JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

pubs.acs.org/JAFC
Article

Application of Ambient Ionization Mass Spectrometry for the Screening of Pesticide Contaminants on *Cannabis* Plant Materials

Megan I. Chambers and Walter B. Wilson*

Cite This: *J. Agric. Food Chem.* 2026, 74, 26969−26981
Read Online

ABSTRACT: As ambient ionization mass spectrometry is increasingly used for screening due to its ability to rapidly detect trace-level contaminants, this study developed a direct analysis in the real-time−mass spectrometry (DART-MS) method to investigate pesticides commonly used in *Cannabis* cultivation. While 108/113 pesticides were detected by the DART-MS method, evaluation of instrumental parameters revealed that the positive-ionization mode and a gas temperature of 350 °C were most effective for detecting pesticides. Experiments investigating major pesticide fragments and determining the lowest concentration at which the pesticide could be detected were also performed. Analysis of *Cannabis* plant materials spiked or treated with pesticides during cultivation demonstrated the applicability of this method to actual samples. The results of this study reveal that DART-MS can successfully screen for pesticide residues in *Cannabis* and serve as a qualitative screening tool to inform subsequent quantitative analyses.

KEYWORDS: *Cannabis sativa, pesticide residues, mass spectrometry, DART-MS, screening methods*

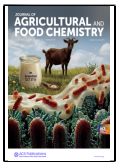
INTRODUCTION

The increase in the decriminalization, legalization, and commercialization of*Cannabis sativa* products in the United States and worldwide has led to a pressing need to increase guidance, regulation, and quality of *Cannabis* products to maintain consumer safety. To help ensure the safety and quality of *Cannabis* products, various properties and characteristics were tested. For example, depending on state regulations, the products may be tested (qualitatively and/or quantitatively) for cannabinoids, terpenes, heavy metals, toxic elements, mycotoxins, residual solvents, and moisture. Pesticides are another class of compounds that are investigated during *cannabis* testing. Pesticides are substances that are commonly used to help maintain the overall health of a plant or crop by preventing or removing certain types of pests (e.g., weeds and predators) that can negatively impact crop quality and yield.[1] *Cannabis* plants are among the myriad of crops that are vulnerable to pests and often treated with pesticides. However, pesticides, especially those that are more persistent, can negatively impact human health and increase vulnerability to adverse health effects.[2] Some examples of adverse effects from pesticides include carcinogenicity, endocrine disruption, reproductive toxicity, developmental toxicity, neurological disorders, acute toxicity, and respiratory health problems.[3−5] Research studies focused on identifying and understanding these adverse effects help define the maximum residue limits (MRLs) and action levels (i.e., the recommended levels that should not be exceeded) for different pesticides and contaminants of concern. This is ultimately aimed at improving the quality and safety of *Cannabis* products and minimizing human health impacts when pesticide use is not properly regulated, administered, or controlled.[1]

Strict guidelines have been instituted in countries that have federally legalized the use of *cannabis*, which help ensure the quality, safety, and efficacy of *cannabis* products.[6] For example, because *Cannabis* is legal and regulated at the federal level in Canada, the control of pesticide use is stricter there than in the United States; Canada has established a list of 96 pesticides that must be tested in *Cannabis* products.[7] In the United States, because *Cannabis* is currently federally scheduled as a controlled substance, the regulations regarding which pesticides can be used for *Cannabis* cultivation, and the concentrations at which they remain in finished products, are determined at the state level and can vary between states. This does not take into consideration the pesticides used on *Cannabis* plants and products within the illicit and unregulated markets. The variability in human exposure to pesticide residues is further confounded by potential sources in illicit and unregulated markets that are generally unknown. The challenges of reducing human exposure to pesticides are compounded by the fact that hundreds of pesticides exist, are often present at low concentrations, and can occur in diverse complex matrices (e.g., *cannabis* and derived products), all of which increase the difficulty of analyzing these residues.[8,9]

Pesticides are typically analyzed by gas chromatography (GC) or liquid chromatography (LC) coupled with mass spectrometry (MS) or Raman spectroscopy.[1,10] GC-MS/MS and LC-MS/MS are regarded as the most effective techniques

Received: January 16, 2026
Revised: July 23, 2026
Accepted: August 18, 2026
Published: August 24, 2026



https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

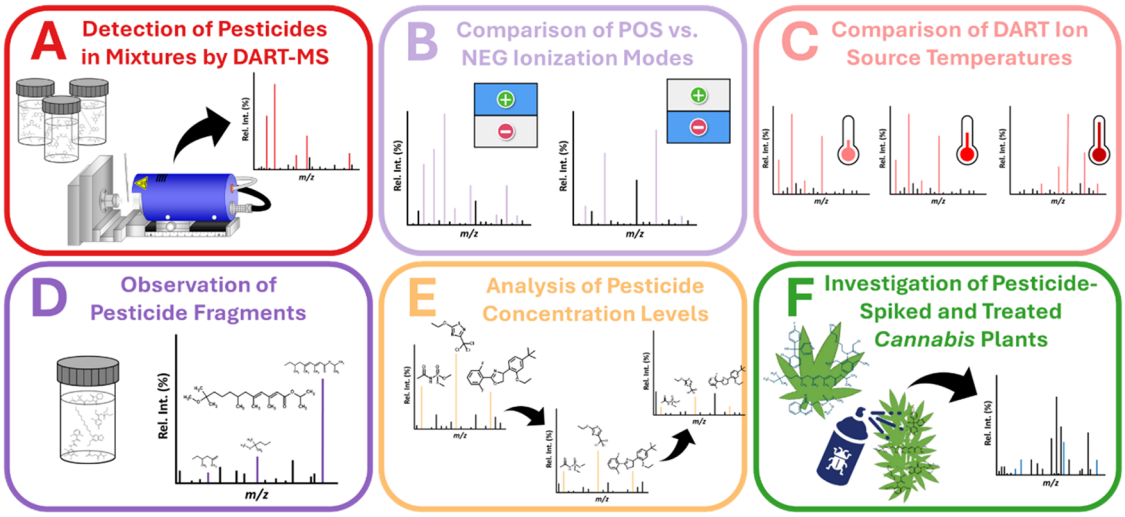


Figure 1. Scheme demonstrating the experimental design for the method development and application (top; purple) and method optimization (bottom; green) portions of the study presented herein: (A) DART-MS analysis of pesticide mixtures; (B) comparison of pesticide DART mass spectra collected in positive- and negative-ionization modes; (C) comparison of the effect DART ion source temperature has on the detection of pesticides; (D) observation of pesticide fragments observed in the DART mass spectra; (E) analysis of pesticide concentrations detectable by the developed DART-MS method the DART-MS; and (F) investigation of *Cannabis* plant materials spiked with pesticide mixtures or treated with pesticides during cultivation.

for the identification and quantification of pesticide residues. Following sample preparation and extraction to produce a solution that can be injected into the system and to remove potential interferences, these techniques have been used to examine a wide variety of food products, including fruits, vegetables, spices, beverages, and animal-derived products.[11−14] [Granados-Povedano 2023] Several studies have used GC-MS, GC-MS/MS, and LC-MS/MS to qualitatively and/or quantitatively examine hundreds of pesticides on *Cannabis* plants and dried flower samples (legal and illicit samples), *Cannabis* oils, concentrates, and hash products.[15−20] One of the features that makes these approaches even stronger is the incorporation of tandem MS/MS or high-resolution mass spectrometry (HRMS). While these techniques can analyze samples for pesticide residues, they can do so only after the time-consuming sample preparation and cleanup steps that render the samples suitable for injection into a chromatographic system.[21] In other words, they do not have the benefit of analyzing a product with no sample preparation and achieving results in just a couple of minutes, if not less. The incorporation of an analytical technology at the front end (i.e., prior to analysis by GC-MS/MS or LC-MS/MS) could provide a significant amount of information including but not limited to, such as an approximate number of pesticides in the sample, the presence of various cannabinoids (both natural and semisynthetic), knowledge about possible coeluting pesticides/compounds, unexpected matrix interferences, and assist with determining samples that need to be submitted for further laboratory testing. With respect to the data output, the benefit of incorporating a high-resolution technique capable of nontargeted analysis (NTA) provides not only comprehensive information at the front end but also offers the capability for retrospective analysis, particularly with the interest toward incorporating machine learning (ML) and artificial intelligence (AI) into data processing procedures, and offers information beyond the identification of known pesticide molecules, such as fragments, metabolites, byproducts, and could reveal the presence of contaminants disregarded by conventional techniques.[22−25] Recent methods demonstrating the advantages of combining HRMS and NTA capabilities for the comprehensive screening of pesticides and other contaminants of concern are leading this area of food/agricultural research.[24,26−28] This information could be provided by performing an extraction and running the extract through a system. However, some techniques offer the added benefit of providing this information without requiring sample preparation. Depending on the type of technology implemented, this information could be available in seconds or minutes.

An example of such technology is direct analysis in real time-mass spectrometry (DART-MS), a type of ambient ionization mass spectrometry (AIMS) technique that has become increasingly popular for rapid analyses and screening on the front end prior to confirmatory methods.[29] AIMS techniques, such as DART-MS, often offer advantages, including minimal to no sample preparation, rapid analysis time, real-time information, the need for only a small amount of sample for analysis, and direct detection of analytes on various surfaces (e.g., pesticides on food and plants).[30] This could be particularly helpful for determining surface concentrations in field-level monitoring of pesticide residues on plant surfaces or for identifying pesticide drift.

