Application of direct analysis in real-time mass spectrometry (DART-MS) in forensic science: a comprehensive review

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Abstract
Background: As the rate of crime is constantly increasing, the workload on the forensic analyst also piles up. The availability of a limited number of seized samples makes it crucial to directly analyze the sample, thereby preventing wastage in the prior steps of sample preparation. Due to such needs, the forensic community is consistently working on broadening the usage of direct analysis in real-time mass spectrometry (DART-MS). DART-MS is a relatively new technique for rapid mass spectral analysis. Its use for chemical analysis credits its ability to analyze the sample at atmospheric pressure.

Main body: This article gives insight into the ionization mechanisms, data analysis tools, and the use of hyphenated techniques like thermal-desorption-DART-MS, infrared-thermal-desorption-DART-MS, Joule-heating thermal-desorption-DART-MS, etc. This review summarizes the applications of DART-MS in the field of Forensic Science reported from 2005 to 2021. The applications include analysis of drugs, warfare agents, gun-shot residues, ink differentiation, and other forensically relevant samples. The paper also presents the relation between the type of DART-MS technique and the ionization mode used for a particular class of compounds.

Conclusion: The review follows that the high-resolution mass-spectrometers or low-resolution mass-spectrometers systems in the positive or negative mode were highly dependent on the type of analyte under investigation. Drugs, inks, dyes, and paints were mainly analyzed using the positive ionization mode in the HRMS technique. The examinations of fire accelerants predominantly used the positive ionization mode in the LRMS technique. Moreover, the limit of detection values obtained from the qualitative screening of street drugs were of ppb level, indicating high sensitivity of DART-MS. Considering the work done in the past years, there are potential future research needs of this technology, especially in forensic science.

Keywords: Forensic science, Direct analysis in real-time, Mass spectrometry, DART-MS

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Background
Forensic science is the application of scientific principles in the legal domain. The main motto of this discipline is to ensure effective and timely delivery of justice. Forensics is a multi-disciplinary branch and has incorporated principles from various disciplines like biology, chemistry, physics, serology, and anthropology. This set of principles lay a guideline and set a standard that ensures high quality of work. The Principle of Analysis, one of the most formidable principles in Forensic Science, states that "The analysis can be no better than the sample analyzed". Thus, it is of utmost importance to properly collect and preserve the evidence so that the sample can be accurately analyzed.

But, the process of investigation is not hurdle-free. Some of the factors responsible for inaccurate results are improper sealing of crime scenes, lack of proper collection and sampling, availability of minute quantities, a low workforce in forensic labs, and high workload. As many such factors determine the effectiveness of the analysis, which eventually holds the fate of the accused and the victim, it is crucial to ensure that the results obtained are as accurate as possible. Being a forensic scientist, one way to achieve this is to minimize the obstacles which arise in the processes performed after the sample has already been collected and sent to the lab. Instrumental parameters like sensitivity, specificity, and rapidity often test the performance of analytical techniques. The technique applied and the instrument used must be highly sensitive as the desired analyte might be present in very minute quantities. Also, the rapid increase in crime has led to an escalation in the number of samples to be analyzed. Thus, emphasizing the need for employing time-effective techniques to bestow timely justice.

One of the most reliable modern techniques used for analysis is mass spectrometry. This technique aids in the identification of the unknown sample while allowing both qualitative and quantitative estimations. This versatile technique has been extensively used in forensic science, especially when the sample is diminutive. Over the last few decades, various modifications and adaptations have been implemented in the mass spectrometer to refine its performance. The use of different ionization sources, detectors, carrier gases, and hyphenation with other techniques are a few ways to enhance the accuracy of the results. Among hyphenated techniques, mass spectrometry is one of the most versatile instrumentation techniques. It provides a high-resolution mass...
number and consequently aids their identification (Kim and Jee 2010).

To reduce the burden on the analyst while saving time and energy, led to the introduction of **Ambient Ionization Techniques**. “Ambient mass spectrometry” referred to as “direct ionization mass spectrometry,” is a subfield of analytical mass spectrometry (MS). The pivotal milestone in the recent development of this new family of ionization methods is that it requires almost no sample preparation while facilitating the sample to be probed without any chemical separation (Ackerman and Noonan 2009). These ambient ionization methods are distinguished as they operate in open air and have the ability to probe the surface of samples of any shape and size (preferably small). Thereby significantly expanding the analyst’s toolbox in various sectors like imaging, homeland security detection, drug discovery, forensic, and quality control while maintaining the sample’s integrity (Harris and Nyadong 2008). These ambient ionization techniques are a developmental breakthrough in MS as several samples can be examined in their native state only. They can be classified (Table 1) as spray or jet-based; electric-discharge-based, and ambient gas, heat and laser-assisted desorption/ionization-based.

The transfer of the ionization process from the mass spectrometer into the open air has resulted in a remarkable expansion. This further increases the flexibility of these techniques and their applications. Due to commercial availability and the advantage of no direct interaction of plasma and sample, one of the most widely used techniques for ambient ionization is DART. In 2005, Cody et al. proposed direct-analysis in real-time (DART) for a rapid and direct examination of the sample. The main perks of this technique are the working of the instrument in the open air, requiring no sample preparation, having no memory effect, and no sample carryover. Thus, allowing a wide range of samples like metabolites, explosives, drugs of abuse, and so on to be rapidly screened and analyzed from different surfaces like skin, glass, clothes, and metals effortlessly (Cody and Laramée 2005). It is an efficient and prompt analytical technique in which the spread of required ion current over the data channel is allowed, safeguarding the valuable analyte signal, which aids in analyzing a vast number of samples.

### DART-MS

The DART ion source was developed in late 2002 by JEOL USA Inc. It was first tested on a mass spectrometer in 2003 and then later patented in 2005. The DART source was first presented at the American Society for Mass Spectrometry Conference (Swider 2013). Since then, it has been used with different types of mass spectrometers.

The helium plasma, generated from an electrical discharge in a ceramic flow cell, is used in an ion source (Ackerman and Noonan 2009). This discharge is a result of applying a potential between a needle-electrode and a ground counter-electrode. The gas exits the glow discharge region through the perforated disk electrode/ground counter electrode, gas heater, and a grid electrode/needle electrode. The solvent-free stream of helium gas consists of excited neutral helium atoms, which ionize and generate protonated water molecules. These water molecules then vaporize the desired analyte molecules by protonating the sample (Jeckelmann 2007). Ionisation occurs when the gas from DART interacts with the sample.

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**Table 1** Categorization of ambient ionization techniques (Harris and Nyadong 2008)

| Classification of ambient ionization techniques | Technique          | Year introduced | Acronym | Full form                                                      |
|------------------------------------------------|--------------------|----------------|---------|----------------------------------------------------------------|
| Spray- or jet-based                            | 2004               | DESI           | Desorption-Electrospray Ionisation                          |
| 2006                                           | DeSSI              | Desorption-Sonic Spray Ionisation                         |
| 2006                                           | EASI               | Easy-Ambient Sonic-Spray Ionisation                        |
| 2007                                           | DAPPI              | Desorption-Atmospheric-Pressure-Photoionization            |
| Electric Discharge-based                       | 2005               | DART           | Direct Analysis in Real-Time                                |
| 2005                                           | ASAP               | Atmospheric-Pressure Solids-Analysis Probe                 |
| 2005                                           | DAPCI              | Desorption Atmospheric-Pressure Chemical Ionisation        |
| 2007                                           | DBDI               | Dielectric-Barrier Discharge Ionisation                     |
| 2007                                           | PADI               | Plasma-Assisted Desorption Ionisation                      |
| Ambient gas-, heat- and laser-assisted desorption/ionization-based | 2007               | ND-EESI        | Neutral-Desorption Extractive Electrospray Ionisation       |
| 2005                                           | ELDI               | Electrospray-Laser Desorption Ionisation                   |
| 2007                                           | IR-LADESI          | Infrared-Laser Assisted Desorption Electrospray Ionisation |
| 2007                                           | LAESI              | Laser-Ablation Electrospray Ionisation                     |
| 2007                                           | MALDESI            | Matrix-Assisted Laser Desorption Electrospray Ionisation   |
with the sample in the gap between the DART source outlet and the orifice of the mass spectrometer. The ionization mechanisms of the DART ion source are penning ionization and proton transfer (Jeckelmann 2007). When a metastable atom transfers its energy to an analyte molecule resulting in the formation of a molecular ion, it is known as the penning ionization process. Whereas, the proton transfer occurs when the analyte molecule has a higher proton affinity than the ionized water cluster (Jagerdeoa and Abdel-Rehim 2009). The amount of target analyte subjected to the ion source is proportional to the intensity of the molecular ion peak. The spectra obtained from the standard calibration curve of the peaks of different concentrations of the standard solution are relatively simple and clean as it majorly consists of $[M+H]^+$ molecular cations (Jang 2009).

