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REVIEW PAPER

Recent advances in the role of mass spectrometry in the analysis of food: a review

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Abstract

Mass spectrometry (MS) is an essential analytical technique in the scientific domains of chemistry, biochemistry, pharmacy, medicine, and many others. The technique is centrally implicated in the quality control of pharmaceuticals, foods, atmospheric and forensic analytes, polymers and the structure elucidation of unknown compounds. Foods are an intricate combination of carbohydrates, oils, vitamins, amino acids, polyphenols and nutrients that give a wide range of flavours and aromas. MS therefore due to its great selectivity and specificity has proven to be a very effective method for characterising and estimating food components. The main employment of MS in food-related applications was probably gas chromatography mass spectrometry which enables derivatized polar isolates and natural volatiles to be easily examined even if the mixtures should contain over 100 ingredients. The technique due to its capabilities and the ease with which it interacts with widely used chromatographic techniques is particularly useful for the analysis of food as regards nutritional content and adulterations. This review intends to present an overview of some recent applications of MS and its associated techniques in the analysis of food.

Keywords Gas chromatography-mass spectrometry · MALDI · Gas spectrometry · Electrophoresis · Immunoassays

Introduction

Technological procedures that are vital for the dictation of food and foodstuffs form the core of research in food functionality and safety [1]. The complex matrix of food composition detection which covers trace elements, diversity and multiple sources is difficult to be satisfactorily established by conventional analytical methods of GC, HPLC and simple instrumental analysis hence the popularity of MS in food composition dictation [2]. MS has seen wide applications in food analysis, biological analysis and protein identification. Furthermore, high and low melting point substances, volatile and non-volatile components, high and low ionic components are also analysed using MS-based techniques [3]. MS-based detectors give excellent sensitivity, selection, recovery, minimum interference and reproducibility [4]. Diverse food residues like meats, fruits, vegetables are analyzed using MS. MS combines powerful chromatographic separation in identifying and confirming the existence of target compounds [5]. It is a potential approach for the wide range of applications like elucidating the structures of compounds, investigating degradation mechanisms and

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identifying separated compounds [6]. GC-MS has particularly evolved as an important technique for food contamination analysis in recent years and is comfortably used for low molecular weight identification [7]. Moreover, MS and biology are now so entwined that an MS journal covers the fundamentals of proteomics research [8]. MS can also be used to determine the mass-charge ratio (m/z) of one or more molecules in a sample, so that the precise molecular weight of a sample's constituent parts can easily be ascertained [9]. Since MS can be used to determine the molecular weight of a molecule, it indirectly contributes to the identification of isotopes [10]. There are presently numerous fields (Geochemistry, Oil and Gas surveying chemical and petrochemical industry, environmental monitoring and others) that use mass spectrometers. Prior to being ionised, the samples are vaporised in order to transition them into the gas phase, positively charged molecules are produced when ionisation strips the molecule of its electrons. The electrical current flowing through the ions is then measured to find the sample's charge [11]. The central roles that mass spectrometry plays in food analysis are both qualitative and quantitative including recognition of substances contained in unidentified samples, testing for cancer [12], characterising proteins [13], evaluating drinking water, finding explosive residues, tracking medications used in clinical drugs development, recognising arson's use of fire accelerant [14] and etcetera. A summary of these MS roles are illustrated in Fig. 1.

Food is a necessity for all living organisms. Within the body, food serves three basic purposes. Its main function is to supply our body with vital nutrients such proteins, fats, carbohydrates, vitamins, and minerals and energy [15]. By influencing our dietary preferences through taste, smell, texture, colour and other factors, food also serves auxiliary purposes [16]. The third function of food is to modulate our body's physiological processes. These roles are ascribed to the distinctive chemical elements found in each food. The aim of this review is to provide a summary of the applications of MS in detecting adulterants in food samples. Some associated procedures to the MS technique are also discussed.