The DART system operates by introducing a sample into an open-air gap between the DART ion source and the mass spectrometer inlet, which exposes the sample to a heated, electrically charged stream of metastable gas (usually helium) and, in turn, desorbs and ionizes the sample for analysis by mass spectrometry.[29,31,32] Depending on the carrier gas, proton affinity, and ionization potential of the analyte, and the presence of additives or dopants, ionization mechanisms including protonation, deprotonation, and adduct formation are possible.[29,31,33] This technique has been used in the qualitative and quantitative analysis of pesticides in various food and environmental matrices, particularly to ensure that pesticide concentrations are below levels deemed to be unsafe for human consumption.[32,34−42]

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

DART-MS has been used previously for the detection, quantification, and differentiation of cannabinoids in complex *Cannabis* matrices, including plant materials and derived products.[43−46] Although DART-MS has been used for either pesticide detection or cannabinoid analysis in *Cannabis* materials, no previous study has focused on screening pesticides in *Cannabis* plant materials. Therefore, the study presented herein, summarized in Figure 1, focuses on the development and evaluation of a DART-MS method for rapid analysis of pesticides commonly used in *Cannabis* cultivation. Pesticide mixtures were analyzed to determine the ability of DART-MS to detect m/z values consistent with their protonated $[M + H]^+$ and deprotonated $[M - H]^-$ masses, as well as major fragment peaks, when applicable. All pesticide mixtures were analyzed in positive- and negative-ion modes to determine which mode detected the greatest number of pesticides. In addition, three different gas temperatures were investigated to determine the optimal conditions for detecting the widest range of pesticides. To provide quantitative information, experiments were performed to determine the lowest concentrations of the pesticides that the DART-MS method could detect. Although not a quantitative method, this allowed for comparison to the pesticide action levels recommended by the AOAC for quantitative protocols. Using the approach described, *Cannabis* plant materials were analyzed by DART-MS to test the method. These samples include pesticide-spiked *Cannabis* leaves and *Cannabis* plants cultivated with known pesticides.

MATERIALS AND METHODS

Chemicals and Materials

Pesticide mixtures (CAN-CAN-KIT) were purchased from SPEX CertiPrep (Metuchen, NJ) at nominal concentrations of either 100 μg/mL (Pesticide Mixture 1 to Pesticide Mixture 6) or 1000 μg/mL (Pesticide Mixture 7). All pesticide mixtures were in acetonitrile, except for Pesticide Mixture 6, which was in a 1:1 ratio of acetonitrile to methanol. The 113 pesticides and pesticide isomers in these mixtures are listed in Table S1, which includes the pesticide names, chemical structures, chemical formulas, and their classification (e.g., insecticide, miticide, fungicide). Pierce LTQ Velos ESI Positive and Negative Calibration Solutions were purchased from Thermo Scientific (Waltham, MA). Ultrahigh purity helium (99.999%) gas was obtained from Roberts Oxygen Company (Rockville, MD). Acetonitrile and methanol were purchased from Fisher Scientific (J.T. Baker Brand, Hampton, NH). Phytocannabinoid Mixture 11 was obtained from Cayman Chemical (Ann Arbor, MI), containing the following cannabinoids in acetonitrile: cannabidivarin (CBDV), tetrahydrocannabivarin (THCV), cannabinol (CBN), cannabichromene (CBC), cannabidiol (CBD), Δ^8-tetrahydrocannabinol (Δ^8-THC), Δ^9-tetrahyrdocannabinol (Δ^9-THC), cannabigerol (CBG), cannabidiolic acid (CBDA), tetrahydrocannabinolic acid (THCA), and cannabigerolic acid (CBGA). Several leaf segments were selected from a dried bulk hemp plant material for the experiments involving pesticide-spiked *Cannabis* material. Cuttings from fresh *Cannabis* plants (hemp variety) treated with pesticides were obtained locally from a collaborator and did not undergo any sample preparation prior to analysis by DART-MS. These samples were accompanied by a treatment list with the pesticides and oils used to treat the plants, the dates each treatment was applied, and the reasons/targets for each pesticide. The plants from which the cuttings were obtained are used solely for research purposes and are not available to the public for retail or resale.

Operation of DART-MS Instrument

A DART SVP-201 (standard voltage and pressure) ion source (IonSense Inc., Saugus, MA) coupled to a Q-Exactive Orbitrap Mass Spectrometer (Thermo Fisher Scientific, Waltham, MA) was used for all DART-MS analyses in the current study. A DART Thermo Ion Max Vapur Interface (IonSense Inc., Saugus, MA), positioned between the DART ion source and the mass spectrometer, facilitated ion transfer. DART SVP Software Version 2.4.4.2 was used with a PC-based web interface. The "Free Run" mode gives the operator the ability to directly control the DART ion source and relevant parameters, including system status (i.e., standby with nitrogen gas, run with helium gas), temperature of the DART gas stream, ionization mode (i.e., positive- or negative-ion modes), and the linear rail system, if needed. Ultrahigh-purity helium gas was used at a constant flow rate of 2.29 L/min. The DART gas temperature varied between 250, 350, and 450 °C depending on the experiment. The DART ion source was operated in both positive- and negative-ion modes over a range of m/z 75 to m/z 1125. Additional properties of the mass spectrometer include a resolution of 35,000 (proportional to 1/sqrt (m/z)), an automatic gain control (AGC) target of 3e6 (the number of ions injected into the analyzer), and a capillary temperature of 250 °C. Q-Exactive Tune 2.2 Software was used for instrument setup and operation. Data processing was performed using Foundation 2.0 SP1 and Xcalibur 2.2 SP1.

Acquisition of Mass Spectral Data

The Q-Exactive mass spectrometer was calibrated with calibration solutions to assess mass accuracy on a weekly basis and daily prior to conducting DART-MS experiments, evaluating the lowest levels at which the pesticides could be detected. This ensures that a mass tolerance of 0.004 $\Delta m/z$ (±4 mDa or 0.004 Da) can be used when developing the pesticide screening approach.

All chemical standards and plant samples were analyzed in triplicate during each DART-MS acquisition by using a manual sampling technique. For liquid samples (i.e., pesticide mixtures), the closed end of a melting-point capillary (Corning Incorporated, Tewksbury, MA) was inserted into the sample and presented to the heated DART gas stream for approximately 5 s. This process was repeated two more times during the same DART-MS acquisition, and the replicates were averaged to create a comprehensive chemical profile for each sample. For plant materials, the closed end of the capillary tube was rubbed against either fresh or dried *Cannabis* leaves. After three leaves were sampled during the same DART-MS acquisition, the mass spectral data were averaged to create a single chemical profile representative of the leaves and any pesticides on their surfaces if present. After replicates were averaged, the background was subtracted from a surrounding section of the total ion chromatogram to minimize the background interferences.

Preparation and Analysis of Pesticide Samples

DART-MS analyses were performed on the pesticide standard mixtures at their received nominal concentrations to determine which pesticides were detectable in positive- and/or negative-ion modes at gas temperatures of 250, 350, and 450 °C. Pesticides were reported as detected if either a protonated $[M + H]^+$ mass in positive-ion mode or a deprotonated $[M - H]^-$ mass in negative-ion mode was observed within 0.004 $\Delta m/z$ (±4 mDa or 0.004 Da) of the theoretical mass and had an ion count greater than 500. Pesticides were not reported if a peak consistent with their theoretical mass was not detected or fell outside the mass tolerance window, or if a peak consistent with the theoretical mass was detected but had an ion count below 500.

In the experiments aimed at determining the approximate lowest concentration at which a pesticide could be detected, serial dilutions prepared using the pesticide mixture stock solutions with nominal concentrations of 100 μg/mL (Pesticide Mixtures 1 to Pesticide Mixture 6) or 1000 μg/mL (Pesticide Mixture 7) and were diluted with either acetonitrile (Pesticide Mixtures 1 to Pesticide Mixture 5, and Pesticide Mixture 7) or 1:1 acetonitrile:methanol (Pesticide Mixture 6). The following concentrations were prepared: 100, 10, 1, 0.5, 0.4, 0.2, 0.1, 0.06, 0.05, 0.04, 0.02, and 0.01 mg/L. Calibrated pipettes were used to prepare the serial dilutions because solutions are commonly prepared volumetrically in *Cannabis* testing laboratories. These concentrations were selected based on the action levels

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

reported by the AOAC International Standard Method Performance Requirements (SMPR) 2018.011.[47] These serial dilution solutions were analyzed in positive-ion mode at 350 °C. In addition, because endosulfan sulfate and azadirachtin were detected in negative-ion mode rather than positive-ion mode and were both in Pesticide Mixture 3, this mixture was also included in the experiment and analyzed in negative-ion mode at 350 °C to determine the lowest concentration at which these two pesticides could be detected. For these experiments, to reduce the risk of mistaking background and interferents for pesticide peaks, a mass tolerance of 0.003 $\Delta m/z$ (±3 mDa or 0.003 Da) was used in the DART-MS analyses.