DART has the benefit of no exposed voltage or radioactive material (Cody and Laramée 2005). The elemental composition using rapid data acquisition rates, simplicity of design, wide range of observed mass, and exact mass measurements formulate accurate information. It can actively ionize non-polar neutrals and utilizes the gas-phase ionization technique (Bennett and Steiner 2009). Because of the exclusion of the solution-phase processes, DART often requires the analyte to be volatile. DART-MS is fundamentally a non-contact and non-destructive technique that reduces the possibility of sample cross-contamination, toxic waste generation, and sample loss. To an extent, there is the preservation of the integrity of the sample, as no sample preparation is required (Nilles and Connell 2009). When the samples are present in limited quantity, this distinctive feature allows the same sample to undergo other corresponding investigations. Although the development of DART-MS was for quantitative analyses, it successfully provides semi-quantitative information, yielding a rough estimation of the content of targeted compounds (Vaclavika and Rosmus 2010). Sample pre-treatment for improving the sensitivity of DART as this preconcentrates the analytes is another approach. At present, the mechanism of DART, its sensitivity, quantitation capabilities, and the effect of matrix on the analysis for a wide range of compounds have not been fully characterized. Pursuing this technique in research will continue to expand the use of DART-MS in the field of forensic (Sisco and Forbes 2021).

**Instrumentation of DART-MS**

The instrumentation of DART-MS (Fig. 1) includes the various components of the set-up, the mechanisms on which the technique works, and the working of the system which the forensic scientist utilizes to produce the analytical procedures to obtain measurements/data.

The main components of DART-MS are ion source and the mass spectrometer. An ion source is a device where the conversion of the sample under examination to its atomic or molecular ions. Depending on the strength of the ionization, these sources can be Hard-Ionisation Sources or Low-Ionisation Sources. In Hard-Ionisation Sources, the parent ions of the given analyte fragments during the ionization. However, negligible fragmentation of parent ions takes place in Low-Ionisation Sources. The most commonly used carrier gases in the ion source are Helium and Nitrogen. Nitrogen being readily available in the atmosphere tends to be a cheaper and greener alternative to helium, and its use has been well-demonstrated (An and Liu 2019; Song and Chuah 2020; Sisco and Staymates 2020). These gases form excited species and react with the reagent molecules, which are then allowed to collide with the sample analytes. Helium gas forms electronic excited species and attains a high energy excited state. These excited helium atoms react with the atmospheric water and form water clusters. The Nitrogen gas

![Fig. 1 Schematic diagram of the DART system (Dane 2010)](image-url)
forms vibronic excited species and attains a comparatively low energy excited state. Thus, enabling the ionization of only those analytes which have a lower ionization potential than that of nitrogen’s vibronic excited state. The mass spectrometer is an integral part of the DART-MS arrangement. It functions by selectively detecting the desired analyte according to its mass to charge ratio (m/z). According to the resolution produced, the mass spectrometers can be either of high resolution or low resolution. The high-resolution mass-spectrometers (HRMS) have comparatively much better instrumental parameters like accuracy, selectivity, and sensitivity. Contrary, the low-resolution mass-spectrometers (LRMS) detect the m/z of the analytes with comparatively less precision. Some of the HRMS analyzers are Fourier-transform (FT) - ion cyclotron resonance (ICR), time-of-flight (TOF), and orbitrap mass analyzers and, some of the LRMS analyzers are quadrupole and linear ion trap mass analyzers. The ion source and the mass analyzer usually have an interface of vacuum as it prevents the collision of theformed ions and prohibits any unwanted loss of energy.

Depending on the type of carrier gas in use, the different ionization mechanisms occur in DART. Based on the nature of gas, ion polarity, and the presence of dopants, a DART ion source can result in three types of ions. These ions are metastable species, positive ions, and negative ions. They are produced based on the ionization mechanism that the sample analyte undergoes. These ionization mechanisms are penning ionization method and atmospheric pressure chemical ionization method. Penning ionization method is a type of chemical ionization in which the gas ions are electrically excited and are then allowed to collide with the target analyte molecules. This collision results in the formation of a cationic species of the analyte. In addition, the release of a high-energy electron occurs, and the excited gas ion comes back to the ground state.

Atmospheric pressure chemical ionization method is similar to chemical ionization but for less thermally stable compounds with small molecular weight. It is also known as the proton transfer method. It has two modes, positive ionization mode and negative ionization mode. In positive ionization mode, the given analyte and the carrier gas collide; it leads to the formation of [M+H]+ analyte ions, either due to addition or proton transfer. The majority of the work done in forensic sciences has made use of this method. Whereas in negative ionization mode, the given analyte and the carrier gas collide; the analyte forms either [M-H]− ions due to proton abstraction or [M+X]− ions due to attachment of an anion. In positive mode, the interaction of metastable helium ions with atmospheric water molecules generates a “pseudo molecular” ion. This gives rise to hydronium clusters, which then transfer the protons to the sample. In negative mode, reactions between the metastable helium ions and oxygen–water clusters form the dominant ion and their corresponding adducts (Samms and Jiang 2011).

In the working of a commercial DART ion source, the electrical discharge source runs at a discharge current of the order of 2 mA and, the plasma gas temperature is around 50–60 °C inside the DART ion source (Shelley and Wiley 2008), whereas the gas flow rate is of 1–2 L min⁻¹ and a direct current potential of 1000–5000 V is used (Cody and Laramée 2005). A typical value of +250 V for positive-ion detection and −250 V for negative-ion detection at the exit grid is used (Dane 2010). Due to its non-reactive property, either Helium or Nitrogen gas makes use in the ionization source (Dane 2010). The gas flows through an axially segmented tube where a glow discharge generates by applying an electrical potential in the middle of a discharge needle and a grounded counter electrode. The corona discharge produces excited atoms, ions, and electrons (Cody and Laramée 2005; Gross 2013; Rummel and McKenna 2010). The discharge produced is passed along a perforated electrode, and the cations separate from the gas stream. The resultant gas is then heated and allowed to pass through the third electrode. Here, the extraction of anions and electrons occurs. Thus, the gas flowing from the glow discharge chamber into the tube consists of only metastable species (Gross 2013; Cody and Laramée 2005; Dane 2010). The space between the exit of DART and the mass spectrometer atmospheric-pressure ionization (API) interface consists of the sample which is to be ionized (Dane 2010). The exit grid guides the reagent and the analyte ions towards the API interface and then into the mass spectrometer (Gross 2013). The sample introduction method for a particular analyte is also crucial as it increases reproducibility and maximum desorption temperature. These methods are on-axis methods like direct approach or direct sampling via glass microcapillary or off-axis method like non-proximate configuration. Other methods include sample preconcentration or sample clean-up and thermal desorption. The employment of off-axis methods is majorly due to their extensive screening, as the source scans a large surface area.

Direct analysis in real-time (DART)-time of flight (TOF)-mass spectrometry (MS) is a rapid confirmatory instrumental method that allows for the rapid identification of target analytes. This method produces high-quality data which is suitable for confirmatory analysis. It also makes the task significantly more efficient than the traditional analytical methods. Moreover, DART coupled with the TOF detector provides a high-resolution mass spectrum almost instantaneously for several compounds.
DART-TOF-MS provides a fast-screening method for forensic laboratories. The significant advantages in a forensic laboratory are speed of analysis, ability to analyze samples in-situ (cloth surfaces, swipes, tablets), and the ability to use the same sample preparation for subsequent analysis (Swider 2013). The sample analyte subjected to evaluation may not be volatile, making it difficult for them to reach the MS inlet. For such samples, increasing the extent of desorption is one feasible solution. Introducing a method of heating the sample analyte independent of the DART-MS system is a probable solution. Some of these methods are:

1. TD-DART-MS-thermal-desorption (TD)-DART-MS allows for samples to be introduced on wipes using an auxiliary thermal desorption unit. Its applications are presumptively identifying the contents of drug evidence, classification of cathinone through neutral loss spectra, and quantitation of a suite of different compounds (Jones and Sisco 2020). Low concentrations of non-pharmaceutical Fentanyl (NPF) in blood can be effectively analyzed by targeting solid trace contaminations using TD-DART-MS (Sisco and Verkouteren 2017).

2. IRTD-DART-MS-infrared-thermal-desorption (TD)-DART-MS also allows the sample introduction into a thermal disrober via wipes. But here, an IR lamp is used instead of resistive heater, which attains temperature as high as 600 °C (Forbes and Verkouteren 2019). This technique has been demonstrated for the analysis of inorganic explosives (Forbes and Sisco 2018).

3. JHTD-DART-MS-Joule-heating thermal-desorption (JHTD)-DART-MS works by ohmic heating of the nichrome wire. The wire attains a very high temperature, around 750 °C, and the liquid sample on it, for further analysis (Forbes and Sisco 2017).

4. ionRocket-DART-MS: This technique makes use of a copper pot which is heated to provide temperature-programmed up to 600 °C. Thus, making it possible to analyze several chemical compounds (Barnett 2019; Bridge and Marić 2019; Frazier and Benefield 2020).