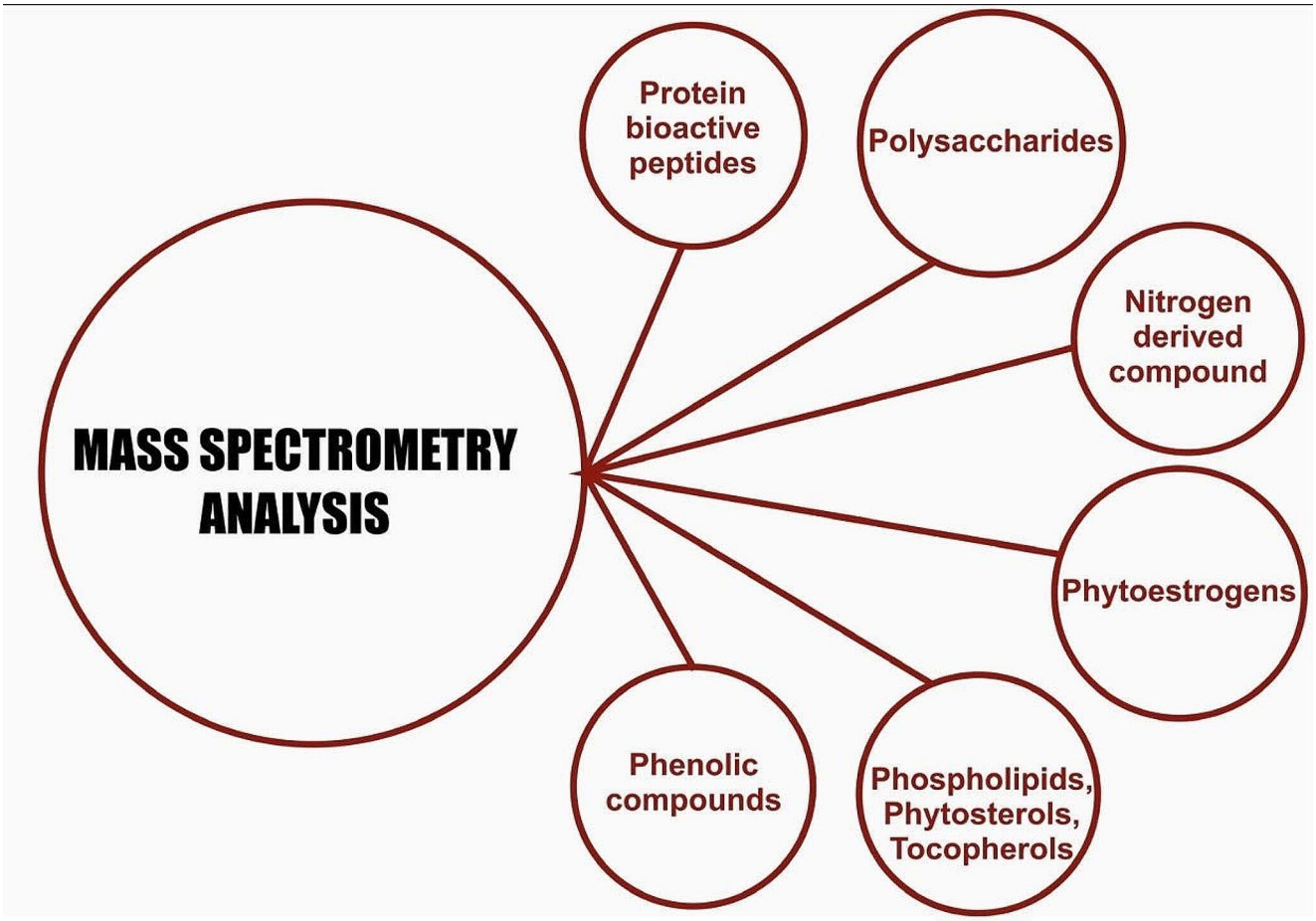

Fig. 1 Demonstrates the principal functions of mass spectrometry in food analysis [17]

Methodology

Scientific articles used for this review were retrieved from the following petroleum journals and databases covering the periods from 2010–2023: "Science Direct (https://www.sciencedirect.com/)", "SPIE Digital Library (https://www.spiedigitallibrary.org/?SSO=1)", "ACS publications (https://pubs.acs.org/journal/esthag)", SETAC Journals (https://setac.onlinelibrary.wiley.com/)". The keywords used in the searches were: "Mass spectrometry," " Gas spectrometry," " Electrophoresis," and "immunoassays."

The history of mass spectrometry

The history of MS dates back more than 100 years to the early investigations of gas excitations in charged environment [18]. The technique's core underpinnings were progressively improved during the ensuing fifty years. Gas chromatography's full potential as a highly precise, quantitative tool for exploring chemicals was realised following the pairing of the technique with mass spectroscopy in 1959. Isotopes were discovered as a result of MS's accuracy [19].