Preparation and Analysis of Pesticide-Spiked *Cannabis* Plant Materials

Pesticide Mixture 1 and Pesticide Mixture 4 were selected as the representative solutions for the experiments that involved spiking the dried *Cannabis* plant material, as outlined in Figure 2. Several leaves

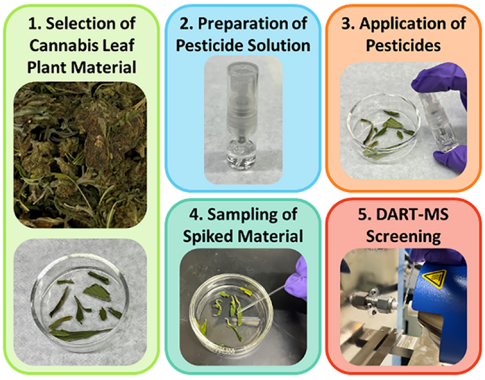


Figure 2. Experimental design for the application of pesticides on *Cannabis* plant material: (1) select several *Cannabis* leaves; (2) prepare the pesticide solution mixtures; (3) spray the pesticides onto the dried leaf material; (4) sample the leaves using a manual capillary tube sampling technique; and (5) screen the samples by DART-MS.

from the bulk material were selected and laid in glass dishes. A set of leaves was prepared for each of the two pesticide mixtures to be tested. Pesticide solutions (nominal 10 μg/mL) were prepared from the stock standards (nominal 100 μg/mL) and deposited into a 2 mL spray bottle for application. Leaves were spiked with the respective solution and allowed to dry for approximately 30 min prior to analysis by DART-MS. Based on the results obtained from the analysis of the pesticide mixture standards, the pesticide-spiked dried hemp plant materials were analyzed by DART-MS in positive-ion mode at a DART gas temperature of 350 °C. Samples were screened in triplicate using the capillary tube sampling approach. With the understanding that the method used to spray the pesticides onto the material in this study is not equivalent to a commercial or industrial sprayer in terms of consistency, we sampled several leaves during the same DART-MS acquisition and average the replicates to address any heterogeneity introduced. Tweezers were not used to present leaf pieces to the DART gas stream due to the fragility of the dried leaf material. Peaks consistent with the high-resolution protonated $[M + H]^+$ masses of pesticides detected in the spiked leaves were compared with those in the respective solutions and detected during the control experiments for the pesticide mixture standards. In addition, high-resolution masses consistent with the protonated masses of cannabinoids were compared with the values obtained during analysis of the 11-Cannabinoid Mixture. The cannabinoids included in the 11-Cannabinoid Mixture were THCV/CBDV ($[C_{19}H_{26}O_2+H]^+$ calc. 287.2006), CBN ($[C_{21}H_{26}O_2+H]^+$ calc. 311.2006), CBC/CBD/Δ^8-THC/Δ^9-THC ($[C_{21}H_{30}O_2+H]^+$ calc. 315.2319), CBG ($[C_{21}H_{32}O_2+H]^+$ calc. 317.2475), CBDA/THCA ($[C_{22}H_{30}O_4+H]^+$ calc. 359.2217), and CBGA ($[C_{22}H_{32}O_4+H]^+$ calc. 361.2373).

Analysis of Pesticide-Treated *Cannabis* Plant Materials

These samples were analyzed by DART-MS using the same instrumental parameters and sampling approach as described above for the pesticide-spiked hemp materials. For the fresh hemp plants, the high-resolution protonated masses of pesticides detected in the plant material by DART-MS were compared to the provided pesticide treatment list. The process of verifying the high-resolution masses of protonated cannabinoids consistent with the 11-cannabinoid mixture was repeated for this experiment.

RESULTS

Analysis of Pesticide Mixtures by DART-MS in Positive-Ion Mode

The results obtained for each of the three different gas temperatures analyzed in positive-ion mode were very similar. The number of pesticides detected (including isomers) was 100 at 250 °C, 104 at 350 °C, and 103 at 450 °C. The differences between the temperatures were the following: (1) a peak consistent with endosulfan I/II was only detected at 350 °C; (2) a peak representative of spinetoram J was only detected at 450 °C; and (3) masses consistent with protonated Spinosad A and D were detected at 350 and 450 °C but not at 250 °C. Figure 3 shows an example of a DART mass spectrum of Pesticide Mixture 4 analyzed in positive-ion mode at 350 °C. In this mixture, 13 of 14 pesticides were detected and are shown as the labeled colored peaks in Figure 3A (m/z 175 to m/z 300) and Figure 3B (m/z 300 to m/z 375). Because positive-ion mode at 350 °C detected the most pesticides, the mass spectra for the remaining pesticide mixtures analyzed under these conditions are shown in Figures S1−S6.

It is interesting to note that only two pesticides with $[M + H]^+$ greater than m/z 700 were detected in positive-ion mode: (1) Spinosad A ($[C_{41}H_{65}NO_{10}+H]^+$ calc. 732.4681) and (2) Spinosad D ($[C_{42}H_{67}NO_{10}+H]^+$ calc. 748.4994). Most pesticides with a theoretical protonated mass greater than m/z 700 were not detected, including azadirachtin ($[C_{35}H_{44}O_{16}+H]^+$ calc. 721.2702), spinetoram J ($[C_{42}H_{69}NO_{10}+H]^+$ calc. 748.4994), spinetoram L ($[C_{43}H_{69}NO_{10}+H]^+$ calc. 760.4994), abamectin (B1b) ($[C_{47}H_{70}O_{14}+H]^+$ calc. 859.4840), and abamectin (B1a) ($[C_{48}H_{72}O_{14}+H]^+$ calc. 873.4995). However, as discussed below, azadirachtin and abamectin B1a were detected in negative-ion mode at certain temperatures.

Analysis of Pesticide Mixtures by DART-MS in Negative-Ion Mode

Although the different gas temperatures used to analyze pesticides in negative-ion mode produced results similar to one another, none yielded better results than those obtained in positive-ion mode. Only 61, 65, and 73 pesticides were detected in negative-ion mode at 250 °C, 350 °C, and 450 °C, respectively, based on their deprotonated masses. There was greater variation in the results between the different gas temperatures. It is worth noting that abamectin B1a, azadirachtin, and endosulfan sulfate were not detected in positive-ion mode at all but were detected in negative-ion mode at one or more of the gas temperature settings.

To provide a visual comparison of the collected data between positive- and negative-ion modes, the DART mass spectra obtained in negative-ion mode at 350 °C for all pesticide mixtures are shown in Figures S7−S12. Table S2 summarizes the results of pesticide DART-MS analysis at 350

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

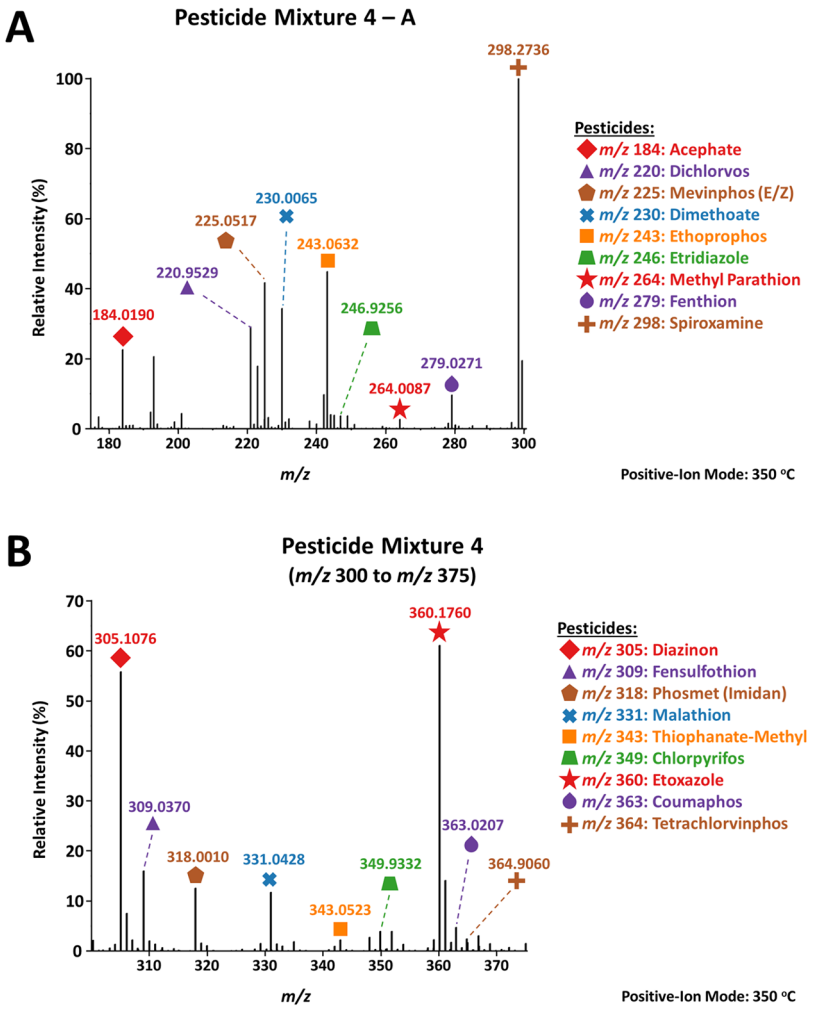


Figure 3. DART mass spectra showing the pesticides detected in Pesticide Mixture 4 when analyzed in positive-ion mode at 350 °C over the mass ranges of m/z 175 to m/z 300 (Panel A) and m/z 300 to m/z 375 (Panel B). The high-resolution peaks consistent with the protonated $[M + H]^+$ masses of pesticides are labeled according to the legends shown to the right of the mass spectra.

°C and whether each was detected in both ionization modes, neither, or only one.

Comparison of DART-MS Ionization Modes

Across the three temperatures, a total of 105 (93%) pesticides were detected in positive-ion mode, while only 77 (68%) were detected in negative-ion mode. Of the 113 pesticides that were analyzed in this study, a total of 108 (96%) were detected by DART-MS in at least one ionization mode at one or more gas temperatures. Figure S13 provides details on each pesticide and whether it was detected at the various gas temperatures in each ionization mode, while a chart summarizing these data is shown in Figure S14.

Only five pesticides were not detected in either positive- or negative-ion modes at any gas temperature used in this study. The five pesticides whose $[M + H]^+$ and $[M\text{-}H]^-$ were not detected in positive- or negative-ion mode, respectively, with their calculated protonated and deprotonated masses were (1) pentachloronitrobenzene, $[C_6Cl_5NO_2+H]^+$ calc. 293.8444, $[M\text{-}H]^-$ calc. not available; (2) piperonyl butoxide, $[C_{19}H_{30}O_5+H]^+$ calc. 339.2170, $[C_{19}H_{30}O_5-H]^-$ calc. 337.2021; (3) etofenprox, $[C_{25}H_{28}O_3+H]^+$ calc. 377.2111, $[C_{25}H_{28}O_3-H]^-$ calc. 375.1966; (4) spinetoram L, $[C_{43}H_{69}NO_{10}+H]^+$ calc. 760.4994, $[C_{43}H_{69}NO_{10}\text{-}H]^-$ calc. 758.4849; and (5) abamectin B1b, $[C_{47}H_{70}O_{14}+H]^+$ calc. 859.4838, $[C_{47}H_{70}O_{14}-H]^-$ calc. 857.4682. The deprotonated mass for pentachloronitrobenzene is reported as "not available" because no proton can be removed from its chemical structure.