The interpretation of mass spectra is the heart of this technique. A mass spectrum is a plot of intensity vs. mass-to-charge ratio (m/z). It is a pattern representing the distribution of ions by their m/z ratio of the sample. Due to the unique and individualizing features of the spectra, tools may be used, which help in characterizing the mass spectra produced. A matrix formation from the mass spectra of various known samples is analyzed using different data analysis tools. Depending on the nature of the examination, these tools can be either statistical or non-statistical (Fig. 2). In 2017, statistical analysis of mass spectra from biodegrading bottled lubricants from skin samples were analyzed using hierarchical clustering analysis (HCA) and principal component analysis (PCA). This revealed 12 distinct groupings and significant chemical differences based on key chemical components and minor additives (Maric and Harvey 2017).

i. Hierarchical clustering analysis (HCA) groups similar samples. It feeds the mass spectral data matrix into the algorithm, which aims to distinguish the mass spectra of individual samples (Box and Hunter 2005). The output of HCA is a dendrogram indicating the overall similarity between the samples analyzed.

ii. Principal component analysis (PCA) is a tool for feature extraction. It obtains the data from the mass spectral matrix and then highlights those features which aid in grouping and classifying the data based on certain commonalities (Box and Hunter 2005).

iii. Random forest analysis (RFA) is used to analyze unknown spectra. Several decision trees are created, with each decision tree containing a set of rules to differentiate samples within the mass spectral data matrix. The classification model formed can then be used to organize mass spectra from unknown samples (Box and Hunter 2005).

iv. Kendrick mass defect (KMD) is applied to polymeric species and takes a given molecular fragment and sets it as an integer value, the Kendrick mass. The defect between the Kendrick mass and nominal mass is then obtained and plotted. The KMD plot then identifies polymers with the same repeating units by their horizontal alignment (Hughey and Hendrickson 2001).

v. Neutral loss spectra is in use to identify similar fragmentation patterns among compounds undergoing high fragmentation. The formation of the spectrum is by plotting the difference, obtained by subtracting the m/z value of each fragment ion from its molecular mass. The difference is the neutral part of the compound, lost in the creation of each fragment ion. This tool helps identify compounds having similar core structures but different substitutions (Fowble and Shepard 2018).

Main text

Forensic applications of DART-MS

Successful utilization of DART-MS has been for the examination various chemical substances from varying
surfaces. Some of the significant analytical classes include chemical warfare agents, pigments, metabolites, pesticides, explosives, drugs of abuse, etc. (Cody and Laramée 2005). In the forensic domain, the inference drawn from the analysis of the sample is of utmost importance. It is better to use HRMS-DART techniques like TOF-DART-MS for rapid mass spectral analysis. Some of its applications include (Gross 2013):

- Screening of trace amounts of explosives/chemical warfare agents/drugs present on any surface
- Study of compound metabolites from urine and plasma
- Examination of inks
- Analysis of flavors and fragrances, etc.

**Drugs**

A drug is any substance which upon consumption may affect either the physiology or psychology of the consumer. Drug samples have been successfully analyzed from different surfaces using DART-MS (Cody and Laramée 2005). Active research of drugs is chiefly due to their recent aggravation in the exploitation of recreational drugs. These recreational drugs can be classified into different categories, depending on the effect they cause to the consumer.

- Analgesic drugs are those drugs that provide the consumer relief from pain. They are commonly known as “painkillers.” In 2005, (Cody and Laramée 2005) an API-TOF-MS (AccuTOF/LC, JEOL Ltd., Japan) was used for the instant detection of Acetaminophen from pain killers. Similarly in 2009, (Steiner and Larson 2009), a narcotic analgesic, Oxycodone, was subjected to rapid detection using a DART ion source coupled to a JEOL AccuTOF mass spectrometer (JMS-T100LC).
- Stimulants are those drugs that enhance the activity of the messenger cells. They make the consumer feel energetic due to increased signaling between the brain and the body cells. Cocaine is a very commonly used recreational drug that is often abused and is of high forensic relevance. In 2009, screening of cocaine and its metabolites from human urine samples was done using a DART-TOF, JMS-T100LC AccuTOF (JEOL, Peabody, USA) (Jagerdeoa and Abdel-Rehim 2009). Kawamura et.al proposed a simple method for simultaneous detection of Methamphetamine (MA), 3,4-Methylenedioxyamphetamine (MDMA), and their metabolites in urine (Kawamura and Kikura-Hanajiri 2011).
- Hallucinogens consist of drugs which cause a change in perception, feelings, and thoughts. The most commonly encountered hallucinogen is cannabis. The
active ingredients screened are tetrahydrocannabinol (THC) or its derivatives, synthetic cannabinoids, and cannabimimetics (Table 2). In 2015, synthetic hallucinogens, N-methoxybenzyl (NBOMe) compounds, were directly analyzed from a blotter paper using DART-MS, operated in positive-ion mode and controlled by Mass Center software version 1.3.4m (JEOL Inc. Tokyo, Japan) (Poklis and Raso 2015). The identification of powdered synthetic cannabinoids using a combination of DART-TOF-MS and NMR (Marino and Voyer 2016). Such a combination led to a higher detection and signal separation power while decreasing load on wet chemistry and solvent usage.

In the forensic domain, the sample procured is often adulterated or mixed with other substances. Receiving pure drug samples as tablets, pills, or vials is an uncommon scenario. The effect of a matrix often creates a hurdle for rapid yet accurate analysis. Thus, various experiments performed using DART-MS for identification with the drug as the target analyte. In 2006, (Williams and Patel 2006) used to compare the analysis of drugs by DART used with other API methods. Drugs were also detected using TLC coupled with DART-MS (Steiner 2011). Pioneer work for the on-site identification of designer drugs using DART SVP source with Vacuum interface (IonSense, Inc. Saugus, MA, USA), (Brown and Oktem 2016). Duvivier et al. performed a comparative analysis of THC from intact hair samples using DART-MS with Orbitrap, quadrupole Orbitrap, triple quadrupole, and quadrupole time-of-flight mass analyzers (Duvivier and van Beek 2016). In another study, several metabolites were detected while excluding external contaminations. DART further provides lower analysis time as compared to traditional segmented hair analysis (Duvivier and van Putten 2016).

The plants containing psychoactive compounds are widely in use as “legal highs.” To ease this illegal distribution while preventing their seizure, they undergo adulteration (Table 3). These adulterants include substances like dried leaves, talc powder, food supplements, etc. The identification of psychoactive drugs from bulk material and their quantification can be efficiently done by DART-MS (Fowble and Musah 2019). In 2019, a study was performed to detect psychoactive materials and the spatial distribution mappings of endogenous molecules simultaneously. Such a study established a direct link between an individual via fingerprint identification and the substances contacted (Fowble and Shepard 2019). Doping substances like cocaine and methadone were quantified from urine by the use of a SPME-coated mesh as sampling system. The extraction with thin-film-coated mesh preconcentrated the analytes and increased the sensitivity of test (Rodriguez-Lafuente and Mirnaghi 2013). In 2015, detection of drugs and metabolites from urine was conducted via SPME, which led to an increase in the signals by more than an order of magnitude as compared with direct analysis (LaPointe and Musselman

Table 2 Different techniques used for the screening of THC, its derivatives, synthetic cannabinoids, and cannabimimetic

| Year of study | Technique used | Conclusion of study |
|---------------|----------------|---------------------|
| Musah and Domin (2012) | DART SVP100™ Ion Source (IonSense, USA) interfaced to AccuTOF (JEOL, Peabody, USA) | Cannabinoids mixed with botanical material were tested. Due to the lack of pure samples, only tentative identification of individual cannabinoids within the mixture was possible. |
| Takahashi and Uchiyama (2013) | JMS-T100LC AccuTOF (JEOL, JAPAN) | JWH-213, a designer drug, was detected in herbal products. |
| Duvivier and van Beek (2014) | DART-SVP™ Ion Source (IonSense, USA) coupled to an Exactive Orbitrap HRMS (Thermo Fisher Scientific, USA) | Pre-screening for THC without sample preparation was done by probing complete locks of hair using DART-MS. |
| Jacobs and Steiner (2014) | DART SVP100™ Ion Source (IonSense, USA) interfaced to AccuTOF (JEOL, Peabody, USA) | The chromophore formed during the Duquenois-Levine test with marijuana sample was detected and characterized for its structure. |
| Lesiak and Musah (2014) | AccuTOF (JEOL, Peabody, USA) configured with a DART-SVP™ Ion Source (IonSense, USA) | Identification of Cannabinoids in commercially available herbal spice products, concentrations within the range of 4–141 mg/g of material |
| Habala and Valentová (2016) | LTO Orbitrap XL™ Hybrid Ion Trap-Orbitrap Mass Spectrometer (Thermo Scientific™) configured with a DART-SVP™ Ion Source (IonSense, USA) | Six synthetic cannabinoids were identified from herbal material, either directly as plant parts or as an extract in methanol. |
| Davidson and Sasiene (2020) | Pro Linear Ion-Trap (LIT) mass-spectrometer operated with Heated-Electrospray Ionization (HESI) source. An Agilent Technologies 6538 UHD Accurate-Mass Quadrupole Time-of-flight (Q-TOF) mass spectrometer operated DART SVP100™ Ion Source (IonSense, USA) mounted to the Q-TOF with a Vapur™ interface (IonSense, USA). | The fragmentation pathway was identified for the identification of novel N-alkylated synthetic cathinone. |
| Application | Technique | Conclusion |
|-------------|-----------|------------|
| Differentiation of seeds from Datura genus by seed analysis (Lesiak and Cody 2015) | DART SVP100™ Ion Source (IonSense, USA) coupled to AccuTOF (JEOL, Peabody, USA) | The variance of Principal Components (PCs) was 98.02% and the leave-one-out cross-validation (LOOCV) was 89.26% |
| Identification of psychoactive pepper from a variety of supplements (Lesiak and Musah 2016) | DART-SVP™ Ion Source (IonSense, USA) coupled to AccuTOF-HRMS (JEOL, Peabody, USA) | The variance of principal components was 70.92%, and the LOOCV was 95.72% |
| To measure Mitragynine in kratom plants (Fowble and Musah 2019) | DART-SVP™ Ion Source (IonSense, USA) coupled to AccuTOF-HRMS (JEOL, Peabody, USA) | The linear range of quantification was 5-100 μg mL⁻¹ mitragynine in methanol extracts with an LLOQ of 5 μg mL⁻¹. The lowest concentration was found in the dried leaves of the live plant and the highest in the capsules, with a range of 2.76–20.05 mg/g |
| Detection of atropine and scopolamine from twenty-four nightshade plant species by directly testing the cross-section of the seeds (Beyramysoltan and Abdul-Rahman 2019) | DART-SVP™ Ion Source (IonSense, USA) coupled to AccuTOF-HRMS (JEOL, Peabody, USA) | Mass measurements were in the range m/z 40-700 of seeds of species in five genera, namely Atropa, Brugmansia, Datura, Hyoscyamus, and Mandragora |
| Differentiation of species of 11 different psychoactive plants using SPME sampling (Appley and Beyramysoltan 2019) | DART-SVP™ Ion Source (IonSense, USA) coupled to AccuTOF-HRMS (JEOL, Peabody, USA) | The relative importance of the various m/z values were explored by PCA and RD results |
| Differentiation of hemp cultivars by temperature programmed using ionRocket for thermal desorption (Dong and Liang 2019) | DART Ion Source (IonSense, USA) equipped with a Thermo LTQ XL mass spectrometer (Thermo Scientific, USA) | A 99.3 ± 0.3% classification accuracy was obtained |
| To quantify mescaline in cacti of the Echinopsis genus (Longo and Musah 2020) | DART-SVP™ Ion Source (IonSense, USA) coupled to AccuTOF-HRMS (JEOL, Peabody, USA) | As per the FDA guidelines, the mean relative errors and coefficients of variance were all within 15%. But, the LLOQ samples were within 20% Quantification of mescaline was in the range of 1–100 ppm. The micro punching technique took around 0.01 mL or 2–3 mg of the sample and dissolved it in 1 mL of methanol. The concentration of the drug was approximately 0.5–2 mg/mL |
| Analysis of different Ayahuasca plant species, containing N,N-dimethyltryptamine (Zhou and Wang 2020) | DART-SVP™ Ion Source (IonSense, USA) coupled to a Q Exactive hybrid quadrupole-Orbitrap mass spectrometer (Thermo Fisher Scientific, USA) | The micro punching technique took around 0.01 mL or 2–3 mg of the sample and dissolved it in 1 mL of methanol. The concentration of the drug was approximately 0.5–2 mg/mL |

