

Ambient Ionization Mass Spectrometry in Food Science: Recent Advancement and Applications

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ABSTRACT

Ambient mass spectrometry (AMS) is the collective term for a set of techniques that enable ions to be generated from condensed phase specimens in atmospheric conditions before being gathered and examined by a mass spectrometer. Direct molecular identification of a variety of raw food specimens is made possible by AMS with little to no sample pretreatment. Due to AMS's excellent sensitivity and selectivity with analysis, it is progressively used in the disciplines of food science and industry. A variety of solid and liquid samples could be directly analyzed using ambient ionization methods and MS. A unique opportunity to examine the spatial-chemical data from a variety of food samples is also presented by MS imaging. This article discusses that the AMS principle, how it can be used to analyze a variety of food samples, its benefits and drawbacks, as well as the impact AMS has on food chemistry and the difficulties it presents. This article provides an outline of the most recent and popular AMS methods in the food business, rather than a systematic review.

Key words: Ambient ionization mass spectrometry, Direct analysis in real time mass spectrometry, Mass spectrometry imaging, Atmospheric ionization, Food analysis.

1. INTRODUCTION

The global population is increasing, which has resulted in a rise in food demand and, consequently, in the field of food science as well as the food industry. Despite this, food safety incidents were common [1], driven by the desire to maximize profits. As a result, in recent times, there has been an increase in concern regarding the purity and safety of food. The analysis of food safety, however, is a significant challenge in modern society due to the diversity and chemical sophistication of food samples, which result in trace concentrations of a variety of analytes, including pathogenic organisms, trace metals, chemical additives, biotoxins, surreptitious contaminants, organic contaminants, etc. [2,3]. Although conventional technologies, such as chromatographic techniques and ELISA [4], might identify chemical components in food samples, these techniques are usually preceded by a long list of time-consuming sample pretreatment phases. The direct and effective evaluation of food business specimens in the prevailing food industry may not be acceptable, especially for the techniques discussed above. Therefore, the development of powerful and efficient tools for the evaluation of various types of complex food samples is sorely needed [5].

Mass spectrometry (MS) has gained prominence as a powerful and versatile tool for analytical and bioanalytical analysis. The chief factor in this immense success and applicability is MS's unmatched abilities to recognize, measure, and characterize atoms and molecules of varying sorts, proportions, and dimensions [6]. The combination of high responsiveness, specificity, and faster detection has long been recognized as a significant advantage of MS. It takes much more than just the ability of an analyzer to differentiate between various (m/z) ratios for MS to be used to recognize chemical substances in a mixture, including determining the structural makeup of large biomolecules. This problem was resolved for samples that were in the solution phase with the introduction of electrospray ionization (ESI) [7]. The

ESI method involves nebulizing the solution to create a fine spray of droplets under conditions where evaporation of the solvent occurs as the droplets traverse the ambient interface, consequently introducing ionic species into the spectrometer [7].

Analytical chemistry underwent a revolution thanks to the introduction of desorption ESI (DESI) by Takats *et al.* (2004). The simultaneous dissociation and ionization of solutes from a specimen in their natural state is made possible by DESI ionization [8]. DART, another widely used atmospheric ionization methodology, was developed not long after DESI was first introduced [9]. The above methods were combined to form the captivating field of ambient ionization. Ambient ionization MS (AIMS) enables quick analysis of specimens in their natural state with little to no sample preparation required. The ambient ionization field has developed significantly since the introduction of DESI and DART ionization, leading to the development of multiple additional methodologies and their use in numerous sectors.

2. AMBIENT IONIZATION TECHNIQUES

In general, there are three main categories of AIMS techniques. Using solid-liquid extraction methods, particles from an analyte's surface are either extracted or desorbed. Ionization is typically accomplished using an ESI mechanism [10]. Plasma desorption methods utilize plasma

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to generate ions through methodologies comparable to those used in ambient pressure chemical ionization [11]. As a final step, laser ablation processes utilize infrared (IR) or UV lasers to ablate and desorb substances from the specimen surface [12]. With the development of AIMS processes, each of these categories has expanded, now including the analysis of a wide range of sample types, from modest volatile chemicals to sizable preserved biomaterials.

Wang *et al.* first created the low-cost, readily accessible technique known as paper spray (PS) ionization in 2010 [13]. In PS ionization, the sample is applied to a triangular paper [13]. The analyte electrosprays from the tip of the triangular paper after it has dried, a spray solvent has been added, and high voltage has been applied [13]. PS, in contrast to many other ionization methodologies, facilitates instant access to a number of sampling strategies, including surface analysis, the direct assessment of dried blood spots, and the isolated compounds from a TLC band [13].

In contrast to other ambient MS (AMS) methods, EESI-MS isolates the sample from the electric field and avoids chemical regulator contamination to the greatest extent possible. The following are some of the key characteristics of EESI: (a) monitoring that is ongoing and remote; (b) *in vivo* investigation; (c) capability to analyze polar and non-polar compounds; (d) simpler sample treatment procedures; (e) monitoring ion-molecule and ion-ion reactions; (f) ability to analyze liquid, gas, aerosol samples, etc.; and (g) ability to be easily coupled with other instruments [14]. With iEESI-MS, the bulk sample is directly injected through the capillary with a specific flow rate of extractive solutions (such as methanol or water) biased with high voltage [14]. The extractive solvent was infused into the sample to extract the analytes, which were then carried through the bulk sample along the gradient of the electric field toward the nearby mass spectrometer (MS) for analysis [14]. The distinguishing characteristics of iEESI-MS include the following: (i) direct chemical characterization within bulk samples as opposed to on the surface; (ii) the solvent used is easily changeable; (iii) least amount of sample prior preparation; (iv) no sheath gas; (v) faster analysis time; (vi) little sample consumption, straightforward processes; and (vii) simplicity of integration with various types of MS which are all advantages [14].