Historically, analytical procedures have been categorized based on how they operate. For instance, nuclear magnetic resonance (NMR), mass spectrometry (MS), polymerase chain reaction (PCR), infrared (IR), immunological techniques (e.g. biosensors), atomic spectroscopy (AS), high-pressure liquid chromatography (HPLC), capillary electrophoresis (CE), gas chromatography (GC), microwave-assisted extraction (MAE), purge and trap (PAT) and automatic thermal desorption (ATD) [20]. Each of these techniques although having its own benefits and limitations, offer particular information about the constituents to be examined in relation to their chemical and physical properties has its own benefits and limitations when it comes to food analysis [21]. It is outside the purview of this study to describe the plethora of analytical techniques frequently employed in food analysis. However, some information about the aforementioned sub-disciplines, intended to give little insight into the intricacy of the multitude of methodologies currently employed in food analysis will be provided. The advantages of MS; high selectivity, least response time, high sensitivity in food analysis within the past few years are worth noting [22]. Liquid chromatography (LC) and, to a lesser extent, capillary electrophoresis (CE) are two more separation techniques that have been commonly utilized in conjunction with MS for identifying and quantifying food constituents over the past ten years. For its inability to reach the recently established standards set by the food authorities such like the FDA, particularly with regard to the required number of identification points, single quadrupole MS has been limited to screening applications [23]. Conversely though, tandem mass spectrometry has consequently evolved into a generic tool for dictating and measuring analytes (mostly pollutants) in the analysis of food [24]. This review intends to provide a summary of the applications of MS and its associated procedures in detecting adulterants in food samples.

Principle of mass spectrometry

MS measures the specimen fragments or ions that occur from the breakdown of organic molecules. The fundamental concept requires the bombardment of organic matter [25] where a compound is attacked with a beam of electrons to generate positively charged ions. Peak intensity of each ion is represented by a mass spectrum. Ion detection is proportionate to ion abundance, ion differentiation is based on the m/z ratio, and ion separation is dependent on charge, mass, and velocity [26].

A diversified characterization of the elaborate food proteomes is now possible thanks to highly dynamic technological advancements in mass spectrometer instrumentation, which have increased sensitivity, resolution, and speed [27]. Additional advancements in this area include the involvement of orthogonal severance techniques, like ion mobility (IMS) and CE [28].

The LC HRMS techniques

Two primary methods are commonly used in making chemical outlines for food authenticity and quality while using LC-HRMS and LC-MS techniques in targeted and non-targeted studies [29]. Targeted methods are due to special characteristics of a particular group of determined compounds, or some set of chemical substances originating from the same line or at least having a similar structural characteristic [30]. The different LC-MS techniques; separation MS techniques, Direct MS techniques, desorption MS techniques are illustrated in **(**Fig. 2**).**

They can be carried out by both LC-HRMS and LC-MS (/MS) procedures. To address food authenticity and integrity, the levels of the targeted components are subsequently utilized for food markers [31]. Generally speaking, this method necessitates an earlier quantization stage employing standards for every component that is being targeted [32]. The quantification of certain compounds may however be challenging when food products are involved because as mentioned earlier, they have very complicated matrices [33].

Since food sample matrices are complex and contain a wide range of biologically active composites having varying physicochemical properties and structures, LC-MS/MS

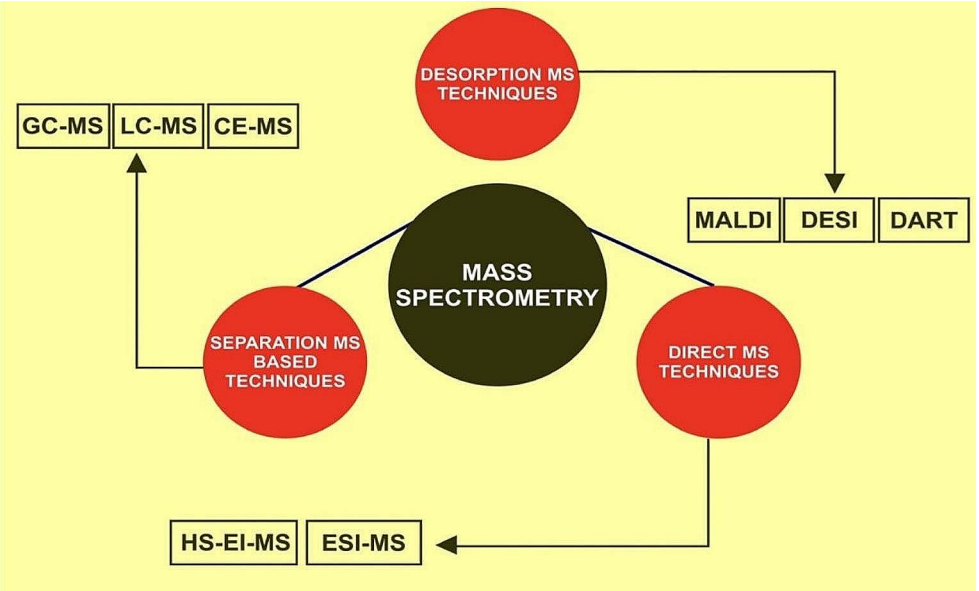

Fig. 2 Different techniques involved in mass spectrometry [34]