Table 3 Applications of various psychoactive plants and the technique used for their analysis, along with the conclusion of the study
in the extensive area of research of drugs.

The drug samples of forensic pertinence execute an extremely crucial role in the transmission of justice. It is therefore of extreme importance to not only screen the sample but also to provide confirmatory data. As DART-TOF-MS generates high-quality data, it is comparatively more appropriate for such confirmatory investigations. DART-MS was used for screening of an appetite suppressant, Dimethylamylamine (DMAA) from its supplements and urine samples. Important qualitative information was obtained from instant and highly accurate mass measurements (Lesiak and Adams 2014). Table 4 enlists the steady growth of the applications of DART-TOF-MS in the extensive area of research of drugs.

To carry out a given task with consistency, the validation of the method is very critical. Ensuring the use of relevant processes and application of the best analytical parameters gives an overall good performance. One of the many performance indicators is the limit of detection (LOD). It is the minimum quantity/concentration of the sample/analyte that the instrument can detect. For a device, this value varies with the type of analyte used. Table 5 is a compilation of the LOD values for different drugs sampled from different matrices and surfaces. With an established LOD at 250 ng/mL, Methadone from unprocessed urine was analyzed by DART-MS with positive identification rates of 87 and 91%, for DART-TOF-MS and DART-QTRAP-MS platforms, respectively (Beck and Carter 2016). In 2019, Zhang et al. investigated nine drugs and metabolites and obtained LODs ranging from sub ng/mL to hundreds of ng/mL (Zhang and Zhang 2019). Blood spots containing codeine, propanolol, bisoprolol, and methadone were analyzed after treating with organic solvents and the LOQ values were under 0.5 ng mL⁻¹ (Gómez-Rios and Tascon 2018).

**Explosives**

Explosives are reactive substances that produce an explosion with the release of energy; light, heat, sound, and pressure. These substances have potential energy stored in them and explode when triggered. In the field of forensic, the detection of explosives holds a very great significance. Thus, it is crucial to have an analytical technique that can be employed efficiently to detect a wide variety of explosives, especially of liquid and solid form (Cody and Laramée 2005). Along with direct analysis of the sample, DART-MS also provides a rapid presumptive screening. These explosives can be detected from any surface like metal, glass, wood, tape, polymers, etc. Although it has been observed that porous substances tend to retain the target analyte, thereby causing disruption in the DART gas stream and reducing the overall signal strength. Another factor was the thermal property of the explosive, which is directly proportional to the desorption area (Sisco and Forbes 2021).

DART-MS and its variants make extensive use for the detection of a range of explosives. Some of the commonly analyzed organic explosives include Dinitrotoluene, Trinitrotoluene Trinitrobenzene, Nitroglycerine, PETN, RDX, HMX, etc. With the increase in technology, many new explosives are available in the market. The detection of new compounds with existing methods is a challenge. Thus, DART-MS has also evolved by using alternative sample introduction techniques like TD-DART, QuickStrip, ionRocket, etc. Some of the recent studies on various explosives are in Table 6.

Raman spectroscopy coupled to DART-MS had led to the formation of orthogonal signatures that provided the capability of unique differentiation among explosives, binders, plasticizers, and additives (Bridoux and Schwarzenberg 2016). IRTD-DART-MS created a discrete temperature profile, each species desorbed at its optimal desorption temperatures (Forbes and Sisco 2018). This technique also detected potassium perchlorate from flash powder and potassium nitrate, and sulfur from black powder (Bezeremer and Forbes 2020). In 2019, KMD analyzed the polymeric components of each sample, pre- and post-blast, and inferred that the post-blast residues were less oxygenated and more unsaturated (Gaiffe and Cole 2019).

In cases of terrorism, to avoid suspicion, the explosive material is hidden, and their screening becomes quite a task. When the sample tested is suspected to be a part of the post-blast residue, its testing becomes very difficult as the explosive material is present only in very minute quantities. In such cases where the analyte is already present in trace amounts, the sample preparation required for testing is an uphill task. Thus, emphasis on the need for the use of DART is the need of the hour.