Some of the main advantages of DART-MS include its high sensitivity, specificity, and speed of analysis; its simplicity of use; and the avoidance of a time-consuming sample preparation process [Figure 1] for food analysis [15]. Both DESI and DART were created around the same time, but DART is a renowned plasma-based AIMS methodology

because it directly desorbs and ionizes analytes using a plasma-based ion source [15]. In DART, an electrical potential difference is applied to a flow of N₂ or He gas. Analytes subsequently desorb directly from the specimen surface as a result of plasma being created by a variety of thermodynamically stable species, ions, and electrons [15].

Matrix-assisted laser DESI (MALDESI) was created in 2006 by combining the MALDI and ESI ionization methods [16]. Similar to MALDI, pulsed laser illumination [16] is applied to tissue specimens that have been doped with matrix solutions or to dried sample particles that have both an analyte and a matrix component. The analyte is subsequently desorbed. For the analysis of unprocessed specimens like tissue, mid-IR lasers are frequently employed, taking advantage of the properties of water as a matrix [16]. ESI is implemented orthogonally to ionize the desorbed particles and send the ions to the MS system [16]. Initial developments succeeded in expanding their relevance to MS imaging (MSI). Sampson *et al.* increased the number of analytes and types of samples that MALDESI could analyze by utilizing liquid-phase MALDESI [17].

Rapid evaporative ionization MS (REIMS) was first developed to differentiate between cancerous and non-cancerous tissue in real-time while also carrying out surgical treatments [18]. During a surgical procedure, the tissue is first vaporized, then ionized using an electrocautery knife. The MS receives the ionized analytes for assessment.

3. AMS IN FOOD ANALYSIS

3.1. Liquid and Viscous Samples

The utilization of AMS techniques for liquid and viscous samples is listed in Table 1. It is critical to implement and promote metabolomics as a diagnostic instrument, even though it can be used to characterize a variety of metabolites present in milk products and ascertain whether they are substantially connected to the feeding system, particularly in unrestrained real-world farming practices [19]. Segato *et al.* evaluated the multi-modal DART-HRMS's capacity to monitor three milk production franchises in 2022 [20]. The goal of the study was to evaluate DART-HRMS's ability to differentiate between milk specimens from lowland and Alpine farms to discover biological markers associated with dietary forage. The quality of the milk was assessed in 88 samples altogether. Among these, 18 specimens were obtained from Alpine farms during the summer season, and 70 different milk specimens across the 4 seasons were obtained from lowland farms [20]. Milk was produced by cows on the farms in the lowlands that contained

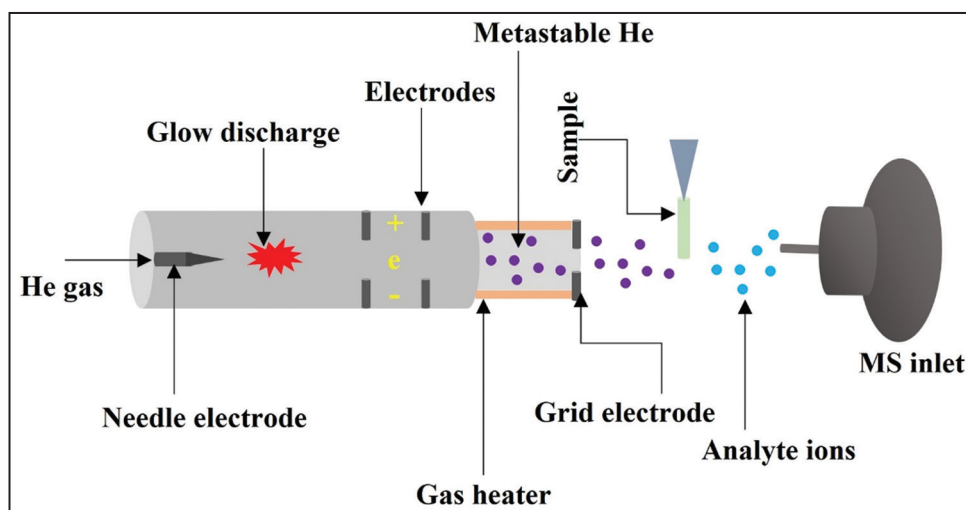


Figure 1: Schematic illustration of DART ionization technique.

Table 1: AMS analysis of liquid and viscous samples.

Ionization technique	Desorption mechanism	Ionization mechanism	Sample	Analytes	LOD	RSD	References #
DART	Plasma desorption	Corona discharge	Milk	Energetic compounds (creatinine, glucose, acetolactate); low-weight molecules (nogramine), amines (glucosamine, N-acetyl-glucosamine), and organic acids (oleic acid)	NR	11%	[20]
			Beer	Ethanol	0.15%	±1.0%	[22]
			Alcoholic drinks	aspartame, saccharin, acesulfame-K, neotame, sucralose, cyclamate and alitame	v/v <ng/mL	NR	[25]
PSI	Liquid extraction	electrospray	Extra virgin olive oil	Tyrosol, hydroxytyrosol and phenolic derivatives	10–30 ng/mL	9-11%	[28]

NA: Not applicable; NR: Not reported, LOD: Limit of detection, RSDL: Relative standard deviation, DART: Direct analysis in real time, PSI: Paper spray ionization

glucosamine, N-acetylglucosamine, amines, and organic acids [20]. Alpine milk's metabolic profile was identified by 11 lactate-related ions and the predominant monoacylglycerol molecules, which can be distinguished by their C16:0 and C18:0 structural characteristics. According to the study, DART-HRMS offers a streamlined procedure that enables access to the chemical composition directly from diluted milk samples. In addition, this approach makes use of chemometrics and low-level data fusion [20].