and LC-MS are shown to be valuable procedures in food authenticity and integrity analysis [24 h] although, a more selective and sensitive technique like LC-HRMS is usually required. Because they ensure a clear identification of the elemental composition of target compounds and enable their separation from other co-eluting isobaric compounds, high-precision mass measurements and precise mass measurements are becoming the most effective methods for making analysis of food samples [35]. A selection of applications using targeted LC-HRMS techniques for food integrity and authenticity are summarized in Table 1.

Polyphenols are often utilized as biological markers in targeted LC-HRMS techniques, taking into account a single class of polyphenols or a larger collection [36]. Even in the case of plant-based food products, polyphenols may not always be the optimal solution to the analytical puzzle; alternative substances may be used instead [37]. Investigated the occurrence of bijou biologically active lipids which occur as markers to distinguish between different species of rice, while [38] studied a categorization of cocoa from various geographic regions and the fermentation status using low molecular weight carbohydrates.

Ionization technique

A potential analytical technique for figuring out and visualizing the structural dispersal of particular chemical constituents based on the value of their molecular weights is mass spectrometry imaging (MSI) which is sometimes known as imaging mass spectrometry (IMS). In essence, MSI is an analytical technique that is two dimensional has capacity to identify whole particles in tissues or tissue slices even without the need for separation, extraction, or purification [39]. The general MSI process is rather straightforward [40]. As shown in (Fig. 3), the overall overview of the workflow for MSI and the ionization processes of the most popular ways utilize it. Depending on the matrix type, thin-section samples are placed on a plate, ions are then created and identified by a mass spectrometer through the use of an ion beam, a laser or charged solvent droplets [41]. Each and every data point yields a mass spectrum. Every single mass occurrence is represented as a scaled fake color in a single dataset that is created from these data. Under MS/MS, target molecules on tissues can be seen and recognized. MALDI, SIMS, and DESI are some ionization processes.

LC-MS

Liquid chromatography has potential for analyzing common nutritional ingredients in food and feed [42]. There are some parallels between food and feed when it comes to using LC for analysis. Selection and examination of analytes pertinent to the two fields was made by the authors drawing from years of exposure to application chemistry in food and feed investigations [43]. The common challenges and unique characteristics of every analyte which they present for the application of LC techniques across several phases of technique development (chromatographic separation, detection and sample preparation) are covered in this study [44].

LC-based analytical techniques have been applied for food product characterization in a number of inventive research efforts. By analyzing the hypoglycemic potentials, composition of phenols and the antioxidant capacity of native Colombian fruits and their byproducts, A scholar, characterized the products in samples of the species from *Solanaceae* family and chlorogenic acid was shown to be

Table 1 A selections of applications using targeted LC-HRMS techniques for food and chromatographic separation

Compounds	Mass spectrometry and chromatographic separation	Data analysis	References
Derivatives of Kaempferol	Ascentis Express Fused-core C18 column (100 × 2.1 mm, 2.7 µm) Gradient elution (0.4 mL·min − 1): A) water with 0.1% formic acid (B) acetonitrile with 0.1% formic acid H-ESI (−) Q-TOF (full-scan mode 100–1700 m/z)	-	[45]
Polyphenols	Waters XTerra MS C18 column (250 × 4.6 mm, 5 µm) Gradient elution (0.8 mL·min − 1): (A) water with 0.5% acetic acid (B) water:acetonitrile 1:1 (v/v) with 0.5% acetic acid H-ESI (−) Q-TOF (full-scan mode 50–1500 m/z)	PCA, ANOVA AND SLDA	[28]
Polyphenols (berry fruit juice)	Phenomenex C18 column (100 × 2.1 mm, 2.6 µm) Gradient elution (0.3 mL·min − 1): (A) water with 0.1% formic acid (B) methanol with 0.1% formic acid H-ESI (±) Q-TOF (full-scan mode 50–1000 m/z)	PCA-DA and OPLS-DA	[46]
Polyphenols (red spice paprika)	Syncronis C18 column (100 × 2.1 mm, 1.7 µm) Gradient elution (0.25 mL·min − 1): (A) water with 0.01% acetic acid (B) acetonitrile H-ESI (−) LTQ-Orbitrap (full-scan mode 100–1000 m/z)	PCA	[47]
Low molecular weight carbohydrates (cocoa beans)	BEH X-Bridge Amide column (150 × 4.6 mm, 3.5 µm) Gradient elution (0.4 mL·min − 1): (A) water with 0.1% ammonium hydroxide (B) acetonitrile with 0.1% ammonium hydroxide H-ESI (+) TOF (full-scan mode 50–1200 m/z)	PLS-DA, PCA and ANOVA	[48]
Polyphenols (cranberry-based extracts)	Ascentis Express C18 column (150 × 2.1 mm, 2.7 µm) Gradient elution (0.3 mL·min − 1): (A) water with 0.1% formic acid (B) acetonitrile with 0.1% formic acid H-ESI (−) Q-Orbitrap (full-scan mode 100–1500 m/z)	PLS and PCA	[49]
Small bioactive lipids (rice)	Acquity UPLC BEH C18 column (50 × 2.1 mm, 1.7 µm) Gradient elution (0.5 mL·min − 1): (A) water with 10 mM ammonium hydroxide (B) acetonitrile:isopropanol 90:10 (v/v) H-ESI (−) Q-TOF (full-scan mode 50–1200 m/z)	PCA and OPLS-DA	[50]