**Gun-shot residues**

Gun-shot residues are the residues discharged from the firearm because of the burning of the propellant material in the cartridges. Gun-shot residues are the residues discharged from the firearm because of the burning of the propellant material in the cartridges. These residues are complex mixtures, which depend on the chemical composition of the propellant mixture, the type of projectile used, and the scrapings of the barrel. The evaluation of the gun-shot residues (GSR) aids the forensic scientist in evaluating various things. For instance,
| Application                                                                 | Technique                                                                                           | Ionization mode in DART source                                                                 | Reference                                                                 |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Detection of adulterants and contaminants in drugs                        | DART ion source coupled to an AccuTOF orthogonal TOF-MS                                              | Both positive and negative ionization mode                                                      | (Fernandez and Cody 2006)                                                 |
|                                                                           | DART-TOF (JEOL, Peabody, USA)                                                                        | Positive ionization mode                                                                       | (Newton and Fernandez 2008; Nyadong and Harris 2009)                       |
|                                                                           | AccuTOF-MS (JEOL, Japan) with DART Ion Source (IonSense, USA)                                       | Positive ionization mode                                                                       | (Chernetsova and Bochkov 2011)                                            |
|                                                                           | DART-SVP100™ Ion Source (IonSense, USA) linked with JMS-T100LP AccuTOF (JEOL, Peabody, USA)        | Positive ionization mode                                                                       | (Samms and Jiang 2011)                                                   |
|                                                                           | DART-SVP™ Ion Source (IonSense, USA) equipped with 6530 Accurate-Mass Quadrupole, TOF-MS (Agilent Technologies, USA) | Positive ionization mode                                                                       | (Zhou and Zhang 2011)                                                    |
|                                                                           | DART ionization coupled to a QqTOF-MS                                                               | Both positive and negative ionization mode                                                      | (Vaclavik and Krynitsky 2014)                                             |
| Determining the active component in several drugs/pharmaceuticals        | AccuTOF-DART (JEOL, Peabody, MA) and DART Ion Source (IonSense, USA)                                | Positive ionization mode                                                                       | (Ropero-Miller and Stout 2007; Howlett and Steiner 2011; Lesiak and Cody 2014; Chernetsova and Bochkov 2010) |
|                                                                           | DART-SVP100™ Ion Source (IonSense, USA) and JMS-T100LP AccuTOF (JEOL, Peabody, USA)                | Positive ionization mode                                                                       | (Likar and Cheng 2011)                                                   |
|                                                                           | AccuTOF-DART-MS (JEOL, Peabody, MA) and DART-SVP™ Ion Source (IonSense, USA)                        | Positive ionization mode                                                                       | (Lesiak and Musah 2013; Musah and Cody 2014; Kuki and Nagy 2015)          |
|                                                                           | DART-SVP100™ Ion Source (IonSense, USA) and JMS-T100LP AccuTOF (JEOL, Peabody, USA)                | Positive ionization mode                                                                       | (Easter and Steiner 2014; Samms and Jiang 2011)                           |
|                                                                           | TD-DART-MS interfaced to a JMS-T100LP AccuTOF (JEOL, Peabody, USA)                                 | Positive ionization mode                                                                       | (Sisco and Verkouteren 2017)                                             |
|                                                                           | JMS-T100LP AccuTOF (JEOL USA, Peabody, MA) connected to DART-SVP™ Ion Source (IonSense, USA), along with TD-MS | Both positive and negative ionization mode                                                      | (Robinson and Sisco 2018)                                                |
| Identifying drug residuals on surfaces bearing fingerprints or from fluid matrices | DART-SVP100™ Ion Source (IonSense, USA) and JMS-T100LP AccuTOF (JEOL, Peabody, USA)                | Both positive and negative ionization mode                                                      | (Bennett andSteiner 2009; Sisco andNajarro 2018)                         |
|                                                                           | A DART® ion source (IonSense, USA) interfaced to AccuTOF® 100 TOF-MS (JEOL, Peabody, USA)         | Positive ionization mode                                                                       | (Grange and Sovocool 2011)                                               |
|                                                                           | SALDI-MS using an AXIMA TOF-MS  (Shimadzu Pvt. Ltd.) API source from DART Ion Source (IonSense, USA) and JMS-T100LP AccuTOF (JEOL, Peabody, USA) | Positive ionization mode                                                                       | (Lim and Rowell 2013)                                                   |
| Application                          | Technique                                                                 | Ionization mode in DART source | Reference                                           |
|-------------------------------------|---------------------------------------------------------------------------|--------------------------------|-----------------------------------------------------|
| Identifying marker compounds in herbal drugs | AccuTOF-TLC single-reflection TOF-MS (JEOL, Peabody, USA) equipped with a DART Ion Source (IonSense, USA) | Positive ionization mode          | (Kim and Jee 2010; Moore and Garvin 2017)           |
|                                     | AccuTOF-DART-MS (JEOL, Peabody, USA) configured with a DART-SVP™ Ion Source (IonSense, USA) | Positive ionization mode        | (Lesiak and Musah 2014)                             |
|                                     | 6520 Accurate Mass quadrupole TOF-MS (Agilent Technologies, USA) equipped with a DART SVP™ Ion Source (IonSense, USA) | Positive ionization mode        | (Wang and Li 2014)                                 |
|                                     | DART Ion Source (IonSense, Japan) coupled to a JMS-T100TD TLC-TOFMS      | Positive ionization mode        | (Jang 2009)                                       |
| Analysis of sexual lubricants       | AccuTOF-DART (JEOL, USA)                                                  | Positive ionization mode        | (Musah and Cody 2012)                               |
|                                     | DART Ion Source (IonSense, USA) and JMS-4000LC AccuTOF (JEOL, JAPAN)     | Both positive and negative ionization mode | (Maric and Bridge 2016)                           |
|                                     | DART-SVP100™ Ion Source (IonSense, USA) and 4G LC- plus AccuTOF (JEOL, Peabody, USA) | Positive ionization mode        | (Maric and Harvey 2017)                            |
|                                     | DART Ion Source (IonSense, USA) and JMS-4000LC AccuTOF (JEOL, JAPAN)     | Both positive and negative ionization mode | (Moustafa and Bridge 2017)                        |
|                                     | DART-100 Ion Source (IonSense, USA) and AccuTOF (JEOL)                   | Both positive and negative ionization mode | (Proni and Cohen 2017)                            |
|                                     | DART-SVP Ion Source (IonSense, USA) and JMS-4000LC AccuTOF-LP 4G (JEOL, JAPAN) | Both positive and negative ionization mode | (Baumgarten and Marić 2018)                       |
|                                     | AccuTOF-DART (JEOL, USA) HRMS with resolving power of 6000 FWHM (full width at half maximum) | Positive ionization mode        | (Coon and Beyramysoltan 2019)                      |
|                                     | DART-SVP Ion Source (IonSense, USA) and JMS-4000LC AccuTOF-LP 4G (JEOL, JAPAN) | Positive ionization mode        | (Bridge and Marić 2019)                            |
### Table 5  Experimentally found LOD for various drug samples spiked with methanol in different matrices

| Drug category                                                                 | Compound                        | Approx. LOD  | Ionization mode in DART source |
|-------------------------------------------------------------------------------|---------------------------------|--------------|---------------------------------|
| 1. Cocaine and its metabolites from urine (Jagerdeoa and Abdel-Rehim 2009)   | Ecgonine methyl ester (EME)      | 22.9 ng/mL   | Positive ionization mode        |
|                                                                                | Benzoylecgonine (BZE)            | 23.7 ng/mL   |                                  |
|                                                                                | Cocaine (C)                      | 4.0 ng/mL    |                                  |
|                                                                                | Coca ethylene (CE)               | 9.8 ng/mL    |                                  |
| 2. Anti-diabetic drugs (Zhou and Zhang 2011)                                  | Metformin                       | 100 ng/mL    | Positive ionization mode        |
|                                                                                | Nateglinide                      | 100 ng/mL    |                                  |
|                                                                                | Gliclazide                       | 20 ng/mL     |                                  |
|                                                                                | Rosiglitazone                    | 20 ng/mL     |                                  |
|                                                                                | Glibenclamide                    | 1000 ng/mL   |                                  |
|                                                                                | Glipizide                        | 500 ng/mL    |                                  |
|                                                                                | Gliquidone                       | 200 ng/mL    |                                  |
| 3. Codeine and its derivatives (Howlett and Steiner 2011)                     | Oxycodone                        | 0.3 mg/mL    | Positive ionization mode        |
|                                                                                | Hydrocodone                      | 0.7 mg/mL    |                                  |
|                                                                                | Codeine                          | 0.5 mg/mL    |                                  |
| 4. Opioids (Lim and Rowell 2013)                                              | 6-MAM                            | 200 ng       | Positive ionization mode        |
|                                                                                | Heroin                           | 1000 ng      |                                  |
|                                                                                | Methadone                        | 2 ng         |                                  |
|                                                                                | Nicotine                         | 20 ng        |                                  |
|                                                                                | Noscapine                        | 20 ng        |                                  |
| 5. Nicotine (Kuki and Nagy 2015)                                              | Nicotine                         | 0.1 ng/cm2   | Positive ionization mode        |
| 6. Date rape drugs (Chen and Hsu 2016)                                        | p-Chloroamphetamine              | 1404 ng/mL   | Positive ionization mode        |
|                                                                                | 4-Fluoromethamphetamine         | 112 ng/mL    |                                  |
|                                                                                | Ketamine                         | 527 ng/mL    |                                  |
|                                                                                | Methyline                        | 20 ng/mL     |                                  |
|                                                                                | 3,4-Methylenedioxyxypyrvalerone  | 100 ng/mL    |                                  |
|                                                                                | p-Methylcathinone                | 50 ng/mL     |                                  |
|                                                                                | Methamphetamine                 | 65 ng/mL     |                                  |
|                                                                                | Nimetazepam                      | 153 ng/mL    |                                  |
|                                                                                | γ-Hydroxybutyrate                | 703 ng/mL    | Negative ionization mode        |
Table 5 (continued)

| Drug category | Compound | Approx. LOD | Ionization mode in DART source |
|---------------|----------|-------------|-------------------------------|
| 7. Fentanyl and Fentanyl analogues (synthetic opioids) (Sisco and Verkouteren 2017) | Acetyl Fentanyl | 0.222 ng | Positive ionization mode |
|  | Acryl Fentanyl | 0.145 ng |  |
|  | Benzyl Fentanyl | 0.0864 ng |  |
|  | Butryl Fentanyl | 0.140 ng |  |
|  | Carfentanil | 0.197 ng |  |
|  | Cyclopentyl Fentanyl | 0.165 ng |  |
|  | Despropionyl Fentanyl | 0.160 ng |  |
|  | Fentanyl | 0.142 ng |  |
|  | ortho-Fluorobutyryl Fentanyl | 0.296 ng |  |
|  | para-Fluoroisobutyryl Fentanyl | 0.351 ng |  |
|  | Furanyl Fentanyl | 0.199 ng |  |
|  | β-Hydroxythiofentanyl | 0.292 ng |  |
|  | Isobutyryl Fentanyl | 0.183 ng |  |
|  | 4-Methoxy Butyryl Fentanyl | 0.101 ng |  |
|  | 4-Methoxy Fentanyl | 0.262 ng |  |
|  | trans-3-Methyl Fentanyl | 0.144 ng |  |
|  | Valeryl Fentanyl | 0.0807 ng |  |
|  | Buprenorphine | 0.473 ng |  |
|  | Heroin | 2.55 ng |  |
|  | Methadone | 0.0529 ng |  |
|  | Naloxone | 0.0930 ng |  |
| 8. Rodenticides (Robinson and Sisco 2018) | Brodifacoum | 14.8 ng | Positive ionization mode |
|  | Bromadiolone | 24.6 ng |  |
|  | Chlorophacinone | 81.0 ng |  |
|  | Difenacoum | 4.7 ng |  |
|  | Diphacinone | 12.9 ng |  |
|  | Pindone | 15.0 ng |  |
| 9. Benzodiazepines (Jones and Sisco 2020) | Alprazolam | 0.2 ng | Positive ionization mode |
|  | Bromazepam | 0.50 ng |  |
|  | Clonazolam | 1.00 ng |  |
|  | Deschloroetizolam | 0.10 ng |  |
|  | Diclazepam | 0.10 ng |  |
|  | Estazolam | 0.20 ng |  |
|  | Etizolam | 0.10 ng |  |
|  | Flunitrazepam | 0.10 ng |  |
|  | Lorazepam | 1.00 ng |  |
|  | Midazolam | 0.10 ng |  |
|  | Nimetazepam | 0.10 ng |  |
|  | Oxazepam | 0.50 ng |  |
|  | Temazepam | 0.2 ng |  |
|  | Zolazepam | 0.05 g |  |
Table 6  Applications of varied Explosive compounds, the type of mass analyzer and the Ionisation mode used for their analysis

