Analysis of Drugs of Abuse in Biofluids by Low Temperature Plasma (LTP) Ionization Mass Spectrometry, *Analyst*, 2010, **135**(5), 927–933, DOI: 10.1039/b920155f.

18 L. Gao, X. Shi and X. Wu, Applications and Challenges of Low Temperature Plasma in Pharmaceutical Field, *J. Pharm. Anal.*, 2021, **11**(1), 28–36, DOI: 10.1016/j.jpha.2020.05.001.

19 Y. Wu, M. Li, R. Liu, J. Li, Y. Guo, D. Yang, W. Xu and K. Hou, Photothermal Desorption and Reagent-Assisted Low-Temperature Plasma Ionization Miniature IT-MS/MS for On-Site Analysis of Illicit Drugs in Saliva and Urine, *Anal. Chem.*, 2025, **97**(5), 2801–2808, DOI: 10.1021/acs.analchem.4c05146.

20 X. Wang, Z. Hua, Z. Yang, H. Li, H. Liu, B. Qiu and H. Nie, Low–temperature Plasma–probe Mass Spectrometry Based Method for Determination of New Psychoactive Substances in Oral Fluid, *Rapid Commun. Mass Spectrom.*, 2018, **32**(11), 913–918, DOI: 10.1002/rcm.8112.

21 N. Na, M. Zhao, S. Zhang, C. Yang and X. Zhang, Development of a Dielectric Barrier Discharge Ion Source for Ambient Mass Spectrometry, *J. Am. Soc. Mass Spectrom.*, 2007, **18**(10), 1859–1862, DOI: 10.1016/j.jasms.2007.07.027.

22 N. Na, C. Zhang, M. Zhao, S. Zhang, C. Yang, X. Fang and X. Zhang, Direct Detection of Explosives on Solid Surfaces by Mass Spectrometry with an Ambient Ion Source Based on Dielectric Barrier Discharge, *J. Mass Spectrom.*, 2007, **42**(8), 1079–1085, DOI: 10.1002/jms.1243.

23 K. Dryahina, M. Polášek, J. Jašík, K. Sovová and P. Španěl, Ion Chemistry in Dielectric Barrier Discharge Ionization: Recent Advances in Direct Gas Phase Analyses, *Mass Spectrom. Rev.*, 2024, **45**, 193–217, DOI: 10.1002/mas.21914.

24 A. Pape and O. J. Schmitz, Dielectric Barrier Discharge in Mass Spectrometry – An Overview over Plasma Investigations and Ion Sources Applications, *TrAC, Trends Anal. Chem.*, 2024, **170**, 117420, DOI: 10.1016/j.trac.2023.117420.

25 C. Conway, M. Weber, A. Ferranti, J. Wolf and C. Haisch, Rapid Desorption and Analysis for Illicit Drugs and Chemical Profiling of Fingerprints by SICRIT Ion Source, *Drug Test. Anal.*, 2024, **16**(10), 1094–1101, DOI: 10.1002/dta.3623.

26 M. Weber, J.-C. Wolf and C. Haisch, Effect of Dopants and Gas-Phase Composition on Ionization Behavior and Efficiency in Dielectric Barrier Discharge Ionization, *J. Am. Soc. Mass Spectrom.*, 2023, **34**(4), 538–549, DOI: 10.1021/jasms.2c00279.

27 K. M. Thaler, L. Gilardi, M. Weber, A. Vohburger, Z. Toumasatos, A. Kontses, Z. Samaras, J. Kalliokoski,

P. Simonen, H. Timonen, M. Aurela, S. Saarikoski, S. Martikainen, P. Karjalainen, M. Dal Maso, J. Keskinen, R. Niessner, G. A. Pang and C. Haisch, HELIOS/SICRIT/Mass Spectrometry for Analysis of Aerosols in Engine Exhaust, *Aerosol Sci. Technol.*, 2021, **55**(8), 886–900, DOI: 10.1080/02786826.2021.1909699.

28 Z. Zhang, M. Qie, L. Bai, S. Zhao, Y. Li, X. Yang, K. Liang and Y. Zhao, Rapid Authenticity Assessment of PGI Hongyuan Yak Milk Based on SICRIT-QTOF MS, *Food Chem.*, 2024, **442**, 138444, DOI: 10.1016/j.foodchem.2024.138444.