To analyze two volatile phenols in grape juice quantitatively, Rafson and Sacks (2021) investigated the effectiveness of thin film sorbent sheets made of direct immersion poly (dimethyl siloxane) and coupled with (DI-SPMESH-DART-MS) direct analysis in real time MS [21]. Multiple reaction tracking mode was used to collect data, while the MS was in negative-ion mode of operation. Semi-volatile odorants could be accurately and sensitively measured in soluble and grape juice specimens thanks to the experimental setup's high throughput. Four volatile phenols that are relevant to the standard of grape juices – 4-ethylphenol, 4-ethylguaiaicol, 4-methylguaiaicol, and guaiaicol – underwent enhancement and verification utilizing the [DI-SPMESH-DART-MS] method. Twenty-four samples were subjected to a DI-SPMESH-DART-MS analysis with detection limits of 0.5–3 g/L in model juice solutions [21]. Volatile phenols could be detected with good accuracy (72–137%) in actual grape juices. Guaiaicol measurements in some cultivars, however, showed poor accuracy, and measurements of 4-methylguaiaicol were hampered by interactions with other volatile phenols [21].

The amount of ethyl alcohol in alcoholic drinks was measured quantitatively using DART-MS [22]. A simple adjustment in the DART-MS functionality was made to extract headspace fumes in the DART gas stream, and this alteration was used to generate a method for measuring ethanol concentration. Quantitative information was, then, extracted from samples with known ethyl alcohol concentrations to assess the effectiveness of this method. In addition, assessed was the capacity to re-analyze samples. Measurements were accurate and within 1% v/v when ethanol reference materials were quantified with known ethanol concentrations [22].

A broad-spectrum antibiotic called chloramphenicol (CAP), which was previously used in veterinary medicine, has serious toxicological effects

on humans and can lead to conditions like aplastic anemia. The use of CAP in livestock, including honeybees, has been prohibited in several countries due to its toxic effects, which are not dose dependent [23].

To determine CAP in honey, Li *et al.* (2019) used QTRAP MS coupled with a DART ion source [23]. By comparing results obtained from the HPLC-MS method, the accuracy of the DART-MS method was determined [23]. By improving the sample preparation process, a sensitive detection of CAP residue in honey at levels lower than 1.0 g/kg was made possible. Several samples of honey that were obtained from a market in China were examined using the techniques. Since the two methods' results are in good accord, it is possible to use DART-MS/MS as a technique for the precise detection of veterinary drug traces in complex matrixes. Compared to the HPLC-MS method, the DART-MS method is simpler, quicker, and less expensive per analysis. It also has fewer matrix effects [23].

Artificial sweeteners are useful additives that can be used to adjust the sweetness of food. In addition, they have few or no calories, which help regulate insulin levels and body weight [24]. Overconsumption of artificial sweeteners could have a negative impact on people's health [24]. As a result, regulatory oversight of the existence of strong sweeteners in various types of foods is required to protect consumers. The concentrations of various sweeteners in alcoholic beverages must be determined using a direct and effective analytical method because sweeteners are frequently combined with other additives to enhance the flavors of alcoholic beverages. A few reports of multiple sweeteners being found in other foods at the same time have been made. A reliable approach based on direct assessment combined with QTRAP MS was reported by Li *et al.* (2021) to simultaneously screen and quantify artificial sweeteners in alcoholic beverages [25]. More importantly, the technique has a high sensitivity and specificity for identifying artificial sweeteners in alcoholic beverages such as beer, wine, Chinese liquors, and whisky that are bought at the store. The results suggested that the method suggested here might be effective for widespread application in typical quality control tests of artificial sweeteners [25].

The most prized type of olive oil, extra virgin olive oil, must adhere to strict standards for molecular composition, manufacturing, aroma, and taste perception. Depending on the quality, olive oil can be divided into a number of categories. It has a molecular structure

that is quite distinct from other edible fats and offers a variety of health benefits [26]. An apparent correlation exists between the presence of a particular monounsaturated fatty acid, such as oleic acid, and a reduced risk of cardiovascular fatality and stroke [26]. In addition, polar oxidants (tyrosol and hydroxytyrosol) and lipophilic antioxidants (tocopherols) may inhibit atherogenesis [27]. Analytical methods with the highest level of accuracy and selectivity should be used to analyze these compounds. The experiments may be very challenging and time-consuming due to a lack of suitable reference standards and the interference of analytical conditions with their chemical stability. For instance, dialdehydes, an ester derivative, easily interconvert into acetals, and hemiacetals when present with acidic methanol.

By combining PS-MS and microwave-enabled acid hydrolysis, Bartella *et al.* (2020) reported a novel and incredibly time-efficient method to analyze tyrosol and hydroxytyrosol derivatives [28]. The accuracy of the method is ensured by tandem MS and deuterated internal standards, which together represent an unrivaled analysis procedure for localizing small compounds in sophisticated mixtures like olive oil. With an intraday relative standard deviation (RSD%) range of five to nine and an interday (RSD%) range of nine to eleven after several weeks of operation, the system's repeatability was excellent. The threshold for detection was established to be (10–30 ng/mL) [28].

3.2. Solid and Bulk Samples

The uses of AMS techniques in solid and bulk samples are displayed in Table 2. Human perception of flavor is influenced by interactions with flavors, fragrance, sensory properties, vision, and audio [29]. Evaluation platforms that can collect both qualitative and quantitative chemical information can be used to objectively characterize vegetable quality characteristics [29] that are reflective of the human sensory experience. Due to their ability to operate in ambient conditions and minimal sample preparation requirements, AMS platforms present an appealing alternative that enables a high-throughput method for high-quality analysis [30]. Mason *et al.* (2021) evaluated the ability of DART-MS and REIMS for quality-based classification and rapid

monitoring of peppers [31]. DART-MS demonstrated the capacity to distinguish between capsule colors and astringency based on chemical fingerprints, in contrast to REIMS, which could identify pepper market classes. Capsaicin, vitamin C, and coumaric acid were among the substantial bioactive components in human nutrition that may have been discovered as a result of the DART-MS analysis. The findings of this study indicate the potential of these methods as simple, dependable techniques for increased inspection of pepper quality [31].