Observation of Major Pesticide Fragments

In addition to the detection of peaks consistent with the high-resolution protonated masses of pesticide molecules, protonated major fragment peaks were observed for several pesticides. Previously published studies were used as a starting point to identify fragments associated with the pesticides investigated in the current DART-MS study.[48−50] Fragmentation may occur due to temperature or molecular instability. Based on the results of determining which ionization mode and gas temperature yielded the highest number of detected pesticides, an initial investigation of pesticide fragments was conducted in positive-ion mode at 350 °C, followed by experiments at 250 and 450 °C. Mass spectra collected in negative-ion mode were also checked for major pesticide fragments, but only 9−15 were observed across the various gas temperatures (data not shown).

In positive-ion mode at 350 °C, 45 peaks consistent with the protonated $[MF+H]^+$ masses of known major fragments from 28 pesticides within the various mixtures are presented in Figure S15. This table also includes the fragment chemical formula, calculated $[MF+H]^+$, experimental $[MF+H]^+$, $\Delta m/z$,

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

Table 1. Approximate Lowest Pesticide Concentrations Detected by DART-MS, with Reference to the Lowest Action Level (ppm) Listed by AOAC International.[47]

pesticide	lowest concentration detected by DART-MS (μg/mL)	AOAC lowest action level listed (ppm)	pesticide	lowest concentration detected by DART-MS (μg/mL)	AOAC lowest action level listed (ppm)
abamectin (avermectin B1a)	ND[a]	0.05	imazalil	≤0.01[b]	0.01
abamectin (avermectin B1b)	ND[a]	0.05	imidacloprid	≤0.01	0.01
acephate	≤0.01[b]	0.1	iprodione	≤0.01[b]	0
acequinocyl	0.1	0.1	jasmolin I	0.02	NL[c]
acetamiprid	0.02	0.1	jasmolin II	0.4	NL[c]
aldicarb	≤0.01[b]	0.1	kinoprene	≤0.01[b]	0
allethrin	0.02	0.1	kresoxim-methyl	0.02	0.1
azadirachtin[d]	100	0.1	malathion	≤0.01[b]	0.05
azoxystrobin	≤0.01[b]	0.02	metalaxyl	0.02	0.2
benzovindflupyr	≤0.01[b]	0.1	methiocarb	≤0.01[b]	0.1
bifenazate	0.04	0.01	methomyl	≤0.01[b]	0.4
bifenthrin	1	0.01	methoprene	≤0.01[b]	0
boscalid	0.02	0.1	methyl parathion	≤0.01[b]	0.1
buprofezin	≤0.01[b]	0.1	mevinphos (E/Z)	≤0.01[b]	0.1
carbaryl	≤0.01[b]	0.2	MGK 264 (endo/exo)	≤0.01[b]	0.2
carbofuran	≤0.01[b]	0.2	myclobutanil	≤0.01[b]	0.01
chlorantraniliprole	0.2	0.2	naled (Dibrom)	0.05	0.1
chlorfenapyr	0.04	0.1	novaluron	≤0.01[b]	0
chlorpyrifos	≤0.01[b]	0.1	oxamyl	1	0.5
cinerin I	0.1	NL[c]	paclobutrazol (impurity/cis/trans)	≤0.01[b]	0.05
cinerin II	0.2	NL[c]	pentachloronitrobenzene	ND[a]	0.2
clofentazine	≤0.01[b]	0.1	permethrins (cis/trans)	0.1	0.04
clothianidin	0.04	0	phenothrins (cis/trans D-phenothrin)	≤0.01[b]	0
coumaphos	≤0.01[b]	0.1	phosmet (Imidan)	≤0.01[b]	0.02
cyantraniliprole	0.4	0	piperonyl butoxide	ND[a]	1
cyfluthrin (baythroid)	0.10	0.1	pirimicarb	≤0.01[b]	0
cypermethrins (I–IV)	0.04	0.05	prallethrin	0.02	0.1
cyprodinil	≤0.01[b]	0	propiconazole (I/II)	≤0.01[b]	0.1
daminozide	ND[a]	0.05	propoxur (Baygon)	≤0.01[b]	0.1
deltamethrin	0.2	0	pyraclostrobin	0.04	0
diazinon	≤0.01[b]	0.1	pyrethrin I	0.04	0.5
dichlorvos	≤0.01[b]	0.1	pyrethrin II	0.05	0.5
dimethoate	≤0.01[b]	0.1	pyridaben	0.02	0.1
dinotefuran	0.02	0	resmethrin	≤0.01[b]	0
dodemorph	≤0.01[b]	0	spinetoram (J)	ND[a]	0.1
endosulfan I/II[d]	0.05	0	spinetoram (L)	ND[a]	0.1
endosulfan sulfate[d]	≤0.01[b]	0	spinosad (A)	100	0.06
ethoprophos (prophos)	≤0.01[b]	0.1	spinosad (D)	100	0.06
etofenprox	ND[a]	0.1	spirodiclofen	0.02	0
etoxazole	≤0.01[b]	0.01	spiromesifen	0.02	0.01
etriadiazole (terrazole)	≤0.01[b]	0	spirotetramet	0.02	0.02
fenoxycarb	≤0.01[b]	0.1	spiroxamine	≤0.01[b]	0.1
fenpyroximate (E)	0.02	0.1	tebuconazole (Folicur)	≤0.01[b]	0.01
fensulfothion	≤0.01[b]	0	tebufenozide	0.02	0
fenthion	≤0.01[b]	0	teflubenzuron	0.04	0
fenvalerate (sanmarton)	0.1	0	tetrachlorvinphos	≤0.01[b]	0
fipronil	≤0.01[b]	0.1	tetramethrin	≤0.01[b]	0
flonicamid	≤0.01[b]	0.1	thiacloprid	≤0.01[b]	0.1
fludioxonil	10	0.02	thiamethoxam	0.02	0.05
fluopyram	≤0.01[b]	0	thiophanate-methyl	10	0
hexythiazox	0.02	0.1	trifloxystrobin	≤0.01[b]	0.01

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

Table 1. continued

[a]ND: not detected by the DART-MS method. [b]0.01 was the lowest concentration examined in this study; the actual lowest levels detectable by DART-MS may be less than 0.01 μg/mL. [c]NL: not listed by AOAC SMPR 2018.011. [d]The lowest concentration was detected in negative-ion mode.

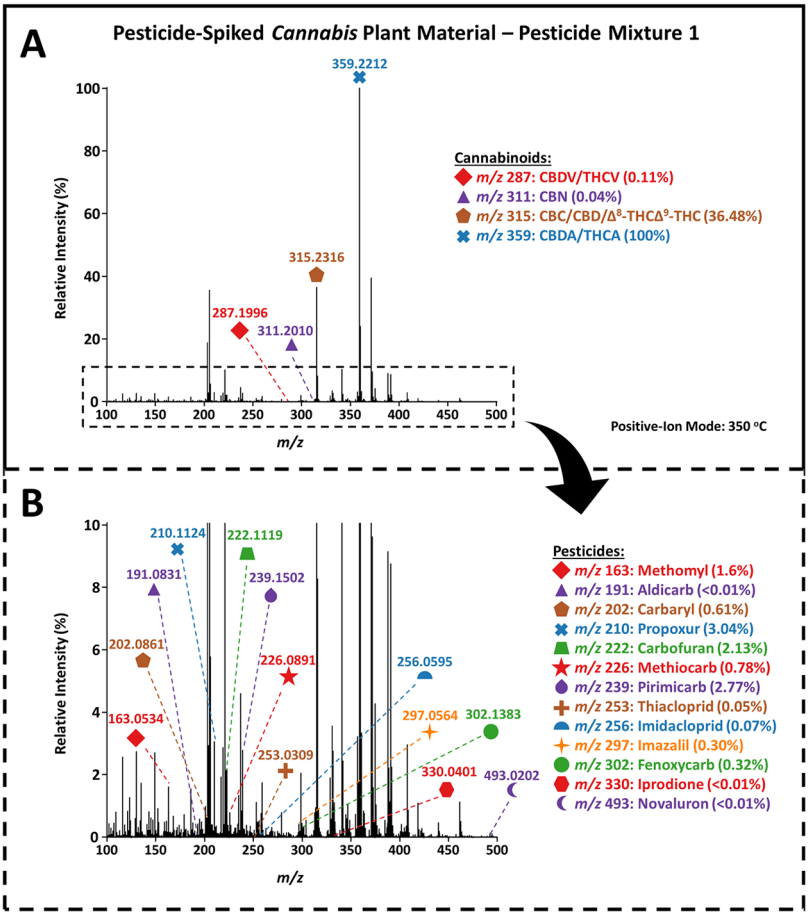


Figure 4. DART mass spectra showing the cannabinoids detected in the dried *Cannabis* plant material spiked with Pesticide Mixture 1 (Panel A) when analyzed in positive-ion mode at 350 °C. The figure also presents the pesticides detected in the sample over a mass range of *m/z* 150 to *m/z* 500 (Panel B). Each of the cannabinoids and pesticides is color-coded and labeled according to the legends shown to the right of the respective mass spectrum.

and the relative intensity of the respective peak. Additional fragments beyond those listed are likely present in the mass spectral data obtained from the DART-MS analysis of the pesticides, but exact fragments associated with individual pesticides, especially those with low *m/z* values, are challenging to identify when evaluated in mixture form.

The protonated mass of a pesticide was observed alongside various protonated fragments in several instances. Figure 16B shows the peak consistent with the protonated $[M + H]^+$ mass of methoprene in Pesticide Mixture 2 at *m/z* 311, with four additional labeled peaks consistent with known protonated fragments at *m/z* 279, *m/z* 237, *m/z* 219, and *m/z* 191. The same was observed for carbaryl and aldicarb in Figure 16A, acephate and mevinphos (E/Z) in Figure 16C, tebufenozide in Figure 16D, and several others not shown in the figure but available in Table S3.