| Application                                                                 | Mass analyzer                                                                 | Ionization mode in DART source        | Reference                        |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|---------------------------------------|-----------------------------------|
| To study the ionization mechanism of LC/NI-APPI-MS by NI-DART               | JMS-T100LC orthogonal TOF-MS (JEOL, Peabody, USA)                              | Negative ionization mode              | (Song and Dykstra 2008)           |
| Detection of organic nitrate and peroxide based explosive compounds, produced by negative mode and positive mode, respectively using helium gas and dopant additions | AccuTOF-DART-MS                                                                | Both positive and negative ionization mode | (Nilles and Connell 2010)       |
| Direct examination of pre- and post-blast residues from various surfaces like metals, wood, glass, foam, asphalt, tape, polymer/metal wires, batteries, synthetic skin substrate, etc. | AccuTOF-DART-MS, JMS-T100LP AccuTOF (JEOL, Peabody, USA) along with a Vapur® API interface Ion Source (IonSense, USA) | Both positive and negative ionization mode | (Sisco and Forbes 2015)        |
| Detection of nitro-organic and peroxide explosives from the residue due to finger contact | Thermo LTQ XL mass spectrometer coupled with DART-SVP™ Ion Source (IonSense, USA) | Positive (HMTD) and negative (TNT, TDB, PETN) ionization mode | (Frazier and Benefield 2020)      |
| Determination of the most efficient experimental parameter for the screening of nitroaromatics, ringed nitro compounds, straight-chain nitro compounds, and peroxide-containing explosives | API Ion Source (IonSense, USA) and a JMS-T100LP AccuTOF (JEOL, Japan) | Positive (TATP) and negative (nitro-organic explosives) ionization mode | (Rowell and Seviour 2012)       |
| Extraction of a single particle from the surface of interest using DART coupled to direct analyte-probed nano-extraction (DAPNe) | DART Ion Source (IonSense, USA) and JMS-T100LC AccuTOF (JEOL, Peabody, MA) | Positive ionization mode              | (Clemons and Dake 2013)          |
| Detection of explosive residues, from surfaces and within solutions         | DART Ion Source (IonSense, USA) and JMS-T100LC AccuTOF (JEOL, Peabody, MA)     | Both positive and negative ionization mode | (Swider 2013)                    |
| Impact of humidity on the DART-MS ion abundance                            | DART-SVP™ Ion Source (IonSense, USA) with an LTQ Orbitrap XL mass spectrometer (Thermo Fisher Scientific, USA) | Positive ionization mode              | (Newsome and Ackerman 2014)      |
| Detection and desorption efficiency of the explosive and its precursor from a Teflon substrate | JEO AccuTOF LC-plus JMS-T100LP TOF-MS (JEOL, Peabody, MA) coupled with a Vapur® API interface Ion Source (IonSense, USA) | Both positive and negative ionization mode | (Sisco and Forbes 2015)         |
| Scanning signatures of nitrate ester explosives in the presence of confounding sugar alcohol precursors and partially-nitrated or dimerized by-products | LC-plus JMS-T100LP AccuTOF (JEOL, Peabody, USA) coupled with a Vapur® API interface Ion Source (IonSense, USA) | Both positive and negative ionization mode | (Sisco and Forbes 2015)         |
| DART-MS coupled with Raman spectroscopy to produce orthogonal signatures from ammunitions like grenades, and rockets | DART-SVP™ Ion Source (IonSense, USA) interfaced to LTQ-Orbitrap XL mass spectrometer (Thermo Scientific, USA) in combination with Raman microscopy | Both positive and negative ionization mode | (Bridoux and Schwarzenberg 2016) |
| Application                                                                 | Mass analyzer                                                                 | Ionization mode in DART source              | Reference                                      |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|---------------------------------------------|-----------------------------------------------|
| Enhancement of compound (2,4,6-trinitrotoluene) identification using DART-MS and isotope pattern matching | JMS-T100LP AccuTOF (JEOL, Peabody, USA) with a DART Ion Source (IonSense, USA) | Negative ionization mode                     | (Liu and Sun 2016)                            |
| Detection of nitrate-, chloride-, and perchlorate-based oxidizers by distinguishing the regimes of vapor generation and thermal decomposition | DART Ion Source (IonSense, USA) with a Vapur hydrodynamic-assist interface (IonSense) and orthogonal JMS-T100LP AccuTOF (JEOL, Peabody, USA) | Both positive and negative ionization mode   | (Forbes and Sisco 2017)                       |
| Use of IRTD coupled with DART-MS for analysis of wipe-based samples by the aid of elevated heating | IRTD-DART-MS with JMS-T100LP AccuTOF (JEOL, Peabody, USA) | Both positive and negative ionization mode   | (Forbes and Sisco 2018)                       |
| Use of nitrogen as the ionization gas | IRTD-DART-MS | Both positive and negative ionization mode | (Forbes and Sisco 2018) |
| Examination of post-blast residues from peroxide-based homemade explosives | DART-SVP™ Ion Source (IonSense, USA) coupled to a Q Exactive™ (Orbitrap) mass spectrometer (Thermo Fisher Scientific, USA) | Positive ionization mode                     | (Black and D’Souza 2019; Black 2019)          |
| Use of wipe sampling with dry cotton swabs for the analysis of post-blast debris produced superior results | DART-SVP™ Ion Source (IonSense, USA) coupled to a Q Exactive™ (Orbitrap) mass spectrometer (Thermo Fisher Scientific, USA) | Positive ionization mode                     | (Black and D’Souza 2019)                      |
| Screening of the post-blast debris from polymer materials by the use of multivariate statistics and Kendrick mass defect analysis tool | Linear trapping quadrupole 161 (LTQ)-Orbitrap XL mass spectrometer (Thermo Fisher Scientific, Waltham, USA) | Positive ionization mode                     | (Gaiffe and Cole 2019)                        |
| Systematic analysis of explosives with helium gas using TD-DART | DART Ion Source coupled to Agilent 6520 Q-TOF mass spectrometer by a Vapur® hydrodynamic assist interface (IonSense, USA) | Both positive and negative ionization mode   | (An and Liu 2019)                             |
| Characterization of sampling introduction platforms which can be coupled to DART-MS | Thermo LTQ XL mass spectrometer coupled with DART-SVP™ Ion Source (IonSense, USA) | Positive (HMTD) and negative (TNT, TDX, PETN) ionization mode | (Frazier and Benefield 2020)                  |
| Analysis of screen wipe samples of seized packages by IRTD-DART-MS | Capillary electrophoresis (CE)-based inorganic oxidizer detector and (IRTD glass-mica bottom plate (Hereaus-Nobelight America, USA) coupled with DART-MS | Negative ionization mode                     | (Bezemer and Forbes 2020)                     |
• Corroborating the wound with the firearm
• The firing was from which firearm
• The suspect fired the firearm or, was it implanted
• Mode of death; suicide, homicide or, accident
• Range of firing, etc.

DART-MS has been used to detect the analytes used in the propellant mixture, ammunition, IED’s, etc. the sample obtained generally includes unburned, partially burned, and completely burned residues (Table 7).

**Chemical warfare agents**

Chemical warfare agents are weapons of mass destruction as they can cause several casualties. Due to their fatal effect, it is essential to detect these chemicals. These chemical agents are designed specifically for a particular purpose. Their use intends to harass or kill their target in mass. Grouping of the warfare agents is according to the intent of use and the effect caused on the target. Studies on several constituents of the nerve agents and the blistering agents have been conducted (Cody and Lamarée 2005). The practicability of applying DART to detect chemical warfare agents, especially on DMMP, the chemical stimulant of sarin gas, is being established by conducting scientific studies in this field (Table 8).

**Fire debris, ignitable liquids, and flammable solvents**

Fire is a product of the rapid oxidation of fuel with the release of heat and energy. To sustain the fire, three parameters, namely fuel, heat, and oxygen, must be present for the chemical reaction to proceed. Together, they form the “fire triangle.” Fuel is the solid/liquid/gaseous substance that burns. Heat is required to start the chemical reaction, whereas oxygen makes use for the combustion of fuel. Depending on the intent, fire may be natural, accidental, or arson. The analysis of the type of fire debris, ignitable liquids, and flammable solvents recovered from the crime scene aids in determining the intent behind the fire. Due to their volatile nature, the analysis of these compounds is traditionally by SPME followed by GC-MS. But their lengthy protocol has recently led to the use of DART-MS as an alternative method for screening these compounds. This modern technique is fast, easy to perform, and compatible with the existing extraction methods (Pavlovich and Musselman 2016).

The following are a few studies done on the compounds of this class (Table 9).