To identify adulterants in saffron specimens, an array of analytical methods has been developed [32]. These methods are accurate and simple to use, but they have a number of drawbacks, such as sample loss, time-consuming sample preparation, and a general inability to perform quality assessment, especially in industrial applications [32]. To distinguish between pure and impure saffron specimens, Fiorino *et al.* (2019) created a technique based on DART and an Orbitrap high-resolution mass analyzer [33]. Pure saffron and saffron specimens adulterated with safflower or turmeric could be distinguished, according to MS spectra acquired in positive ion configuration. Saffron adulteration was clearly defined and started at low inclusion rates, between 5% and 10% [33].

Drugs such as cocaine, dextromethorphan, fentanyl, heroin, and lorazepam were extracted from infant formula using fiber-based SPME tips. Sample responses and sensitivities for the drugs were discovered to be 1–100 ng/mL [34]. There was a noticeable improvement in signal detection when comparing the SPME-DART to a classical DART-MS method for low level drug detection. According to the study, SPME-DART-MS is a practical method for looking for drug residue traces in complex matrices like infant formula [34]. In a different study, Khaled *et al.* (2020) investigated the detection and quantitation of a large number of pharmaceutical drugs with varying physical and chemical properties in complex food matrices like beef tissues with SPME and DART coupled to a MS [35]. DART might successfully ionize 53% of the 98 initially selected target analytes in bovine muscle and quantify them at concentrations that have been at or below the Canadian maximum residue limits and United States regulated tolerance levels. These analytes demonstrated positive outcomes

Table 2: AMS analysis of solid and bulk samples.

Ionization technique	Desorption mechanism	Ionization mechanism	Sample	Analytes	LOD	RSD	References #
DART	Plasma desorption	Corona discharge	Pepper	Vitamin C, p-coumaric acid, and capsaicin	NR	NR	[31]
			Saffron	2,4,6-trimethyltetracos-2-enoic acid, 4,4'-diapophytoene,	<5–10%	NR	[33]
			Baby formula	Cocaine, dextromethorphan, fentanyl, heroin, and lorazepam	2.5–100 ng/mL	NR	[35]
i-EESI	Liquid extraction	electrospray	Tilapia fish	Phosphatidylcholines (PCs), Sphingomyelins (SMs), phosphatidic acids (PAs)	NR	NR	[38]
PSI	Liquid extraction	electrospray	Tomato	Acephate, chlorpyrifos, and cyazofamid	0.01 ppm	9%	[40]
REIMS			Meat	NR	~2.5%	NR	
IR-MALDESI	Electrospray	MALDI	Tomato	Amino acids, terpenes, phenolics, glycosides	NA	NA	[44]
LAESI-MSI	Laser ablation	electrospray	Fruits	Mycotoxin	NA	NA	[49]

NA: Not applicable, NR: Not reported, LOD: Limit of detection, RSD: Relative standard deviation, i-EESI: Extractive electrospray ionization, MSI: Mass spectrometry imaging, MALDESI: Matrix-assisted laser DESI, IR: Infrared, PCs: Phosphatidyl cholines, SMs: Sphingomyelins, PAs: Phosphatidic acids

amidst using just two reference standards for correction, with 62% of detected analytes accomplishing linear correlation coefficients above 0.99 inside the evaluated concentration limit. In addition, upward of 90% of the detected analytes had intraday reproducibility RSDs of <25% and average accuracy within the range of 70–120% of their true concentrations at the 0.5–2 times concentration level [35].

In a related study, Kosek *et al.* (2019) looked at REIMS technology to detect unlisted additives in products such as sausages and burgers that are made from chopped pork and chicken meat [36]. Because it can result in sizable financial gains and a drop in consumer confidence, meat counterfeiting is a substantial economic problem. To bulk up minced meat by concealing, the addition of water with a bulking agent is immoral and hard to identify. Total net protein can be used to gauge the meat's quality, but the methods for doing so are not up to the task of dealing with the highly advanced adulteration techniques used today [36].

The REIMS method had high confidence in its ability to detect adulterants when they were added in concentrations >2.5%. The results might be attained in a brief amount of time. When used as the primary testing technique to ensure the integrity of meat products, REIMS can be thought of as a quick diagnostic test [36].

A typical perfluoroalkyl chemical compound with the properties of hydrooleophobicity, high surface activity, heat resistance, and acid resistance is perfluorooctanoic acid (PFOA) [37]. The stable C-F bond in PFOA makes it difficult to degrade and highly persistent in both the environment and living things [37]. In addition, PFOA has recently been found in high concentrations in human tissues, blood, breast milk, and umbilical cord blood [37]. As a result, there is a lot of concern about PFOA's potential toxicity to both humans and the environment. The most recent research has demonstrated that PFOA has numerous toxic effects on living things, including hepatotoxicity, developmental toxicity, neurotoxicity, immunotoxicity, etc. [37] Phospholipids have been acknowledged to play a significant role in biochemical processes in organisms as a class of endogenous metabolites. Therefore, studying the changes in phospholipids brought on by emerging pollutants in organisms may assist in understanding the possible dangers that these pollutants pose to people and other living things. PFOA-exposed Nile tilapia was profiled for phospholipids in the spleen and liver tissues using iEESI-MS [38]. The iEESI-MS system was able to directly

identify and detect 130 phospholipid signals in the Nile tilapia's tissues. Using PLS-DA and ANOVA, phospholipid signals showed a significant difference in the Nile tilapia tissue between the control group and PFOA exposure groups [Figure 2]. In addition, pathway analysis showed that PFOA significantly affects the metabolism of glycerophospholipids in Nile tilapia [38].