In some cases, fragments were detected under conditions where the protonated pesticide precursor was not. For example, the protonated mass of piperonyl butoxide ($[C_{19}H_{30}O_5+H]^+$ calc. 339.2170) was not detected in positive- or negative-ion mode at 350 °C, possibly due to the peak associated with the protonated mass of resmethrin ($[C_{22}H_{26}O_3+H]^+$ calc. 339.1955) overlapping the peak that would correspond to the protonated mass of piperonyl butoxide. However, as shown in Figure 16B, the protonated major fragment of piperonyl butoxide ($[C_{11}H_{12}O+H]^+$ calc. 177.0910) was detected at *m/z* 177.0911 as the base peak in the mass spectrum for Pesticide Mixture 2.

The mass spectral data collected in positive-ion mode at 250 and 450 °C for each pesticide mixture were also examined to determine whether the pesticide fragments detected at 350 °C were also observed at the other gas temperatures. These results are also shown in Figure S15. Similar results were obtained, with 43 and 44 pesticide fragments detected at 250 and 450 °C, respectively.

Evaluation of Pesticide Concentrations

After determining the ionization mode and gas temperature settings that detected the most pesticides (i.e., positive-ion mode and 350 °C), it was important to try to determine the approximate lowest concentration of the pesticides that the method could detect. These DART-MS settings were used for

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

all pesticides, but the two were detected in negative-ion mode instead. A range of concentrations was prepared and analyzed, from 100 μg/mL (Pesticide Mixture stock solution nominal concentration) to 0.01 μg/mL. Concentrations below 0.01 μg/mL were not evaluated in this study because more accurate results could be obtained by analyzing individual standards rather than pesticide mixtures. In addition to listing the results in Table 1, which indicate the lowest concentration of each pesticide detected by DART-MS, it also includes the Lowest Action Level Listed (in ppm) according to Standard Method Performance Requirements (SMPR) 2018.011 published by AOAC International. It is crucial to note that because the concentrations of the pesticide solutions are in μg/mL, and the AOAC action levels are in ppm of pesticide residues in dried *Cannabis* samples, a direct comparison cannot be made. The concentrations presented here using the developed method are approximate values and, as in the pesticide fragmentation investigation, would benefit from analysis of individual pesticide standards. Some key takeaways include that more than 80% (92 pesticides) were detected at a concentration of 0.1 μg/mL, approximately 75% (86 pesticides) could be detected at 0.05 μg/mL, and that just over half (57 pesticides) were still detected by DART-MS at a concentration of 0.01 μg/mL.

Analysis of Pesticide-Spiked *Cannabis* Plant Material

Based on the results, indicating that DART-MS analyses operated in positive -ion mode at 350 °C detected the most pesticides, all experiments involving the analysis of cannabinoids and *Cannabis* plant materials were conducted in positive-ion mode at 350 °C. Because cannabinoids are an important class of molecules that may cause potential spectral interferences in the DART mass spectra of pesticides in this study, the dried *Cannabis* leaves were first screened and examined for the cannabinoids included in the 11-Cannabinoid Mixture before investigating pesticide residues. The following cannabinoids were detected in the 11-Cannabinoid Mixture DART mass spectrum (Figure S17) with the experimental $[M + H]^+$ and corresponding relative intensity (%): THCV/CBDV at *m/z* 287.2001 (74.89%); CBN at *m/z* 311.2000 (14.40%); CBC/CBD/Δ^8-THC/Δ^9-THC at *m/z* 315.2311 (100%); CBG at *m/z* 317.2479 (11.10%); CBDA/THCA at *m/z* 359.2209 (12.76%); and CBGA at *m/z* 361.2373 (3.50%). Cannabinoids detected in the prespiked *Cannabis* plant material (Figure S18) were CBDV/THCV at *m/z* 287.1978 (0.58%), CBN at *m/z* 311.1987 (0.55%), CBC/CBD/Δ^8-THC/Δ^9-THC at *m/z* 315.2294 (89.47%), and CBDA/THCA at *m/z* 359.2186 (100%). Cannabinoids that have the same $[M + H]^+$ peaks could not be distinguished from each other. The $[M + H]^+$ peaks for CBG and CBGA were not detected in this plant material.

Several leaves from this dried *Cannabis* plant material were selected and spiked with either Pesticide Mixture 1 or Pesticide Mixture 4. The spiked samples were then screened by DART-MS in triplicate (positive-ion mode; 350 °C). The leaves sprayed with Pesticide Mixture 1 were spiked with 14 pesticides, and the leaves sprayed with Pesticide Mixture 4 were spiked with 19 pesticides. Most of the pesticides applied to both sets of leaves were detected: 13 of 14 in Pesticide Mixture 1 and 17 of 19 in Pesticide Mixture 4. The only pesticides that were not detected were oxamyl (Pesticide Mixture 1), etofenprox (Pesticide Mixture 4), and thiophanate-methyl (Pesticide Mixture 4).

During this analysis, the cannabinoid profile of *Cannabis* leaves was reevaluated after spiking. For example, in the leaves sprayed with Pesticide Mixture 1, the following cannabinoids were detected: CBDV/THCV at *m/z* 287.1996 (0.11%), CBN at *m/z* 311.2010 (0.04%), CBC/CBD/Δ^8-THC/Δ^9-THC at *m/z* 315.2316 (36.48%), and CBDA/THCA at *m/z* 359.2212 (100%). These peaks are shown in the mass spectrum of this sample, displayed in Figure 4A. Figure 4B presents the zoomed-in DART mass spectrum acquired when Pesticide Mixture 1 was spiked onto the *Cannabis* plant material. The DART mass spectral data acquired from the analysis of the *Cannabis* leaves spiked with Pesticide Mixture 4 are shown in Figure S19.

Analysis of Fresh Hemp Plant Materials

The cannabinoid content of the fresh *Cannabis* leaves was evaluated by DART-MS, similar to spiked plant material. Detected in this plant material were CBDV/THCV at *m/z* 287.1997, CBN at *m/z* 311.2012, CBC/CBD/Δ^8-THC/Δ^9-THC *m/z* 315.2307, CBG at *m/z* 317.2365, and CBDA/THCA at *m/z* 359.2203. CBGA was also not detected in this plant material.

The cuttings were accompanied by a list of 15 pesticides that had been sprayed on the *Cannabis* plant over the previous several months prior to collection and analysis. The fresh plant samples were screened for pesticides applied within the last 8 weeks; pesticides applied more than 8 weeks prior to testing were assumed to have sufficiently degraded by the time of testing. The developed DART-MS method was used to evaluate the persistence of pesticides on the material based on the application dates provided. Because some pesticides were applied multiple times over the 6-month period, the most recent application date was used to determine how long each pesticide persisted on leaves under the growth conditions. For example, if a pesticide was applied on several different occasions, then only the most recent application date was used during data processing and evaluation. Two of the pesticides applied (pyridalyl and cyflumetofen) were not included in the panel of pesticides for the standard mixtures. Therefore, the mass spectra were screened for high-resolution peaks consistent with the protonated masses of these two pesticides for a tentative assignment.

Ten (10) of the 15 pesticides were detected by DART-MS and are labeled in the mass spectrum presented in Figure S20. The pesticides detected include novaluron (*m/z* 493.0194), chlorfenapyr (*m/z* 406.9765), pyraclostrobin (*m/z* 388.1045), spiromesifen (*m/z* 371.2229), etoxazole (*m/z* 360.1771), boscalid (*m/z* 343.0376), tebuconazole (*m/z* 308.1509), bifenazate (*m/z* 301.1531), and flonicamid (*m/z* 230.0527). Three (3) of the pesticides that were not detected on the plant material (abamectin (B1a), abamectin (B1b), and azadirachtin) were not observed in positive-ion mode at 350 °C in the pesticide standard mixtures when the DART-MS method was being developed. Therefore, the detection of these three pesticides was not expected in the plant material. Another pesticide that was not detected was cyflumetofen ($[C_{24}H_{24}F_3NO_4+H]^+$, calc. 448.1730), one of the two pesticides not included in the standard pesticide mixtures. Therefore, it is not known whether this pesticide is detectable by DART-MS under the conditions used in this study. On the other hand, a peak consistent with the high-resolution protonated mass of pyridalyl ($[C_{18}H_{14}Cl_4F_3NO_3+H]^+$ calc. 489.9753) was detected at *m/z* 489.9724. These two pesticides

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

will be included in a broader panel to assess their screening capabilities using DART-MS. The fifth pesticide not detected in the leaf material was acephate. The last time this pesticide was applied was 48 days prior to DART-MS analysis, so acephate may not be detected on the plant due to degradation. The high-resolution masses consistent with pesticides detected on the plant material and included in the standard mixtures previously analyzed are listed in Table 2, along with the theoretical protonated mass, $\Delta m/z$, and the approximate time frame of the last application.

Table 2. Results from the DART-MS Analysis of Hemp Leaves Treated with Pesticides for Several Weeks[a]

application	pesticide	$[M + H]^+$ calc.	$[M + H]^+$ exp.	difference ($\Delta m/z$)
<1 week	chlorfenapyr	406.9768	406.9765	0.3
>1 week	bifenazate	301.1547	301.1531	1.6
	novaluron	493.0196	493.0194	0.2
	flonicamid	230.0536	230.0527	0.9
>2 weeks	etoxazole	360.1770	360.1771	0.1
>3 weeks	pyraclostrobin	388.1059	388.1045	1.4
	boscalid	343.0399	343.0376	2.3
>4 weeks	spiromesifen	371.2217	371.2229	1.2
>6 weeks	acephate	184.0192	ND	
>7 weeks	tebuconazole	308.1524	308.1509	1.5

[a]The results of this study are shown in Figure 1. ND: not detected.