29 M. F. Mirabelli, E. Gionfriddo, J. Pawliszyn and R. Zenobi, Fast Screening of Illicit Drugs in Beverages and Biological Fluids by Direct Coupling of Thin Film Microextraction to Dielectric Barrier Discharge Ionization-Mass Spectrometry, *Analyst*, 2019, **144**(8), 2788–2796, DOI: 10.1039/C8AN02448K.

30 J. N. Dodds and E. S. Baker, Ion Mobility Spectrometry: Fundamental Concepts, Instrumentation, Applications, and the Road Ahead, *J. Am. Soc. Mass Spectrom.*, 2019, **30**(11), 2185–2195, DOI: 10.1007/s13361-019-02288-2.

31 V. Gabelica and E. Marklund, Fundamentals of Ion Mobility Spectrometry, *Curr. Opin. Chem. Biol.*, 2018, **42**, 51–59, DOI: 10.1016/j.cbpa.2017.10.022.

32 V. Gabelica, A. A. Shvartsburg, C. Afonso, P. Barran, J. L. P. Benesch, C. Bleiholder, M. T. Bowers, A. Bilbao, M. F. Bush, J. L. Campbell, I. D. G. Campuzano, T. Causon, B. H. Clowers, C. S. Creaser, E. De Pauw, J. Far, F. Fernandez-Lima, J. C. Fjeldsted, K. Giles, M. Groessl, C. J. Hogan, S. Hann, H. I. Kim, R. T. Kurulugama, J. C. May, J. A. McLean, K. Pagel, K. Richardson, M. E. Ridgeway, F. Rosu, F. Sobott, K. Thalassinos, S. J. Valentine and T. Wyttenbach, Recommendations for Reporting Ion Mobility Mass Spectrometry Measurements, *Mass Spectrom. Rev.*, 2019, **38**(3), 291–320, DOI: 10.1002/mas.21585.

33 M. Nytka, J. Wan, F. Tureček and K. Lemr, Cyclic Ion Mobility of Isomeric New Psychoactive Substances Employing Characteristic Arrival Time Distribution Profiles and Adduct Separation, *J. Am. Soc. Mass Spectrom.*, 2024, **35**(8), 1733–1742, DOI: 10.1021/jasms.4c00127.

34 H. A. Majeed, T. S. Bos, R. L. C. Voeten, R. F. Kranenburg, A. C. van Asten, G. W. Somsen and I. Kohler, Trapped Ion Mobility Mass Spectrometry of New Psychoactive Substances: Isomer-Specific Identification of Ring-Substituted Cathinones, *Anal. Chim. Acta*, 2023, **1264**, 341276, DOI: 10.1016/j.aca.2023.341276.

35 R. Aderorho and C. D. Chouinard, Determining Protonation Site in Fentanyl Protomers Using Ion Mobility-Aligned MS/MS Fragmentation, *Int. J. Mass Spectrom.*, 2024, **496**, 117185, DOI: 10.1016/j.ijms.2023.117185.

36 R. Aderorho and C. D. Chouinard, Rapid Identification of Xylazine Metabolite Isomers with SLIM IM-MS, *Anal. Methods*, 2023, **16**, 4041–4044 https://pubs.rsc.org/en/content/articlehtml/2024/ay/d4ay00801d.

37 R. Aderorho and C. D. Chouinard, Improved Separation of Fentanyl Isomers Using Metal Cation Adducts and High-Resolution Ion Mobility-Mass Spectrometry (IM-MS), *Drug Test. Anal.*, 2023, **16**, 369–379 https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/dta.3550.

38 C. R. Johnson, H. M. Sabatini, R. Aderorho and C. D. Chouinard, Dependency of Fentanyl Analogue Protomer Ratios on Solvent Conditions as Measured by Ion Mobility–mass Spectrometry, *J. Mass Spectrom.*, 2024, **59**(8), e5070, DOI: 10.1002/jms.5070.