To prevent damage from weeds, insects, fungi, bacteria, larvae, and rodents, pesticides are harmful substances used at different stages of growing fruits and vegetables [39]. Numerous pathologies, including diabetes mellitus, neurodegenerative disorders (Alzheimer's and Parkinson's), autism, hormonal imbalances, high blood pressure, cancer, non-Hodgkin's lymphoma, uterine cancer, and prostate cancer, are associated with pesticide exposure, as per a growing body of research [39]. To monitor the levels of pesticides in tomatoes throughout the pre-harvest periods, Moura *et al.* (2020) used PSI-MS [40]. The samples were divided into field and storage groups. Only this portion of the tomato was examined because the fruit peel is where many pesticides remain [41]. In the samples that had been stored, the levels of pesticides had decreased. Acephate, cyazofamid, and chlorpyrifos concentrations were discovered to be substantially different between the field and stored groups at the conclusion of the pre-harvest periods. Both LODs and LOQs of 0.01 ppm were attained. RSDs were <9%, and recoveries were extremely close to 100% [40].

Large aldehyde intakes have been linked to cancer, diabetes, and cardiovascular disease. For food safety regulation, several nations and organizations have established a range of aldehyde (primarily FA) allowance levels as significant intake sources [41]. As a result, it is essential to create sensitive and quick analytical techniques for calculating aldehyde levels in food. Before aldehyde measurement, sample pretreatment is crucial due to the complicated food matrices. Limiting or even doing away with sample preparation might well be desirable for high analytical throughput and good accuracy. With the extraction and functionalization of aldehydes *in situ* with PS-MS while considering the mildly ionizable characteristics of aldehydes, Lin *et al.* (2022) created an extremely sensitive, high-throughput, and analysis of aldehydes [42]. In the concentration domain of 2–150 μM , the aldehydes [Table 2] showed good linearity with LODs of 0.03–0.15 μM . This technique was used to measure the aldehydes in an array of foods, including meat, fruits, and

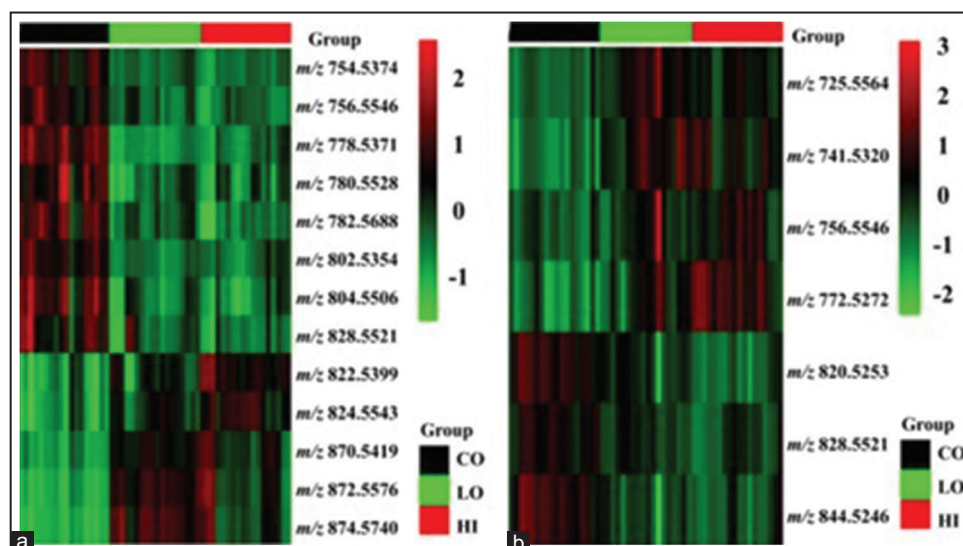


Figure 2: Heatmap of dysregulated phospholipid signals detected by iEESI-MS in positive ion detection mode in different tissue samples of Nile tilapia exposed to perfluorooctanoic acid. (a) Liver sample and (b) spleen sample. (Reproduced with permission from Liu *et al.*, 2022, RSC).

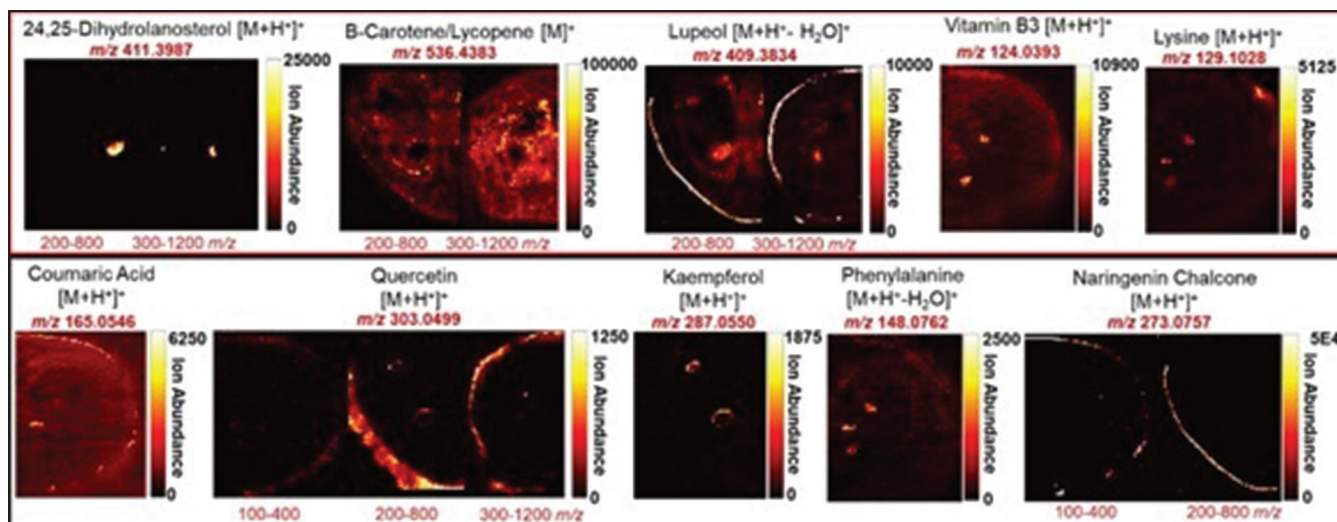


Figure 3: Metabolites found in cherry tomatoes from transverse midsection slices. Three slices were taken to analyze metabolites in three m/z ranges: 100–400, 200–600, and 300–1200. If ions fall in multiple mass ranges they are shown in red font. Ions in the top red box were discovered using discovery-driven methods and those in the bottom black box were found using literature-driven methods (Reproduced with permission from Muddiman *et al.*, [2020], RSC).

vegetables. The proposed method is appealing for screening aldehydes in food, ecologic, and biological materials due to its simplicity, high efficiency, and sensitivity [42].