DISCUSSION

A trend in recent years has been to develop and apply methods for rapid pesticide detection, including on-site and field methods. This idea has been explored in areas including electrochemistry, optical analysis, microfluidic technology, biotechnology, open mass spectrometry ion source, and real-time direct analysis mass spectrometry methods.[1] Mass spectrometry approaches face challenges such as conventional ion sources requiring a high vacuum within a closed structure and the need for extensive sample preparation to decrease matrix interferences.[1] The DART-MS method developed in the current study circumvents some of those challenges. The analysis of the 113 pesticides and isomers by DART-MS serves as a model for developing a rapid, comprehensive screening approach to detect pesticides in a variety of *Cannabis* plants and food/beverage products. Evaluating different ionization modes and gas temperatures helps guide future method development for screening pesticide residues. Based on the observation that the DART-MS screening method appears best suited to analyze pesticides around or below m/z 500, there is room for improvement through additional research to expand the scope and detect a wider range of pesticides. Pesticides that were not detected at 250, 350, or 450 °C in either ionization mode require further investigation, possibly using individual standards or by examining other DART gas temperatures. For example, previous studies have shown that DART-MS can detect some pesticides at even lower temperatures, such as 150 °C for dimethoate and malathion (which were detected at 250 °C in the experiments presented here).[34]

For several pesticides that were not detected as whole protonated or deprotonated molecules, the detection of pesticide fragments provided some insight. This investigation began during efforts to identify the base peak in one of the pesticide mixtures. It was interesting to find that although a protonated or deprotonated mass consistent with piperonyl butoxide was not detected in positive- or negative-ion mode, respectively, the base peak in the mass spectrum of Pesticide Mixture 2 for each of the gas temperatures was consistent with a known major fragment of piperonyl butoxide at nominal m/z 177. When reviewing the current literature on known major pesticide fragments, techniques such as ultrahigh-performance liquid chromatography-electrospray ionization-Quadrupole Time-of-Flight (LC-ESI-QTOF), LC-ESI-MS/MS, and LC-ESI-Q-TOF have been reported for evaluating hundreds of pesticides and their fragments.[48−50] The avoidance of false negatives,[49] observations of pesticide fragmentation at 350 °C, and proposed possible fragmentation mechanisms (e.g., carbamate pesticides can be cleaved at the O−C bond, organophosphate pesticides that do not have phenyl substituents can break down at the carboxylic ester and form an acylium ion)[48] all support the decision to identify possible pesticide fragments detected in the current study. Even though fragments may not be detected due to matrix complexity or because pesticides can be present on plant surfaces at very low concentrations, the overall observation of pesticide fragments by DART-MS highlights a feature of the screening approach worth further exploration. For example, although peaks consistent with major pesticide fragments were observed, analysis of individual pesticide standards would confirm the fragment identities. There also remains the possibility that because the investigation of pesticide fragments in this study was limited to those reported in the referenced literature, there may be fragments of these pesticides that were present but not necessarily detected/attributed to the respective pesticides. If completed in future studies, incorporating the use of unique fragments, along with the precursor ion, would help reduce false positives and support the identification of the pesticides present in the *Cannabis* sample.

The use of individual standards would also help accurately determine the lowest concentration at which each pesticide observed in this study could be detected. Concerns have been raised about the concentration sensitivity of AIMS techniques to matrix effects.[22] Therefore, it is important that investigations to evaluate and maximize the detection of trace residues at low concentrations are performed, such as the initial experiments presented here. Current results demonstrate that DART-MS has the potential to meet AOAC action levels needed for the future development of a validated method to quantify pesticides. If the results had shown that many pesticides could not be detected below 1 μg/mL, the likelihood of developing a DART-MS quantitative method for pesticides at the desired action levels in the future would have been unlikely. However, the results show optimism toward the development of such quantitative methods.

Shifting the discussion to the proof-of-concept presented for the application of the developed method to detect pesticides in *Cannabis* plant materials, several features of the study were successful and demonstrated promising real-world applications. The mass spectral data obtained from analyzing pesticides on the surface of *Cannabis* leaves are far more complex than those from analyzing pesticides in organic solvents and reference standards. Therefore, spiking pesticide mixtures onto the surfaces of dried plant materials assesses their ability to be detected on complex substrates. Although the process of spraying dried plant leaves with pesticides in this study varied widely in consistency and introduced potential heterogeneity, the spray bottle protocol was adequate to demonstrate the

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

proof of concept and detect many of the spiked pesticides when analyzed by DART-MS. Furthermore, allowing the samples to dry at room temperature was important for replicating the traditional pesticide application process as closely as possible and was consistent with previous studies.[51,52] The fact that DART-MS analysis of the spiked *Cannabis* leaves did not detect all of the pesticides administered to the material was not surprising. Several pesticides were detected at very low relative intensities below the ion count threshold. Confidence to assign these peaks or report a positive identification could be achieved through a comprehensive evaluation of the individual pesticide standards.

One real-world consideration when investigating pesticides and environmental contaminants is that although they are typically applied to living plants during growth and storage, pesticides can be found in dried plant materials and finished products (e.g., edibles and concentrates). This demonstrates the persistence of pesticides and their ability to remain present over extended periods. This study was fortunate to receive a few *Cannabis* plant cuttings from a local collaborator, grown strictly for research purposes and not available to the public, for retail purposes or intended for consumption. These samples allowed testing of the developed method on actual *Cannabis* plants treated with pesticides during cultivation, with the added benefit of knowing exactly which pesticides were used and when they were applied. It was beneficial that these plants were grown in a greenhouse, away from typical weather and environmental factors, which allowed for greater control of their growth and health. Therefore, while this experiment does not enable comparison to plants cultivated in an outdoor field, where the persistence of pesticides is likely very different, these experiments could be replicated on additional samples in the future. Another study that would be worth pursuing is the ability of DART-MS to detect pesticides and other adulterants that may pose health risks to consumers in finished *Cannabis* products.

The developed DART-MS method was rapid and efficient, as with most ambient screening approaches, but it has some limitations and additional aspects that need to be further refined. Some of the limitations of a DART-MS screening approach were discussed throughout, such as the need to analyze individual standards by DART-MS to confirm peak assignments for pesticide molecules and fragments and to more definitively determine the lowest pesticide concentrations that can be detected using the proposed method. This leads to another limitation of DART-MS screening approaches: the inability to differentiate between molecules with the same chemical formula in the full-scan mode. Although this was not encountered in the current study, pesticides can share chemical formulas or have the same theoretical protonated/deprotonated masses. This poses the potential risk of misidentification due to isobaric compounds. Because the developed approach can be adapted for DART instruments coupled with alternate MS and MS/MS instruments, the method could be modified to address these occurrences depending on the pesticide concentrations. This concept is beyond the scope of this study and can be investigated in future studies. Nevertheless, laboratories without MS/MS capabilities can still benefit from the developed method. In future studies, the evaluation and detection of pesticide fragments could be incorporated into the method to provide additional identification of the pesticide, especially those that share the same chemical formula.

The issue of within-sample heterogeneity was also discussed, as pesticides are not applied uniformly across an entire plant, leading to variation in their distribution.[30] Within-sample heterogeneity can be especially problematic for AIMS techniques because only a small amount of material is needed for mass spectral profiling. This should be considered during sampling by acquiring several leaves from different locations on the plant, if possible (as partially demonstrated in the spiking experiments), to obtain a good representation of the pesticides applied across the entire plant. Other challenges or limits that exist include (1) matrix interference (e.g., terpenes and lipids);[17] (2) peak overlap with cannabinoids; and (3) misidentification due to lack of structural information or analytical standards.[27] While the studies presented herein did not encounter difficulty stemming from any of these occurrences, the potential remains, and further studies of specificity and reliability should be conducted.

Regarding the expansion of the developed method, although over 100 pesticides were examined in this study, many more could be used for both regulated and illicit *cannabis* cultivation. The potential of this method has been demonstrated, and further studies may be conducted to expand the list of applicable pesticides. Because the screening approach developed in this study is qualitative, there remains an opportunity to develop and implement quantitative or semiquantitative capabilities, especially for determining pesticide bulk concentrations (i.e., w/w of pesticides per dried leaf material). On the basis of semiautomated protocols developed for quantifying small molecules in plant materials by DART-MS, the addition of a quantitation step to the pesticide analysis workflow is feasible.[53−55]

In summary, to the authors' knowledge, this is the first application of DART-MS for multiresidue pesticide detection on *Cannabis* plant materials. This DART-MS method successfully detected 108/113 pesticides, evaluated instrumental parameters (i.e., ionization mode and gas temperature) to maximize the number of detected pesticides, observed major pesticide fragment ions, and determined the approximate lowest concentration at which the pesticides could be detected. The method was then tested using pesticide-spiked and treated *Cannabis* materials, and it successfully detected many of the pesticide residues. The results demonstrate the potential for DART-MS to serve as the analytical technology at the front end of a workflow for testing pesticides on the surface of *Cannabis* materials, such as for field-level monitoring of pesticides on leaves or to examine potential pesticide drift from neighboring fields. It can provide large amounts of informative data, such as an estimate of the number of pesticides in a sample, if there are compounds of interest that could coelute, identify the types of cannabinoids present, and inform decisions about which samples should be submitted for further laboratory testing. The ability to obtain abundant mass spectral data in a matter of seconds without extensive sample preparation is an added benefit of this technique.

While the results presented in this study serve as a proof of concept for screening *Cannabis* for pesticides, additional studies could be conducted to expand on the knowledge presented here. For example, the influence of external factors on pesticide detection, such as weather (rain), flooding, drought, and pest infestations, could be investigated. Another analysis could compare *Cannabis* plants grown in outdoor fields versus those grown in indoor greenhouses, as these plants may be exposed to different pests and predators. Lastly,

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981

the development of quantitative or semiquantitative protocols would further solidify DART-MS's potential for *Cannabis* analysis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jafc.6c00889.