39 R. Aderorho, S. W. Lucas and C. D. Chouinard, Separation and Characterization of Synthetic Cannabinoid Metabolite Isomers Using SLIM High-Resolution Ion Mobility-Tandem Mass Spectrometry (HRIM-MS/MS), *J. Am. Soc. Mass Spectrom.*, 2024, **35**, 582–589, DOI: 10.1021/jasms.3c00419.

40 A. L. Hollerbach, V. S. Lin, Y. M. Ibrahim, R. G. Ewing, T. O. Metz and K. E. Rodda, Elucidating the Gas-Phase Behavior of Nitazene Analog Protomers Using Structures for Lossless Ion Manipulations Ion Mobility-Orbitrap Mass Spectrometry, *J. Am. Soc. Mass Spectrom.*, 2024, **35**(7), 1609–1621, DOI: 10.1021/jasms.4c00200.

41 A. L. Hollerbach, Y. M. Ibrahim, V. S. Lin, K. J. Schultz, A. P. Huntley, P. B. Armentrout, T. O. Metz and R. G. Ewing, Identification of Unique Fragmentation Patterns of Fentanyl Analog Protomers Using Structures for Lossless Ion Manipulations Ion Mobility-Orbitrap Mass Spectrometry, *J. Am. Soc. Mass Spectrom.*, 2024, **35**, 793–803, DOI: 10.1021/jasms.4c00049.

42 C. Ieritano, A. N. Fry, J. N. Dodds, E. S. Baker and W. S. Hopkins, Three Candidates, Two Peaks: Addressing Conflicting Assignments of Fentanyl Protomers with DMS-UVPD, *J. Am. Soc. Mass Spectrom.*, 2025, **36**(9), 1889–1901, DOI: 10.1021/jasms.5c00130.

43 A. Yanini, F. A. Esteve-Turrillas, M. de la Guardia and S. Armenta, Ion Mobility Spectrometry and High Resolution Mass-Spectrometry as Methodologies for Rapid Identification of the Last Generation of New Psychoactive Substances, *J. Chromatogr. A*, 2018, **1574**, 91–100, DOI: 10.1016/j.chroma.2018.09.006.

44 S. Gwak and J. R. Almirall, Rapid Screening of 35 New Psychoactive Substances by Ion Mobility Spectrometry (IMS) and Direct Analysis in Real Time (DART) Coupled to Quadrupole Time-of-Flight Mass Spectrometry (QTOF-MS), *Drug Test. Anal.*, 2015, **7**(10), 884–893, DOI: 10.1002/dta.1783.

45 M. A. Bergström, H. Lövgren, A. Abrahamsson, E. K. Eriksson, M. L. Andersson, M. Komorowska and M. A. B. Axelsson, Rethinking Drug Analysis in Health Care: High-Throughput Analysis of 71 Drugs of Abuse in Oral Fluid Using Ion Mobility–High-Resolution Mass Spectrometry, *J. Anal. Toxicol.*, 2022, **46**(7), 765–775, DOI: 10.1093/jat/bkab114.

46 S. A. Miller, A. R. Forero, L. V. Tose, J. E. Krechmer, F. Muntean and F. Fernandez-Lima, High-Throughput Screening of Fentanyl Analogs, *Talanta*, 2025, **283**, 127191, DOI: 10.1016/j.talanta.2024.127191.

47 A. Michels, S. Tombrink, W. Vautz, M. Miclea and J. Franzke, Spectroscopic Characterization of a

Microplasma Used as Ionization Source for Ion Mobility Spectrometry, *Spectrochim. Acta, Part B*, 2007, **62**(11), 1208–1215, DOI: 10.1016/j.sab.2007.08.004.

48 S. B. Olenici-Craciunescu, A. Michels, C. Meyer, R. Heming, S. Tombrink, W. Vautz and J. Franzke, Characterization of a Capillary Dielectric Barrier Plasma Jet for Use as a Soft Ionization Source by Optical Emission and Ion Mobility Spectrometry, *Spectrochim. Acta, Part B*, 2009, **64**(11–12), 1253–1258, DOI: 10.1016/j.sab.2009.10.001.

49 W. Vautz, A. Michels and J. Franzke, Micro-Plasma: A Novel Ionisation Source for Ion Mobility Spectrometry, *Anal. Bioanal. Chem.*, 2008, **391**(7), 2609–2615, DOI: 10.1007/s00216-008-2181-y.