the predominant constituent using ultra-high performance liquid chromatography-high resolution mass spectrometry (UHPLC-HRMS), and an Orbitrap analyzer of mass [51]. Additionally, the peels of *Solanum quitoense* demonstrated the highest antioxidant capacity [52]. *Passiflora tripartita* fruits demonstrated the highest antioxidant effects among the samples from *Passifloraceae* family. This was based on the ratings of the Global Antioxidant Score (GAS) and the relative antioxidant score (RACI).

These researchers emphasized that the waste portions yielded some auspicious results and so their integration with other functional constituents for the manufacture of nutraceuticals intended for people with disturbances in the metabolism of glucose should be taken into consideration [53]. The impact of far-infrared (FIR) radiation and artificial LED light on isoflavones, phenolic compounds and the antioxidant activity of soybean (*Glycine max*) sprouts was also assessed by [54] in which the identification of six isoflavones: glycitin, genistein, glycitein, genistin, daudzin and daidzein, was done by the use of LC. In the growth chamber, the soybean sprouts were exposed to green (530 nm) LED light and artificial blue (470 nm) and florescent light (control) for three to seven days following sowing [55].

Using LC-HRMS, interesterification indicators triacylglycerol regioisomers in confectionary oils were identified and determined [56]. To get lipids with the right qualities for the confectionery business, it's critical to regulate the degree of positional isomer formation [57]. When the amount of double bonds in a triglyceride molecule is the same and their location is the sole variation, separating triacylglycerol regioisomers can be difficult [58]. The authors' goal was to achieve chromatographic resolution through LTQ-Orbitrap analyzer with atmospheric pressure chemical ionisation (APCI) that would enable robustness in terms of repeatability and reproducibility and allow reliable qualitative and