3.3. AMS Imaging

The analysis of various tissue types with varying densities in a single analysis without using different preparation methods for each tissue presented an intriguing challenge with tomatoes [43]. In 2020, Robichaud *et al.* used IR-MALDESI to metabolically profile cherry tomatoes [44]. The range of metabolites that could be imaged from 100 to 1200 m/z included amino acids, lipids, and the four main classes of secondary metabolites: terpenes, phenolics, glycosides, and alkaloids. The authors discovered endogenous carotenoid hydrocarbons, specifically lycopene and its structural isomer – carotene [Figure 3]. The competitive advantage of IR-MALDESI for fingerprinting metabolomes in plant MSI studies was demonstrated by its capacity to detect classes of metabolites that contain hydrocarbons, such as carotenoids, without the limitations of MALDI [44].

The toxic secondary metabolites known as mycotoxins are produced by a variety of fungi, including penicillium, aspergillus, and fusarium species. These substances have significant effects on the agricultural and food sectors, contaminating a wide array of feed and food products [45]. A significant toxin is patulin, a tetraketide lactone derived from various mold organisms and present in foods and manufactured feeds [46]. Patulin is extremely harmful to humans, animals, and plants. This substance interacts with peptides and amino acids to form adducts that inhibit the synthesis of DNA and RNA. Because patulin is electrophilic, it reacts with glutathione to form covalent modifications, which can deplete glutathione. According to Champdore *et al.* (2007), its electrophilic potential can also cause protein cross-linking between and within molecules [47].

The potential for patulin to spread from fruits and vegetables that have decomposed to unaffected areas is particularly concerning. The high polarity of patulin, which facilitates transmission to the inner surface of fruits and vegetables with a high-water content, may have an impact on diffusion [48]. Using common analytical methods like LC or GC coupled to a detector (UV or MS), the removal and extraction of the sample part for analysis takes a lot of time. Furthermore, these methods only partially reveal the toxin's spatial location within the

sample, making it challenging to determine the analyte's diffusion in food. Da Silva Lima *et al.* (2022) claim that LAESI imaging was used to study the spread of the mycotoxin patulin in fruits from spoiled to unaffected areas [49]. During the sole sample preparation phase, slices of infected and mold-free (control) strawberries and apples were made. Slices were exposed to a 2.94 μm IR beam, which caused the sample compounds to directly ionize and be analyzed by ESI-MS. Even though it was not present in the control samples, patulin was present on every fruit that had mold on it. Patulin was seen to be transferring from the spoiled area to the better and healthier sections of the fruits in LAESI images. The advantages of LAESI imaging over traditional analysis techniques for examining patulin distribution in fruits were highlighted in this report [49].

4. CONCLUSION

Thanks to the quick advancement of AMS techniques, food sample analysis has become simpler, faster, and less expensive. Furthermore, it is now possible to diagnose samples virtually and in actual environments while they are in their natural environment. In the food industry, AMS techniques have evolved into a versatile tool for food safety and quality, providing, to some extent, trustworthy certification support for food authentication. Because there are so many different types of food samples, the mixtures are so intricate, and the analyte concentrations are so low, AMS is faced with a big challenge when it comes to accurately quantifying known and unrecognized directed analytes within different food and operation uniformity. To improve the analytical utility of AMS techniques, factors such as sample injection, repeatability, responsiveness, specificity, inhomogeneity, monotonicity, and exactness must be carefully considered. The repeatability of AMS analysis can be impacted by several variables, including the environment, the sample's geometry and composition, consumer execution, and platform setup. It is crucial to develop ubiquitous and comprehensive datasets of AMS that are independent of MS, ionization methods, and analysis conditions to quickly screen for trace toxic compounds and evaluate the quality of food. In addition, complex MS spectra call for the use of chemometric tools for data analysis; as a result, advancements in automation and machine learning will open up useful new directions for continuing and in-depth studies on AMS in food science.

5. CONFLICTS OF INTEREST

There are no conflicts to declare.