A table presenting information about the pesticide included in this study; DART mass spectra of the pesticides detected in pesticide mixtures analyzed in positive and negative mode at 350 °C; figures summarizing the results from analyzing pesticides under the various DART-MS conditions analyzed; figures and a table presenting the protonated pesticide major fragments detected by DART-MS; and DART mass spectra of the 11-cannabinoid mixture, *Cannabis* plant materials pre/post pesticide spiking, and pesticide-treated fresh hemp *Cannabis* plant analyzed in positive-ion mode at 350 °C (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Walter B. Wilson − *Chemical Sciences Division, Material Measurement Laboratory, National Institute of Standards and Technology, Gaithersburg, Maryland 20899, United States;* orcid.org/0000-0003-1763-781X; Phone: (301) 975-3438; Email: walter.wilson@nist.gov

Author

Megan I. Chambers − *Chemical Sciences Division, Material Measurement Laboratory, National Institute of Standards and Technology, Gaithersburg, Maryland 20899, United States;* orcid.org/0009-0003-4104-1386

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jafc.6c00889

Notes

Certain commercial products are identified in order to adequately specify the procedure; this does not imply endorsement or recommendation by NIST, nor does it imply that such products are necessarily the best available for the purpose.

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The National Research Council (NRC) Research Associateship Program (RAP) is gratefully acknowledged.

■ ABBREVIATIONS USED

Δ^8-THC	Δ^8-tetrahydrocannabinol
Δ^9-THC or THC	Δ^9-tetrahydrocannabinol
AI	artificial intelligence
AGC	automatic gain control
AIMS	ambient ionization mass spectrometry
CBC	cannabichromene
CBD	cannabidiol
CBDA	cannabidiolic acid
CBDV	cannabidivarin
CBG	cannabigerol
CBGA	cannabigerolic acid
CBN	cannabinol
DART	direct analysis in real time
DESI	desorption electrospray ionization
GC	gas chromatography
HRMS	high-resolution mass spectrometry
LC	liquid chromatography
LOQ	limit of quantitation
ML	machine learning
MRL	maximum residue limit
MS	mass spectrometry; National Institute of Standards and Technology
NRC	National Research Council
NTA	non-targeted analysis
ppm	parts per million
QTOF	quadrupole time-of-flight
RAP	Research Associateship Program
SMPR	Standard Method Performance Requirements
SVP	standard voltage and pressure
THCA	tetrahydrocannabinolic Acid
THCV	tetrahydrocannabivarin
TOF	time-of-flight

■ REFERENCES

(1) Xu, L.; Abd El-Aty, A. M.; Eun, J.-B.; Shim, J.-H.; Zhao, J.; Lei, X.; Gao, S.; She, Y.; Jin, F.; Wang, J.; Jin, M.; Hammock, B. D. Recent Advances in Rapid Detection Techniques for Pesticide Residue: A Review. *J. Agric. Food Chem.* **2022**, *70* (41), 13093−13117.

(2) Amvrazi, E. G.; Albanis, T. A. Pesticide Residue Assessment in Different Types of Olive Oil and Preliminary Exposure Assessment of Greek Consumers to the Pesticide Residues Detected. *Food Chem.* **2009**, *113* (1), 253−261.

(3) Damalas, C. A.; Eleftherohorinos, I. Pesticide Exposure, Safety Issues, and Risk Assessment Indicators. *Int. J. Environ. Res. Public Health* **2011**, *8*, 1402−1419.

(4) Karabelas, A. J.; Plakas, K. V.; Solomou, E. S.; Drossou, V.; Sarigiannis, D. A. Impact of European Legislation on Marketed Pesticides — A View from the Standpoint of Health Impact Assessment Studies. *Environ. Int.* **2009**, *35* (7), 1096−1107.

(5) Ye, M.; Beach, J.; Martin, J. W.; Senthilselvan, A. Pesticide Exposures and Respiratory Health in General Populations. *J. Environ. Sci.* **2017**, *51*, 361−370.

(6) Craven, C. B.; Wawryk, N.; Jiang, P.; Liu, Z.; Li, X.-F. Pesticides and Trace Elements in Cannabis: Analytical and Environmental Challenges and Opportunities. *J. Environ. Sci.* **2019**, *85*, 82−93.

(7) Atapattu, S. N.; Johnson, K. R. D. Pesticide Analysis in Cannabis Products. *J. Chromatogr. A* **2020**, *1612*, No. 460656.

(8) Abdulra'uf, L.; Hammed, W.; Tan, G. SPME Fibers for Analysis of Pesticide Residues in Fruits and Vegetables: A Review. *Crit. Rev. Anal. Chem.* **2012**, *42*, 152−161.

(9) Bridoux, M.; Schramm, S. Application of Direct Analysis in Real Time Coupled to Mass Spectrometry (DART-MS) for the Analysis of Environmental Contaminants: Principles and Practices of DART-MS. In *Direct Analysis in Real Time Mass Spectrometry*; Wiley, 2017; pp 193−221 DOI: 10.1002/9783527803705.ch8.

(10) Bernat, A.; Samiwala, M.; Albo, J.; Jiang, X.; Rao, Q. Challenges in SERS-Based Pesticide Detection and Plausible Solutions. *J. Agric. Food Chem.* **2019**, *67*, 12341−12347.

(11) He, Z.; Chen, S.; Wang, L.; Peng, Y.; Luo, M.; Wang, W.; Liu, X. Multiresidue Analysis of 213 Pesticides in Leek and Garlic Using QuEChERS-Based Method and Gas Chromatography-Triple Quadrupole Mass Spectrometry. *Anal. Bioanal. Chem.* **2015**, *407*, 2637−2643.

(12) Lu, D.; Yang, Y.; Luo, X.; Sun, C. A Fast and Easy GC-MS/MS Method for Simultaneous Analysis of 73 Pesticide Residues in Vegetables and Fruits. *Anal. Methods* **2013**, *5* (7), 1721−1732.

(13) Goon, A.; Khan, Z.; Oulkar, D.; Shinde, R.; Gaikwad, S.; Banerjee, K. A Simultaneous Screening and Quantitative Method for