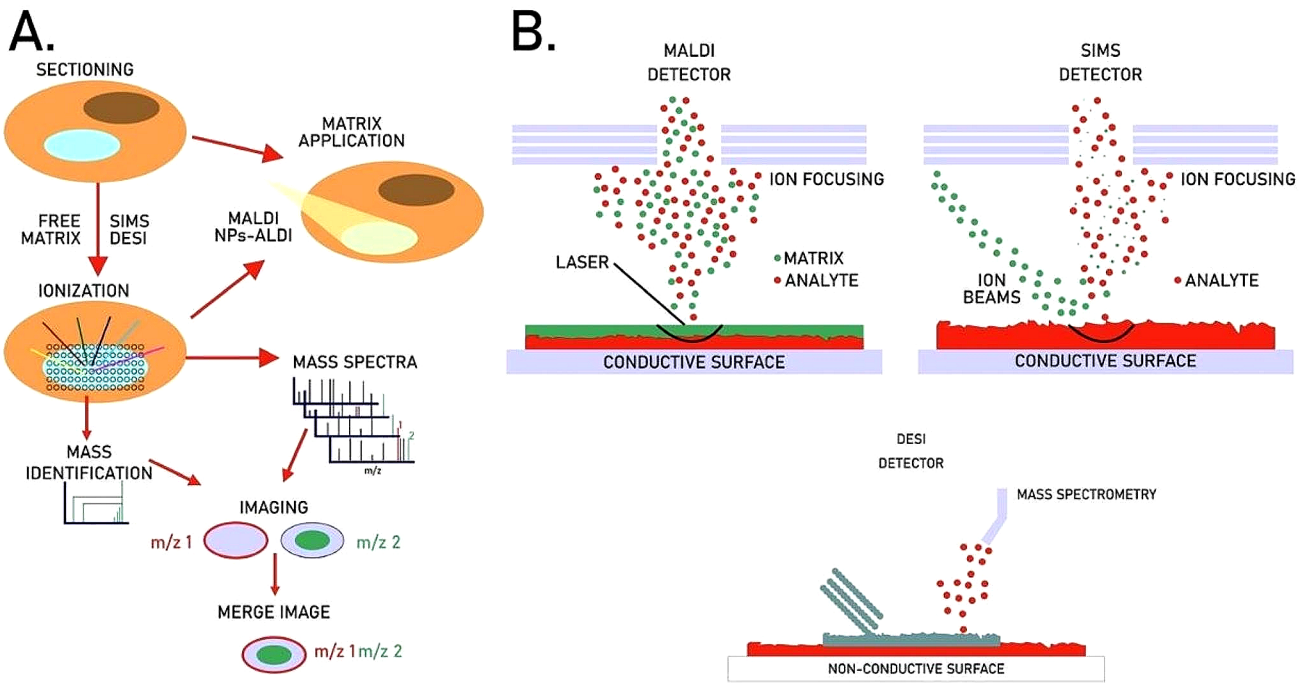

Fig. 3 An illustration of the work flow of mass spectrometry imaging and ionization process [59]

quantitative evaluation of triacylglycerol positional isomers within short retention times [60].

Instrumentation of mass spectrometry

In order to trace the amount of elemental isotopes and analyse the atomic weight of various elements, the first mass spectroscope was created [61] although analysis of bioactive chemicals using a mass spectroscope were only made feasible by the 1950s through the development of methods for vaporising organic molecules. An analyzer, detector, data processor, and ionisation source make up MS [62]. The ions are formed and their paths are maintained at a specific speed by maintaining the analyzer and detector in a vacuum, which prevents air molecules from colliding with the ions [63]. Upon being pumped into the instrument via the inlet, the sample is ionised within the ionisation chamber. Then, ionised species (cations/anions) are separated in the analyzer, resolving the ions according to their m/z ratio [64]. Ultimately, detectors pick up on these ions, and for every identified ionic species, mass spectra are produced that show the relative abundance [65]. **(**Fig. 4**)** displays a schematic illustration of various mass spectrometry techniques.

Utilization of mass spectrometry in food science and related fields

Biological, pharmacological, medical, and criminal investigations are just a few of the disciplines where MS technology has been used [66]. While many effective applications have been created in these domains, there aren't many examples of it being used in food science but as the need for imaging of food products grows, so also grows the number of these investigations [67].

The adulteration of food has a long history that stretches back to the early days of trade [68]. Food adulteration is typically done to boost volume, cover up the presence of lower-quality ingredients, and substitute real ingredients for the seller's financial benefit [69]. Nonetheless, it is imperative to acknowledge that the intentional tampering with food and its false representation to mislead ultimate consumers is illicit globally [70]. This not only has detrimental effects on the economy but also poses significant health risks when illicit substances are incorporated to manipulate the organoleptic quantities of the final food product or instances when the added substance is able to trigger allergic reactions [71]. Because food adulteration has become more sophisticated, it is necessary to create novel analytical procedures to ensure food authenticity and integrity [72].

The extensive range of components that may be available makes food product analysis challenging, this in addition to the diversity and complexity of sample matrices [73]. Apart from concentration levels, food components also vary