6. ACKNOWLEDGMENT

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7. REFERENCES

1. C. Black, O. P. Chevallier, C. T. Elliott, (2016) The current and potential applications of ambient mass spectrometry in detecting food fraud, *TrAC Trends in Analytical Chemistry*, **82**: 268-278.
2. X. Wang, S. Wang, Z. Cai, (2013) The latest developments and applications of mass spectrometry in food-safety and quality analysis, *TrAC Trends in Analytical Chemistry*, **52**: 170-185.
3. Y. Y. Dong, J. H. Liu, W. A. N. G. Sai, Q. L. Chen, T. Y. Guo, L. Y. Zhang, T. W. Tan, (2015) Emerging frontier technologies for food safety analysis and risk assessment, *Journal of Integrative Agriculture*, **14(11)**: 2231-2242.
4. Z. Khan, N. Kamble, A. Bhongale, M. Girme, V. B. Chauhan, K. Banerjee, (2018) Analysis of pesticide residues in tuber crops using pressurised liquid extraction and gas chromatography-tandem mass spectrometry, *Food chemistry*, **241**: 250-257.
5. D. Peng, L. Zhang, C. Situ, Y. Pan, Y. Tao, Y. Wang, Z. Yuan, (2017) Development of monoclonal antibodies and indirect competitive enzyme-linked immunosorbent assay kits for the detection of clenbuterol and salbutamol in the tissues and products of food-producing animals, *Food Analytical Methods*, **10 (11)**: 3623-3633.
6. E. De Hoffmann, V. Stroobant, (2007), *Mass Spectrometry: Principles and Applications*, United States: John Wiley and Sons.
7. J. B. Fenn, M. Mann, C. K. Meng, S. F. Wong, C. M. Whitehouse, (1989) Electrospray ionization for mass spectrometry of large biomolecules, *Science*, **246(4926)**: 64-71.
8. Z. Takats, J. M. Wiseman, B. Gologan, R. G. Cooks, (2004), Mass spectrometry sampling under ambient conditions with desorption electrospray ionization. *Science*, **306**: 471-473.
9. S. Rankin-Turner, L. M. Heaney, (2021) Applications of ambient ionization mass spectrometry in 2020: An annual review. *Analytical Science Advances*, **2(3-4)**: 193-212.
10. A. Albert, J. T. Shelley, C. Engelhard, (2014) Plasma-based ambient desorption/ionization mass spectrometry: State-of-the-art in qualitative and quantitative analysis. *Analytical and Bioanalytical Chemistry*, **406**: 6111-6127.
11. P. Nemes, A. Vertes, A. (2007) Laser ablation electrospray ionization for atmospheric pressure, *in vivo*, and imaging mass spectrometry, *Analytical Chemistry*, **79(21)**: 8098-8106.
12. G. J. Van Berkel, S. P. Pasilis, O. Ovchinnikova, (2008) Established and emerging atmospheric pressure surface sampling/ionization techniques for mass spectrometry, *Journal of Mass Spectrometry*, **43(9)**: 1161-1180.
13. H. Wang, J. Liu, R. G. Cooks, Z. Ouyang, (2010) Paper spray for direct analysis of complex mixtures using mass spectrometry, *Angewandte Chemie*, **122(5)**: 889-892.
14. J. Liu, H. Wang, N. E. Manicke, J. M. Lin, R. G. Cooks, Z. Ouyang, (2010) Development, characterization, and application of paper spray ionization, *Analytical Chemistry*, **82 (6)**: 2463-2471.
15. X. Zhang, X. Ren, K. Chinglin, (2021) Applications of direct analysis in real time mass spectrometry in food analysis: A review, *Rapid Communications in Mass Spectrometry*, **35(6)**: e9013.
16. R. B. Cody, J. A. Laramée, H. D. Durst, (2005) Versatile new ion source for the analysis of materials in open air under ambient conditions, *Analytical Chemistry*, **77(8)**: 2297-2302.
17. J. S. Sampson, A. M. Hawkrige, D. C. Muddiman, (2006) Generation and detection of multiply-charged peptides and proteins by matrix-assisted laser desorption electrospray ionization (MALDESI) Fourier transform ion cyclotron resonance mass spectrometry, *Journal of the American Society for Mass Spectrometry*, **17(12)**: 1712-1716.
18. J. S. Sampson, K. K. Murray, D. C. Muddiman, (2009) Intact and top-down characterization of biomolecules and direct analysis using infrared matrix-assisted laser desorption electrospray ionization coupled to FT-ICR mass spectrometry, *Journal of the American Society for Mass Spectrometry*, **20**: 667-673.
19. A. Tu, D. C. Muddiman, (2019) Internal energy deposition in infrared matrix-assisted laser desorption electrospray ionization with and without the use of ice as a matrix, *Journal of the American Society for Mass Spectrometry*, **30 (11)**: 2380-2391.
20. S. Segato, G. Galaverna, B. Contiero, P. Berzaghi, A. Caligiani, A. Marseglia, G. Cozzi, (2017) Identification of lipid biomarkers to discriminate between the different production systems for Asiago PDO cheese, *Journal of Agricultural and Food Chemistry*, **65(45)**: 9887-9892.
21. J. P. Rafson, G. L. Sacks, (2021) Rapid analysis of volatile phenols from grape juice by immersive sorbent sheet extraction prior to direct analysis in real-time mass spectrometry (DART-MS), *Journal of Agricultural and Food Chemistry*, **69(41)**: 12344-12353.
22. E. Sisco, E. L. Robinson, (2020). Determination of ethanol concentration in alcoholic beverages by direct analysis in real time mass spectrometry (DART-MS), *Forensic Chemistry*, **18**: 100219.
23. X. Q. Li, H. M. Li, S. Xu, Y. Gao, Q. H. Zhang, Y. Zhang, M. Y. Feng, (2019) Rapid quantification of trace chloramphenicol in honey under ambient conditions using direct analysis via real-time QTRAP mass spectrometry, *Food Chemistry*, **276**: 50-56.
24. A. Zyglér, A. Wasik, J. Namieśnik, (2009) Analytical methodologies for determination of artificial sweeteners in foodstuffs, *TrAC Trends in Analytical Chemistry*, **28(9)**: 1082-1102.
25. X. Li, S. Li, H. Li, J. Wang, Q. Luo, X. Yin, (2021) Quantification of artificial sweeteners in alcoholic drinks using direct analysis in real-time QTRAP mass spectrometry, *Food Chemistry*, **342**: 128331.
26. J. López-Miranda, F. Pérez-Jiménez, E. Ros, R. De Caterina, L. Badimón, M. I. Covas, E. Escrich, J. M. Ordovás, F. Soriguer, R. Abia, C. A. de la Lastra, (2010) Olive oil and health: Summary of the II international conference on olive oil and health consensus report, Jaén and Córdoba (Spain) 2008, *Nutrition, Metabolism and Cardiovascular Diseases*, **20(4)**: 284-294.
27. R. Estruch, E. Ros, J. Salas-Salvadó, M. I. Covas, D. Corella, F. Arós, E. Gómez-Gracia, V. Ruiz-Guterrez, M. Fiol, J. Laptera, R. M. Lamuela-Raventos, L. Serra-Majem, (2013) Primary prevention of cardiovascular disease with a Mediterranean diet, *New England Journal of Medicine*, **368(14)**: 1279-1290.
28. L. Bartella, F. Mazzotti, G. Sindona, A. Napoli, L. Di Donna, (2020) Rapid determination of the free and total hydroxytyrosol and tyrosol content in extra virgin olive oil by stable isotope dilution analysis and paper spray tandem mass spectrometry, *Food and Chemical Toxicology*, **136**: 111110.