**Inks, dyes, and paint**

Coloring agents like inks, dyes, and paints are derived when the light spectrum interacts with the light receptors in the eye. These colored substances may be present on the crime scene as trace evidence. Thus, corroborating of the suspect’s presence at the crime scene. Further, being trace evidence, the requirement for the analysis is only of a minute quantity. This examination may also help in individualizing the sample by comparing it with particular control samples. The cases of quality control and assurance also utilize the screening of pigments for investigation purposes. In document analysis, characterization of inkjet inks based on the semi-volatile polymeric differentiated the inks from different cartridges even from the same manufacturer (Williamson and Raeva 2016). DART-MS has a unique ability to detect both organic pigments as well as the compounds within these matrices (Sisco and Forbes 2021). The major advantage of this technique is the minimum risk of damage to the sample surface as it is an indestructible method of analysis (Pavlovich and Musselman 2016). Organic pigments from vehicle paints were screened rapidly by FTIR and further confirmed with DART-MS without requiring any complex sample preparation (Chen and Wu 2017). In 2016, Trejos and Torrione (2016) undertook the formation of an Ink database containing data from various techniques, using the MassHunter Workstation Software Qualitative Analysis (v.B.05.00; Agilent, USA). The following are a few studies done on the compounds of this class (Table 10).

**Miscellaneous**

DART-MS has its utilization in other domains than already mentioned. DART has been used for the direct analysis of active ingredient molecules from ointments/gels from human skin (Williams and Patel 2006). A TSQ Quantum Ultra AM (Thermo Finnigan, USA) triple quadrupole API mass spectrometer, employed for analyzing fragrances from smelling strips (Jeckelmann 2007). A TSQ 7000 triple-quadrupole instrument (Thermo Finnigan) detected the flavors of raw materials (Jeckelmann 2007). Galaxolide, a long-lasting fragrance compound used in shampoo, was detected even in single hair strand using DART. Moreover, similar results were obtained for both wet and dry hair samples. Thus, establishment of standard sample library could aid in semi-quantitative analysis of hair samples (Jeckelmann 2007). In 2010, DART-MS monitored a reaction between ricin and DNA using AccuTOF (JEOL, Peabody, USA) mass spectrometer (Bevilacqua and Nilles 2007). In 2010, DART-MS monitored a reaction between ricin and DNA (Jeckelmann 2007). In 2010, DART-MS monitored a reaction between ricin and DNA using AccuTOF (JEOL, Peabody, USA) mass spectrometer (Bevilacqua and Nilles 2010). Using DART, Zhou et al. developed a protocol for rapid serum metabolic profiling which could reveal the underlying causes of metabolic disorders (Zhou and McDonald 2010). Further studies on metabolic profiling of blood sera revealed the diagnosis of ovarian cancer with high accuracy (Zhou and Guan 2010). In 2011, eight UV filters and four parabens from cosmetic
| Application                                                                 | Mass analyzer                                                                 | Ionization mode in DART source                                           |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Analysis of burned residues of smokeless powders using chemometric (Li 2015) | DART-SVPTM Ion Source (IonSense, USA) interfaced to Thermo-Quest Finnigan LCQ Deca mass spectrometer (San Jose, CA, USA) and Thermo Scientific Exactive Plus mass spectrometer (Thermo Fisher Scientific, USA) | Both positive and negative ionization mode                               |
| Characterization of smokeless powder utilizing sorbent-coated wire mesh which improved the swabbing or vacuum collection (Li 2015; Li and Tice 2016) | DART-SVP™ Ion Source (IonSense, USA) interfaced to Thermo-Quest Finnigan LCQ Deca mass spectrometer (San Jose, CA, USA) and Thermo Scientific Exactive Plus mass spectrometer (Thermo Fisher Scientific, USA) | Negative ionization mode for nitro-organics and positive ionization mode for additives like diphenylamine |
| Detection of components of gunpowder and identification of polymer compounds from 3D printed firearms (Black and Cody 2017) | AccuTOF 4G LC-plus (JEOL, Peabody, USA)                                      | Positive ionization mode                                               |
| Analysis of smokeless powders and its comparison using GC-MS and DART-MS (Lennert and Bridge 2018) | AccuTOF 4G LC-plus (JEOL, Peabody, USA) coupled with DART-SVP™ Ion Source (IonSense, USA) | Both positive and negative ionization mode                               |
| Examination of smokeless powders and gunshot residues by capillary micro-extraction of volatiles dynamic air sampling device (Williamson and Gura 2018) | 6530 Q-TOF MS (Agilent, USA) coupled to DART-SVP™ Ion Source (IonSense, USA) | Positive and negative ionization mode at 250 °C and 200 °C respectively |
| Analysis of smokeless powders using thermal desorption (Lennert and Bridge 2019) | AccuTOF 4G LC-plus (JEOL, Peabody, USA) coupled with DART-SVP™ Ion Source (IonSense, USA) with TD attachment and VAPUR® interface | Both positive and negative ionization mode                               |
| Differentiation of black powders and their substitutes from wipe-based collections (Forbes and Verkouteren 2019) | IRTD unit (twin tube near-infrared emitter (Heraeus Noblelight America, USA), coupled to DART-SVP™ Ion Source (IonSense, USA) and AccuTOF (JEOL, Peabody, USA) | Negative ionization mode                                               |
Table 8: Applications of various chemical warfare agents along with the type of mass analyzer used for their analysis

| Application                                                                 | Mass analyzer                        | Ionization mode in DART source                          |
|----------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------|
| Detection of nanogram level of VX from various surfaces (Laramee and Dupont Durst 2008) | AccuTOF (JEOL, Peabody, USA)         | Both positive and negative ionization mode              |
| Detection of chemical warfare agent (Agent VX) from a porous concrete surface (Nilles and Connell 2009) | AccuTOF (JEOL, Peabody, USA)         | Both positive and negative ionization mode              |
| Use of DART interfaced to Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry to study DMMP and a related compound (Rummel and Steill 2011) | 6210 TOF-MS (Agilent Technologies, USA) | Both positive and negative ionization mode              |
| Detection of DMMP and other organophosphates using Drift-Tube Ion Mobility Spectrometry (DTIMS) coupled with DART-MS (Harris and Kwasnik 2011) | DART-SVP™ Ion Source (IonSense, USA) | Positive ionization mode                               |
| Dependence of temperature and spatial arrangement on the ion abundance in DMMP using DART-MS (Harris and Falcone 2012) | DART-SVP™100 Ion Source (IonSense, USA) coupled to Q-TOF-MS (Bruker, Germany). | Positive ionization mode                               |

Table 9: Applications of various fire debris, ignitable liquids, and flammable solvents along with the type of mass analyzer used for their analysis

| Application                                                                 | Mass analyzer                        | Ionization mode in DART source                          |
|----------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------|
| Detection of arson accelerants from burnt carpet samples (Blackledge 2007) | AccuTOF (JEOL USA, Inc., Peabody, MA, USA) | Positive ionization mode                               |
| Differentiation by visual inspection and chemometric analysis on a series of five types of gasoline (Davis 2015) | Finnigan LQT mass spectrometer (Thermo Fisher Scientific Inc.) | Positive ionization mode                               |
| Study of the polymeric components of the fuel additives (Barnett and Zhang 2018) | Thermo LTQ XL mass spectrometer coupled with DART-SVP™ Ion Source (IonSense, USA) | Positive ionization mode                               |
| Study of neat ignitable liquids and five contaminated substrates by QuickStrip DART-MS configuration (Barnett 2019; Barnett and Bailey 2019) | Thermo LTQ XL mass spectrometer coupled with DART-SVP™ Ion Source (IonSense, USA) | Positive ionization mode                               |

Table 10: Applications of various inks, dyes, and paints along with the type of mass analyzer used for their analysis

| Application                                                                 | Mass analyzer                        | Ionization mode in DART source                          |
|----------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------|
| Analysis if inks using DART-MS (Jones and Cody 2006)                       | JMS-T100LC TOF-MS (JEOL, USA)         | Positive Ionisation Mode                                |
| Detection of MAAQ from security packs using DART-MS (Laramee and Dupont Durst 2008; Pfaff and Steiner 2011) | JMS-T100LC TOF-MS (JEOL, USA)         | Both positive and negative ionization mode              |
| Study of the effects on ink mass spectra by the paper type used (Jones and McClelland 2013) | JMS-T100LC TOF-MS (JEOL, USA)         | Positive ionization mode                               |
| Differentiation of inkjet printer inks of different manufacturers (Houlgrave and LaPorte 2013) | JMS-T100LC TOF-MS (JEOL, USA)         | Positive ionization mode                               |
| Detection and comparison of MAAQ alone and in fingerprints on a glass slide (Clemons and Dake 2013) | JMS-T100LC TOF-MS (JEOL, USA)         | Positive ionization mode                               |
| classification and differentiation of different printer ink samples (Williamson and Raeva 2016) | 6530 Q-TOF-MS (Agilent, USA) coupled to DART-SVP™ Ion Source (IonSense, USA) | Positive ionization mode                               |
| Comparison of known and questioned samples (Chen and Wu 2017)              | DART-Q-Orbitrap tandem mass spectrometer (Thermo Fisher Scientific, USA) | Positive ionization mode                               |
| Comparison of ballpoint inks using DART-MS and direct sample analysis (Drury and Ramotowski 2018) | JMS-T100LC TOF-MS (JEOL, USA)         | Positive ionization mode                               |
| Comparison of DART-MS to pyGC–MS for a clear coat analysis in automotive paints (Manci and Marano 2018) | IonSense® DART® Ion Source and AccuTOF™ 4G LC-plus mass spectrometer (JEOL, USA) | Positive ionization mode                               |
and skincare products were successfully identified and semi-quantitatively analyzed (Haunschmidt and Buchberger 2011). The residues of atrazine, a widespread herbicide, was detected by direct analysis of an unripe pumpkin skin using DAPCI coupled to linear ion trap mass spectrometer (LIT-MS) (Hajslova and Cajka 2011). Bank security devices, containing 1-methylaminoanthraquinone (MAAQ) and o-chlorobenzylidenemalononitrile (CS), and pepper sprays containing capsaicin were analyzed from fabric matrices containing dried sweat and blood. It was found that the matrices did not cause any interference with the target analyte’s peak (Pfaff and Steiner 2011).