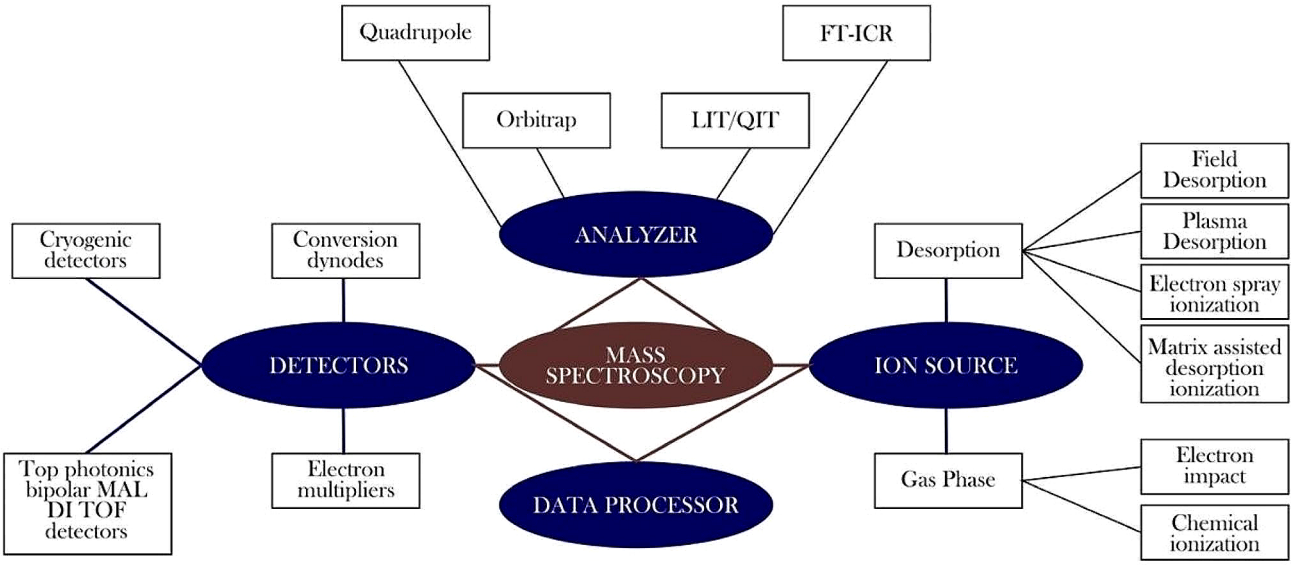

Fig. 4 A schematic illustration of various mass spectrometry

in polarity and structure, ranging from those present at gram per kilogramme and cutting across the ones of trace amounts (low ng/kg and µg/kg) [74]. All of these should be taken into account when choosing which analytical method to use. In order to create an analytical technique for food authenticity and integrity analyses, it is necessary to take into account the extraction methods also for example, sample treatment, separation and determination methodologies as well as recognition and confirmation tactics [75]. Liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) is a modern method employed for this [76].

Lipids

From several aspects of MS analysis, lipids differ somewhat from biomolecules like peptides, oligonucleic acids, and oligosaccharides. Lipids are both hydrophilic and hydrophobic molecules [77], with the former characterized by a high number of hydrogen atoms or –CH2 groups in the molecule that contribute significantly to a loss of mass measured as the composition of the actual mass that follows the integer mass of the species with the molecular ion [78]. Chemical structural properties may frequently be extracted by collision induced dissociation (CID); nevertheless, the lipid's gas-phase ion chemistry encodes this information.

Finding out where metabolites are located in food items or biological specimens can be helpful in evaluating the nutritional roles of biological systems, understanding how to control their quality, and understanding end-use applications like food processing [79]. Food products have seen a lot of use in lipid imaging since lipids make up a significant amount of organic molecules, are found inside cells, and are simple to identify using different types of MS, particularly MALDI-MS [48]. Lipidomic studies frequently employ matrix-assisted laser desorption/ionization (MALDI) mass spectrometry. MALDI produces ions from lipids with little fragmentation by using a laser energy-absorbing matrix [80]. The improvements in MS, which were mainly realised a decade or more ago, have led to notable breakthroughs in our understanding of lipid biochemistry in recent applications of MS to lipid study [81]. Applications of MS in determining the quality of cooking oil were examined. As per the review, mass spectrometry can be an effective tool for analysing characteristics that affect cooking oil quality, such as cyclic aromatic hydrogen compounds, free fatty acids, aldehydes, ketones, epoxides, polymerides, and DAG composition [82].

The availability of more advanced mass spectrometers in biochemical laboratories for the study of lipid biochemistry has been on advancement for lipid mass spectrometry, which may not have been completely recognised [83]. One instance in particular was the application of MS to further our comprehension of the biological function of the gene product SRD5A3, which was formerly identified as steroid 5α-reductase type 3 and its participation in a severe genetic glycosylation problem that affects humans [84]. The affected individuals who lacked this gene had higher plasma levels of polyprenol lipids than dolichols, according to the researchers [2]. also defined SRD5A3 as a NADPH-dependent reductase that saturates the α-isoprene unit of polyprenols to yield the dolichol structure. The Golgi apparatus needs dolichols for N-linked glycosylation, hence the loss of this rate-limiting enzyme decreased the total amount of glycosylation of essential proteins for healthy operation

[85]. The availability of sophisticated instruments for lipidomic research in lipid biochemists' laboratories has led to the development of an MS approach for the analysis of dolichols [83].