29. P. M. Eggink, (2013), *A Taste of Pepper: Genetics, Biochemistry and Prediction of Sweet Pepper Flavor*, Netherlands: Wageningen University and Research.
30. T. Guo, W. Yong, Y. Jin, L. Zhang, J. Liu, S. Wang, Q. Chen, Y. Dong, H. Su, T. Tan, (2017). Applications of DART-MS for food quality and safety assurance in food supply chain, *Mass Spectrometry Reviews*, **36(2)**: 161-187.
31. T. J. Mason, H. M. Bettenhausen, J. M. Chaparro, M. E. Uchanski, J. E. Prenni, (2021) Evaluation of ambient mass spectrometry tools for assessing inherent postharvest pepper quality, *Horticulture Research*, **8**: 160.
32. S. Kiani, S. Minaei, M. Ghasemi-Varnamkhasti, (2018) Instrumental approaches and innovative systems for saffron quality assessment, *Journal of Food Engineering*, **216**: 1-10.
33. G. M. Fiorino, I. Losito, E. De Angelis, M. Arlorio, A. F. Logrieco, L. Monaci, (2019) Assessing fish authenticity by direct analysis in real time-high resolution mass spectrometry and multivariate analysis: Discrimination between wild-type and farmed salmon, *Food Research International*, **116**: 1258-1265.
34. L. Watt, E. Sisco, (2021) Detection of trace drugs of abuse in baby formula using solid-phase microextraction direct analysis in real-time mass spectrometry (SPME-DART-MS), *Journal of Forensic Sciences*, **66(1)**: 172-178.
35. A. Khaled, J. R. Belinato, J. Pawliszyn, (2020) Rapid and high-throughput screening of multi-residue pharmaceutical drugs in bovine tissue using solid phase microextraction and direct analysis in real time-tandem mass spectrometry (SPME-DART-MS/MS), *Talanta*, **217**: 121095.
36. V. Kosek, L. Uttl, M. Jirů, C. Black, O. Chevallier, M. Tomaniová, C. T. Elliott, J. Hajšlová, (2019) Ambient mass spectrometry based on REIMS for the rapid detection of adulteration of minced meats by the use of a range of additives, *Food Control*, **104**: 50-56.
37. C. Chen, J. Wang, S. Yang, Z. Yan, Q. Cai, S. Yao, (2013) Analysis of perfluorooctane sulfonate and perfluorooctanoic acid with a mixed-mode coating-based solid-phase microextraction fiber, *Talanta*, **114**: 11-16.
38. J. Liu, H. Lu, Y. Ning, X. Hua, W. Pan, Y. Gu, D. Dong, D. Liang, (2022) Internal extractive electrospray ionization mass spectrometry for investigating the phospholipid dysregulation induced by perfluorooctanoic acid in Nile tilapia, *Analyst*, **147(17)**: 3930-3937.
39. G. Matthews, (2015) *Pesticides: Health, Safety and the Environment*. United States: John Wiley and Sons.
40. A. C. M. Moura, I. N. Lago, C. F. Cardoso, A. dos Reis Nascimento, I. Pereira, B. G. Vaz, (2020) Rapid monitoring of pesticides in tomatoes (*Solanum lycopersicum* L.) during pre-harvest intervals by paper spray ionization mass spectrometry, *Food Chemistry*, **310**: 125938.
41. B. K. K. K. Jinadasa, C. Elliott, G. D. T. M. Jayasinghe, (2022) A review of the presence of formaldehyde in fish and seafood, *Food Control*, **136**: 108882.
42. Q. Lin, J. Sun, Y. Wang, M. Ye, H. Cheng, (2022) Rapid determination of aldehydes in food by high-throughput reactive paper spray ionization mass spectrometry, *Journal of Food Composition and Analysis*, **114**: 104814.
43. P. Nemes, A. Vertes, (2012) Ambient mass spectrometry for *in vivo* local analysis and *in situ* molecular tissue imaging, *TrAC Trends in Analytical Chemistry*, **34**: 22-34.
44. G. Robichaud, J. A. Barry, K. P. Garrard, D. C. Muddiman, (2012) Infrared matrix-assisted laser desorption electrospray ionization (IR-MALDESI) imaging source coupled to a FT-ICR mass spectrometer, *Journal of the American Society for Mass Spectrometry*, **24(1)**: 92-100.
45. M. Sorahinobar, H. Soltanloo, V. Niknam, H. Ebrahimzadeh, B. Moradi, N. Safaie, M. Behmanesh, M. Bahram, M. (2017) Physiological and molecular responses of resistant and susceptible wheat cultivars to *Fusarium graminearum* mycotoxin extract, *Canadian Journal of Plant Pathology*, **39(4)**: 444-453.
46. M. Watanabe, H. Shimizu, (2005) Detection of Patulin in apple juices marketed in the Tohoku District, Japan, *Journal of Food Protection*, **68(3)**: 610-612.
47. M. de Champdore, P. Bazzicalupo, L. De Napoli, D. Montesarchio, G. Di Fabio, I. Coccozza, S. D'Auria, (2007) A new competitive fluorescence assay for the detection of patulin toxin, *Analytical Chemistry*, **79(2)**: 751-757.
48. P. Restani, (2008) Diffusion of mycotoxins in fruits and vegetables. In: *Mycotoxins in Fruits and Vegetables*, United States: Academic Press, pp105-114.
49. G. Da Silva Lima, G. F., Dos Santos, R. R. F. Ramalho, D. V. A. de Aguiar, J. V. Roque, L. I. L. Maciel, R. C. Simas, I. Pereira, B. G. Vaz, (2022) Laser ablation electrospray ionization mass spectrometry imaging as a new tool for accessing patulin diffusion in mold-infected fruits, *Food Chemistry*, **373**: 131490.