DART-MS was successful in classifying the difference between wood obtained from Red Oak and White Oak. The main advantage was that the sample analysis was within seconds (Cody and Dane 2012). In 2014, Q. Zhang et al. had performed the detection of trace palladium content using DART-MS. Due to the absence of any solvent line, this method minimized cross-contamination and gave good results (Zhang and Bethke 2014).

In 2017, Kern and Crowe (2017) performed the analysis of stains on fabric using DART-HRAM-MS. In this, sample swabs from the stained portion of the suspect’s pants, residue on the ceramic shard, the control chocolate ice cream, and theobromine and caffeine as standards. Further confirmation of tests by LC-MS provided accurate mass information. DART-TOF-MS has also been used to identify the geographic origin of wood at scales. According to the study by Finch and Espinoza (2017), DART-TOF-MS can be used to address wood differences and wood identification at many levels like populations, species, and genera.

The detection by MS is difficult for some compounds as they readily convert to unprotected compounds. Suige et al. analyzed tert-butoxycarbonyl (t-Boc)-protected phenethylamines using DART and sample introduction through a micro-syringe (Sugie and Kurakami 2018). Thermal desorption and pyrolysis coupled with DART-FTMS developed as an analytical method to characterize plastics used in industry, consumer products, and samples from the environment. These experiments eventually revealed rich chemical fingerprints (Zhang and Mell 2019). In 2020, species differentiation from a mixture of larvae developed. This approach utilized DART-HRMS and analyzed aqueous ethanol insect storage suspensions as its samples (Beyramysoltan and Ventura 2020).

Conclusions
DART-MS is one of the newly developed ambient MS ionization techniques. This versatile method has sparked significant interest and opened a gateway for analyzing new applications of a wide variety of samples in the analytical field. The optimization of these techniques with the advantage of high-speed analysis and ease of use will lead to the rapid growth of DART-MS. Areas of rapid screening, quality control, forensic and safety applications, etc. enable this instrument to deal with single compounds or moderately complex mixtures. Further, no requirement of sample preparation aids in the analysis of several samples. The specific determinant for determining the output is the compound class and the instrumental factors.

The domain of forensic science deals with an enormous variety of samples ranging from drugs, explosives to chemical warfare agents to paints, inks, and dyes. These samples are usually not present in abundant quantities. Moreover, the result of these samples plays a very crucial role in the criminal justice system. Thus, it is essential to ensure an accurate analysis. Further, no-hassle sample preparation for DART-MS considerably reduces the chance of sample wastage and saves the sample for re-examination as well. Since 2005, several efforts in this place are now underway. There is the formulation of libraries of spectra for drugs of abuse, explosives, pigments, and other species of forensic relevance. As drugs are the most common evidence, the review focuses on the LOD values of some of the most common drug samples. The LOD value table (Table 5) is a compilation of data over the years. As discussed earlier, the low work power and high workload ratio prevail in Forensic Science Laboratories. Thus, emphasizing rapid screening of commonly seized drugs will save ample time. The LOD values obtained from the qualitative screening of street drugs were of ppb level, indicating high sensitivity of DART-MS. Also, the ionization of most of the samples was in the positive mode. The use of HRMS or LRMS system in positive or negative mode was highly dependent on the type of analyte. Drugs, inks, dyes, and paints were mainly analyzed using the positive ionization mode in the HRMS technique. The examinations of fire accelerants predominantly used the positive ionization mode in the LRMS technique. The experiments on gunshot residues and chemical warfare agents primarily used the HRMS technique. But there was no specific ionization mode observed. The explosives samples analyzed used less of the negative-ionization mode, with no such trend in the MS technique.

While detecting a specific analyte in samples is the prime focus in many forensic labs, the detection of other compounds is equally valuable. The hyphenation of DART with various other techniques makes it highly selective. The hyphenation of planar chromatography with DART-MS is a promising technique for analyzing complex liquids like blood and drink samples. The tuning
of various parameters like experimental factors, solvents, systems, or gas ion sources for HPTLC-DART-MS will enhance the outcome of the analysis. IRTD-DART-MS and TD-DART-MS are other hyphenated techniques having huge research potential in both fundamental and applied analytical chemistry. Presently the competing instruments used in labs are GC/MS or LC/MS. They are more sensitive to DART. For optimization of the DART-MS, the sample can be preconcentrated to enhance the analyte concentration. Although DART-MS has yet not replaced other well-established techniques, DART-MS holds a promising future and has the potential of being the workhorse in almost all analytical laboratories, especially in the field of forensic science.

**Future perspective of DART-MS**

The forensic applications of DART-MS are ever-expanding. Deliberate efforts toward the expansion of the applications of DART-MS will ultimately broaden its horizon. One of the most important works is to check for the reliability and usage of DART-MS while working on real cases. With the collaborative efforts of researchers and forensic experts, we can cross this bridge. Thus, the utility of this technique can be successfully measured and used to its full potential.

The focus is required to find the appropriate gas source to be used in DART-MS. Laboratories are investigating an ideal gas by switching from helium to nitrogen, argon (Dane 2016; Yang and Wan 2013), or even air (Brown and Oktem 2016). This apparent shift needs to be studied intensively to ensure proper detection of the sample without affecting its sensitivity. Determining the most suitable extraction process and the effects of adulterants are a few areas to accomplish. Analyzing the desired compound of interest from different matrices to ascertain its stability for a given time will add a time dimension to DART-MS. This technique may then aid in becoming a confirmatory tool rather than just a screening process. Determining the best packaging material by exploiting rapid surface screening and examining the influence of transference of sample residue is yet another future application of DART. An illustration by Newsome et al. demonstrated analysis of samples meters away using an extended capillary on the inlet of the spectrometer. Forensic applications may also use this scheme when large sample areas are analyzed (Sisco and Forbes 2021).

Further work on comparative studies of various mass spectrometers for their efficient use for particular analytes will determine the most appropriate spectrometer. Moreover, comparative studies of mass spectrometers for their efficient analyte-specific use will establish the most appropriate spectrometer. Creating an extensive resource base, providing forensic chemists with access to training materials, validated methods, optimum operating procedures, and documentary standards will eventually lead to increased adoption of DART-MS. DART-MS being a rapid analytical technique with minimum to no sample preparation can be used directly on the crime scene for evidence evaluation. Thus, research on enhancing the portability of the instrument while maintaining its sturdiness will be beneficial. At present, several barriers to the large-scale adoption of this technique exist. Extensive research and advancement in better analysis tools, creation of universally available data library, availability of validation documents, and relevant material for training will certainly open the doors of this high potential analytical technique.

**Abbreviations**

ABS: Acrylonitrile Butadiene Styrene; API: Atmospheric-pressure ionization; APPI: Atmospheric pressure photoionization; ASAP: Atmospheric pressure solids analysis probe; CE: Capillary electrophoresis; CID: Collisionally induced dissociation; CMV: Capillary micro-extraction of volatiles; DAPCI: Desorption atmospheric pressure chemical ionization; DAPNe: Direct analyte-probed nano-extraction; DAPPI: Desorption atmospheric pressure photoionization; DART-MS: Direct analysis in real-time mass spectrometry; DBDI: Dielectric barrier discharge ionization; DESSI: Desorption electrospray ionization; DeSSI: Desorption-sonic spray ionization; DSA: Direct sample analysis; DTIMS: Drift-tube ion mobility spectrometry; EASI: Easy-ambient sonic-spray ionization; ELDI: Electrospray-laser desorption ionization; FT-ICR: Fourier transform-ion cyclotron resonance; FTIR: Fourier transform infrared spectroscopy; FTMS: Fourier transform microwave spectroscopy; GC: Gas chromatography; GSR: Gun-shot residue; HCA: Hierarchical clustering analysis; HESI: Heated-electrospray ionization; HPTLC: High performance thin layer chromatography; HRMS: High-resolution mass-spectrometry; IDE: Improvised explosive device; IR-LADESI: Infrared laser assisted desorption electrospray ionization; IRTD: Infrared thermal desorption; ITX: Isopropylithoxanthone; JHTD: Joule heating thermal desorption; KMD: Kendrick mass defect; LAESI: Laser-ablation electrospray ionization; LA-ICP: Laser ablation inductively coupled plasma; LLOQ: Lower limit of quantification; LOD: Limit of detection; LOOCV: Leave-one-out cross validation; LRMS: Low-resolution mass-spectrometry; LTO: Linear trap quadrupole; MAAQ: Methylaminooanthraquinone; MALDESI: Matrix-assisted laser desorption electrospray ionization; ND-EESI: Neutral-desorption extractive electrospray ionization; NI: Negative ionization; NBOme: N-methoxybenzyl; NMR: Nuclear magnetic resonance spectroscopy; PADI: Plasma-assisted desorption/ionization; PC: Principal components; PCA: Principal component analysis; PETN: Pentraethythrol tetrantinate; PI: Positive ionization; RDX: Royal demolition explosive; RFA: Random forest analysis; SALDI: Surface assisted laser desorption ionization; SPME: Solid phase micro-extraction; SVP: Standard voltage and pressure; TD: Thermal desorption; THC: Tetrahydrocannabinol; TLC: Thin layer chromatography; TOF-MS: Time of flight mass spectrometry.

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