50 N. Chantipmanee, J. S. Furter and P. C. Hauser, Ambient Ionization Source Based on a Dielectric Barrier Discharge for Direct Testing of Pharmaceuticals Using Ion Mobility Spectrometry, *Anal. Chim. Acta*, 2022, **1195**, 339432, DOI: 10.1016/j.aca.2022.339432.

51 O. E. Olajide, B. Donkor and A. M. Hamid, Systematic Optimization of Ambient Ionization Ion Mobility Mass Spectrometry for Rapid Separation of Isomers, *J. Am. Soc. Mass Spectrom.*, 2022, **33**(1), 160–171, DOI: 10.1021/jasms.1c00311.

52 R. L. Griffiths, A. Dexter, A. J. Creese and H. J. Cooper, Liquid Extraction Surface Analysis Field Asymmetric Waveform Ion Mobility Spectrometry Mass Spectrometry for the Analysis of Dried Blood Spots, *Analyst*, 2015, **140**(20), 6879–6885, DOI: 10.1039/C5AN00933B.

53 C. L. Feider, N. Elizondo and L. S. Eberlin, Ambient Ionization and FAIMS Mass Spectrometry for Enhanced Imaging of Multiply Charged Molecular Ions in Biological Tissues, *Anal. Chem.*, 2016, **88**(23), 11533–11541, DOI: 10.1021/acs.analchem.6b02798.

54 I. K. Webb, S. V. B. Garimella, A. V. Tolmachev, T. C. Chen, X. Zhang, R. V. Norheim, S. A. Prost, B. LaMarche, G. A. Anderson, Y. M. Ibrahim and R. D. Smith, Experimental Evaluation and Optimization of Structures for Lossless Ion Manipulations for Ion Mobility Spectrometry with Time-of-Flight Mass Spectrometry, *Anal. Chem.*, 2014, **86**(18), 9169–9176, DOI: 10.1021/ac502055e.

55 J. C. May, K. L. Leaptrot, B. S. Rose, K. L. W. Moser, L. Deng, L. Maxon, D. Debord and J. A. McLean, Resolving Power and Collision Cross Section Measurement Accuracy of a Prototype High-Resolution Ion Mobility Platform Incorporating Structures for Lossless Ion Manipulation, *J. Am. Soc. Mass Spectrom.*, 2021, **32**(4), 1126–1137, DOI: 10.1021/jasms.1c00056.

56 C. L. Frank, B. M. Jones, E. Efird, M. Hoover, S. Kingsley, H. M. Sabatini and C. D. Chouinard, Profiling Multiple Steroid Subclasses Enabled by Rounded Turn SLIM Ion Mobility, *J. Am. Soc. Mass Spectrom.*, 2025, **36**(12), 2623–2632, DOI: 10.1021/jasms.5c00218.

57 H. M. Sabatini and C. D. Chouinard, SLIM Ion Mobility-Based Analysis of Low Molecular Weight Explosives, *J. Am. Soc. Mass Spectrom.*, 2025, **36**(10), 2022–2025, DOI: 10.1021/jasms.5c00268.

58 A. Bilbao, B. C. Gibbons, S. M. Stow, J. E. Kyle, K. J. Bloodsworth, S. H. Payne, R. D. Smith, Y. M. Ibrahim, E. S. Baker and J. C. Fjeldsted, A Preprocessing Tool for Enhanced Ion Mobility-Mass Spectrometry-Based Omics Workflows, *J. Proteome Res.*, 2022, **21**(3), 798–807, DOI: 10.1021/acs.jproteome.1c00425.

59 S. M. Stow, T. J. Causon, X. Zheng, R. T. Kurulugama, T. Mairinger, J. C. May, E. E. Rennie, E. S. Baker, R. D. Smith, J. A. McLean, S. Hann and J. C. Fjeldsted, An Interlaboratory Evaluation of Drift Tube Ion Mobility-Mass Spectrometry Collision Cross Section Measurements, *Anal. Chem.*, 2017, **89**(17), 9048–9055, DOI: 10.1021/acs.analchem.7b01729.