the Multiresidue Analysis of Pesticides in Spices Using Ultra-High Performance Liquid Chromatography-High Resolution (Orbitrap) Mass Spectrometry. *J. Chromatogr. A* **2018**, *1532*, 105.
(14) Díaz, M. A.; O'Connell, D.; Jordan, S.; O'Connor, C.; Martin, P.; Jones, J.; Garvey, J. Analysis of Pesticide Levels in Honey and Pollen from Irish Honey Bee Colonies Using a Modified Dutch Mini-Luke Method with Gas and Liquid Chromatography-Tandem Mass Spectrometry Detection. *J. Agric. Food Chem.* **2023**, *71*, 12657.
(15) Schneider, S.; Bebing, R.; Dauberschmidt, C. Detection of Pesticides in Seized Illegal Cannabis Plants. *Anal. Methods* **2014**, *6* (2), 515−520.
(16) Gagnon, M.; McRitchie, T.; Montsion, K.; Tully, J.; Blais, M.; Snider, N.; Blais, D. R. High Levels of Pesticides Found in Illicit Cannabis Inflorescence Compared to Licensed Samples in Canadian Study Using Expanded 327 Pesticides Multiresidue Method. *J. Cannabis Res.* **2023**, *5* (1), No. 34.
(17) Moulins, J. R.; Blais, M.; Montsion, K.; Tully, J.; Mohan, W.; Gagnon, M.; McRitchie, T.; Kwong, K.; Snider, N.; Blais, D. Multiresidue Method of Analysis of Pesticides in Medical Cannabis. *J. AOAC Int.* **2018**, *101*, 1948.
(18) Wylie, P. L.; Westland, J.; Wang, M.; Radwan, M.; Majumdar, C. G.; Elsohly, M. Screening for More than 1,000 Pesticides and Environmental Contaminants in Cannabis by GC/Q-TOF. *Med. Cannabis Cannabinoids* **2020**, *3*, 1−11.
(19) Raber, J. C.; Elzinga, S.; Kaplan, C. Understanding Dabs: Contamination Concerns of Cannabis Concentrates and Cannabinoid Transfer during the Act of Dabbing. *J. Toxicol. Sci.* **2015**, *40*, 797−803.
(20) Maguire, W. J.; Call, C. W.; Cerbu, C.; Jambor, K. L.; Benavides-Montes, V. E. Comprehensive Determination of Unregulated Pesticide Residues in Oregon *Cannabis* Flower by Liquid Chromatography Paired with Triple Quadrupole Mass Spectrometry and Gas Chromatography Paired with Triple Quadrupole Mass Spectrometry. *J. Agric. Food Chem.* **2019**, *67* (46), 12670−12674.
(21) Xu, M.-L.; Gao, Y.; Han, X. X.; Zhao, B. Detection of Pesticide Residues in Food Using Surface-Enhanced Raman Spectroscopy: A Review. *J. Agric. Food Chem.* **2017**, *65* (32), 6719−6726.
(22) Hernández-Mesa, M.; Moreno-González, D. Current Role of Mass Spectrometry in the Determination of Pesticide Residues in Food. *Separations* **2022**, *9*, No. 148, DOI: 10.3390/separations9060148.
(23) Bauer, A.; Luetjohann, J.; Rohn, S.; Jantzen, E.; Kuballa, J. Development of a Suspect Screening Strategy for Pesticide Metabolites in Fruit and Vegetables by UPLC-Q-Tof-MS. *Food Anal. Methods* **2018**, *11* (6), 1591−1607.
(24) Canchola, A.; Tran, L. N.; Woo, W.; Tian, L.; Lin, Y. H.; Chou, W. C. Advancing Non-Target Analysis of Emerging Environmental Contaminants with Machine Learning: Current Status and Future Implications. *Environ. Int.* **2025**, *198*, No. 109404, DOI: 10.1016/j.envint.2025.109404.
(25) Hollender, J.; van Bavel, B.; Dulio, V.; Farmen, E.; Furtmann, K.; Koschorreck, J.; Kunkel, U.; Krauss, M.; Munthe, J.; Schlabach, M.; Slobodnik, J.; Stroomberg, G.; Ternes, T.; Thomaidis, N. S.; Togola, A.; Tornero, V. High Resolution Mass Spectrometry-Based Non-Target Screening Can Support Regulatory Environmental Monitoring and Chemicals Management. *Environ. Sci. Eur.* **2019**, *31* (1), No. 42.
(26) Guo, Z.; Zhu, Z.; Huang, S.; Wang, J. Non-Targeted Screening of Pesticides for Food Analysis Using Liquid Chromatography High-Resolution Mass Spectrometry-a Review. *Food Addit. Contam.,:Part A* **2020**, *37* (7), 1180−1201.
(27) Manz, K. E.; Feerick, A.; Braun, J. M.; Feng, Y. L.; Hall, A.; Koelmel, J.; Manzano, C.; Newton, S. R.; Pennell, K. D.; Place, B. J.; Godri Pollitt, K. J.; Prasse, C.; Young, J. A. Non-Targeted Analysis (NTA) and Suspect Screening Analysis (SSA): A Review of Examining the Chemical Exposome. *J. Exposure Sci. Environ. Epidemiol.* **2023**, *33*, 524−536, DOI: 10.1038/s41370-023-00574-6.
(28) Granados-Povedano, M.; Domínguez, I.; Egea-González, F.; Garrido Frenich, A.; Arrebola, F. J. Unified Method for Target and Non-Target Monitoring of Pesticide Residues in Fruits and Fruit Juices by Gas Chromatography-High Resolution Mass Spectrometry. *Foods* **2023**, *12* (4), No. 739.
(29) Cody, R.; Laramee, J. A.; Nilles, J. M.; Durst, H. D. Direct Analysis in Real Time (DART) Mass Spectrometry. *JEOL News* **2005**, *40*, 8−12.
(30) Beneito-Cambra, M.; Gilbert-López, B.; Moreno-González, D.; Bouza, M.; Franzke, J.; García-Reyes, J. F.; Molina-Díaz, A. Ambient (Desorption/Ionization) Mass Spectrometry Methods for Pesticide Testing in Food: A Review. *Anal. Methods* **2020**, *12* (40), 4831−4852.
(31) Gross, J. H. Direct Analysis in Real Time—A Critical Review on DART-MS. *Anal. Bioanal. Chem.* **2014**, *406*, 63.
(32) Jing, W.; Zhou, Y.; Wang, J.; Ni, M.; Bi, W.; Chen, D. D. Y. Dispersive Magnetic Solid-Phase Extraction Coupled to Direct Analysis in Real Time Mass Spectrometry for High-Throughput Analysis of Trace Environmental Contaminants. *Anal. Chem.* **2019**, *91* (17), 11240−11246.
(33) Cody, R. B.; Laramée, J. A.; Durst, H. D. Versatile New Ion Source for the Analysis of Materials in Open Air under Ambient Conditions. *Anal. Chem.* **2005**, *77* (8), 2297−2302.
(34) Crawford, E.; Musselman, B. Evaluating a Direct Swabbing Method for Screening Pesticides on Fruit and Vegetable Surfaces Using Direct Analysis in Real Time (DART) Coupled to an Exactive Benchtop Orbitrap Mass Spectrometer. *Anal. Bioanal. Chem.* **2012**, *403*, 2807−2812.
(35) Edison, S. E.; Lin, L.; Gamble, B.; Wong, J.; Zhang, K. Surface Swabbing Technique for the Rapid Screening for Pesticides Using Ambient Pressure Desorption Ionization with High-Resolution Mass Spectrometry. *Rapid Commun. Mass Spectrom.* **2011**, *25*, 127−139.
(36) Kern, S.; Lin, L. A.; Parrales, L. Practical Considerations for the Rapid Screening for Pesticides Using Ambient Pressure Desorption Ionisation with High-Resolution Mass Spectrometry. *Food Addit. Contam.,: Part A* **2011**, *28*, 1393−1404.
(37) Gómez-Ríos, G. A.; Vasiljevic, T.; Gionfriddo, E.; Yu, M.; Pawliszyn, J. Towards On-Site Analysis of Complex Matrices by Solid-Phase Microextraction-Transmission Mode Coupled to a Portable Mass Spectrometer via Direct Analysis in Real Time. *Analyst* **2017**, *142* (16), 2928−2935.
(38) Gómez-Ríos, G. A.; Gionfriddo, E.; Poole, J.; Pawliszyn, J. Ultrafast Screening and Quantitation of Pesticides in Food and Environmental Matrices by Solid-Phase Microextraction−Transmission Mode (SPME-TM) and Direct Analysis in Real Time (DART). *Anal. Chem.* **2017**, *89* (13), 7240−7248.
(39) Wang, X.; Li, X.; Li, Z.; Zhang, Y.; Bai, Y.; Liu, H. Online Coupling of In-Tube Solid-Phase Microextraction with Direct Analysis in Real Time Mass Spectrometry for Rapid Determination of Triazine Herbicides in Water Using Carbon-Nanotubes-Incorporated Polymer Monolith. *Anal. Chem.* **2014**, *86* (10), 4739−4747.
(40) Guo, T.; Yong, W.; Dong, Y. Automatically High-Throughput Quantification by Paper Spray Ionization Mass Spectrometry for Multiple Pesticides in Wine. *Food Anal. Methods* **2019**, *12*, 1208.
(41) Wang, J.; Du, Q.; You, X.; Lv, Y.; Bi, W.; Li, H.; Chen, D. D. Y. Solvent-Free High-Throughput Analysis of Herbicides in Environmental Water. *Anal. Chim. Acta* **2019**, *1071*, 8−16.
(42) Choi, J.; Choi, W.; Massi, J.; Conaway, M. P.Fast and Accurate Identification of Pesticides by Direct Analysis in Real Time (DART) Ionization with Orbitrap Mass Spectrometry. Thermo Scientific application note: AN64190-EN S 914. 2014.
(43) Chambers, M. I.; Musah, R. A. DART-HRMS as a Triage Approach for the Rapid Analysis of Cannabinoid-Infused Edible Matrices, Personal-Care Products and Cannabis Sativa Hemp Plant Material. *Forensic Chem.* **2022**, *27*, No. 100382.
(44) Chambers, M. I.; Musah, R. A. DART-HRMS Triage Approach Part 2 − Application to the Detection of Cannabinoids and Terpenes in Recreational Cannabis Products. *Forensic Chem.* **2023**, *33*, No. 100469.
(45) Chambers, M. I.; Garosi, B.; Musah, R. A. DART-MS Facilitated Quantification of Cannabinoids in Complex Edible

Matrices—Focus on Chocolates and Gelatin-Based Fruit Candies. *ACS Omega* **2023**, *8* (16), 14459−14469.
(46) Garosi, B.; Chambers, M. I.; Musah, R. A. Utilizing Derivatizing Agents for the Differentiation of Cannabinoid Isomers in Complex Food, Beverage and Personal-Care Product Matrices by Ambient Ionization Mass Spectrometry. *Talanta Open* **2024**, *10*, No. 100328.
(47) Standard Method Performance Requirements (SMPRs) for Identification and Quantitation of Selected Pesticide Residues in Dried Cannabis Materials. 2018 www.eoma.aoac.org/app_f.pdf.
(48) He, Z.; Zhao, L.; Liu, X.; Xu, Y. The Application of In-Source Fragmentation in Ultra-High Performance Liquid Chromatography-Electrospray Ionization -Tandem Mass Spectrometry for Pesticide Residue Analysis. *J. Chromatogr. A* **2020**, *1633*, No. 461637.
(49) He, Z.; Xu, Y.; Zhang, Y.; Liu, B.; Liu, X. On the Use of In-Source Fragmentation in Ultrahigh-Performance Liquid Chromatography-Electrospray Ionization-High-Resolution Mass Spectrometry for Pesticide Residue Analysis. *J. Agric. Food Chem.* **2019**, *67*, 10800.
(50) Muehlwald, S.; Buchner, N.; Kroh, L. Investigating the Causes of Low Detectability of Pesticides in Fruits and Vegetables Analysed by High-Performance Liquid Chromatography − Time-of-Flight. *J. Chromatogr. A* **2018**, *1542*, No. 37.
(51) Cajka, T.; Riddellova, K.; Zomer, P.; Mol, H.; Hajslova, J. Direct Analysis of Dithiocarbamate Fungicides in Fruit by Ambient Mass Spectrometry. *Food Addit. Contam.,:Part A* **2011**, *28*, 2011.
(52) Mainero Rocca, L.; Cecca, J.; L'Episcopo, N.; Fabrizi, G. Ambient Mass Spectrometry: Direct Analysis of Dimethoate, Tebuconazole, and Trifloxystrobin on Olive and Vine Leaves by Desorption Electrospray Ionization Interface. *J. Mass Spectrom.* **2017**, *52* (11), 709−719.
(53) Chambers, M. I.; Appley, M. G.; Longo, C. M.; Musah, R. A. Detection and Quantification of Psychoactive N,N-Dimethyltryptamine in Ayahuasca Brews by Ambient Ionization High-Resolution Mass Spectrometry. *ACS Omega* **2020**, *5* (44), 28547−28554.
(54) Appley, M. G.; Chambers, M. I.; Musah, R. A. Quantification of Hordenine in a Complex Plant Matrix by Direct Analysis in Real Time−High-Resolution Mass Spectrometry: Application to the "Plant of Concern" Sceletium Tortuosum. *Drug Test. Anal.* **2022**, *14* (4), 604−612.
(55) Fowble, K. L.; Musah, R. A. A Validated Method for the Quantification of Mitragynine in Sixteen Commercially Available Kratom (Mitragyna Speciosa) Products. *Forensic Sci. Int.* **2019**, *299*, 195−202.

https://doi.org/10.1021/acs.jafc.6c00889
J. Agric. Food Chem. 2026, 74, 26969−26981