Carbohydrates

When carbohydrates are analysed using MS, various details are revealed, including molecular mass, sequence and constituent simple sugars, linkage type, stereochemistry of the monosaccharide units, anomericity of the glycosidic bond, branching positions and types, modifying groups, types of modifying groups, and monosaccharide types [86]. The mass-to-charge ratio of the gaseous ions created during the conversion of the carbohydrate molecules under vacuum is then determined. Their initial identification is revealed by the mass-to-charge ratio, and this is further clarified by breaking the ions apart through a process known as collision-induced dissociation [87]. Virtual Expert Mass Spectrometrist (VEMS) v3.0 is programmed with a mass list that combines the masses acquired in the first stage of MS with those obtained in the subsequent stages (MSn) [51]. Tropical plants such as sugar cane and maize/corn use a photosynthetic process called the C4 pathway to create sugars [88]. The C3 pathway is a distinct method of photosynthesis used by plants to produce the nectar that bees gather. The proportion of the naturally available carbon-12 to carbon-13 isotopes varies measurably among sugars derived from the C3 and C4 routes. This is been utilized for detecting adulterations in honey by C3 or C4 sugars by the of mass spectrometry and chromatography for isotope analysis [89].

Protein

Using mass spectrometry to investigate proteins is otherwise termed protein mass spectrometry. It is a crucial technique for accessing the characterization and mass measurement of proteins [90]. MS is utilized in dictating proteins and their post-translational alternations, in functional relationships, in the clarification of protein complexes and their subunits as well as in the field of global protein measurement proteomics [91]. The technique is also employable in identifying the interactions existing between different membrane bound proteins and even in localizing proteins to the various vesicles [92]. Electrospray ionisation (ESI) and MALDI are the principal techniques used in MS to ionize proteins [93]. Tandem mass spectrometry and other mass analyzers are employed in conjunction with these ionization procedures. Proteins are typically analyzed using one of two methods: either a "top-down" strategy, in which proteins are examined whole, or a "bottom-up" scheme, where proteins are first broken down into fragments. Larger peptide fragments are analyzed using an intermediate "middle-down" strategy, which is also occasionally employed [94]. Some advantages and limitations however are peculiar to each of these strategies. The top-down strategy of protein analysis for instance is of benefit in that it is useful for locating and characterizing post translational modifications (PTMs), that it has potential access to the complete protein sequence and the fact that protein digestion does not consume time with top-down strategy as with bottom-up strategy. The strategy is however limited by the following; first, it does not work well with intact proteins that are larger than 50 kDa, and secondly the very complex charged spectra generated by multiply charged proteins limit the approach to isolated proteins, or simple protein mixtures at most. Finally, the favoured instrumentation (hybrid ion trap FT-ICR or hybrid ion trap–orbitrap) are expensive to purchase and operate. The bottom –up strategy on the other hand has the advantages of been the most mature and most widely used technique in the identification and characterization of proteins. Secondly, it uses an on-line multidimensional capillary HPLC-MS-MS to identify proteins in digests obtained from extremely complex mixtures like cell lysates and finally, there is the ease of accessing the commercial instruments with the control software and bioinformatics' tools optimized for bottom-up techniques as they are available from several vendors. The technique however shows the limitations of much time consumed in protein digestion, narrow chromatographic peak widths that compromise the acquisition of adequate MS-MS information during elution, incomplete solubilisation and incomplete lysis of proteins [95].

Milk and protein products

By employing LC-MS, it was possible to detect the addition of soy and animal milk adulterants to human milk even though the concentrations present were below the 5% accepted level. Milks are stripped of their proteins and fats, meaning that just a portion of the milk's contents are taken into account for detection. In order for the samples to react with the metabolites, an isotope labeled indicator is usually applied [96]. Associating peaks with components, two distinct isotope labels—one with pure components and the other with a mixture are utilized [97].

Using protein as the target component, UPLC-QTF MS was able to identify adulteration of milk with soybean and pea powder at as low as 1% [98]. Using chemometric instruments, detection was non-targeted. With UHPLC-MS/MS, a technique for measuring the amount of whole milk powder and cow's whey in sheep milk or goat products, such as formulas for babies was produced [99]. Based on software's prediction of the presence of signature peptides given intact protein sequences, the detection was conducted. The

product's foreign protein detection limit ranged from 0.01 to 0.05%. The development of MS allowed for the detection of the unscrupulous addition of cow whey in goat, sheep and buffalo ricotta cheeses. Using whey protein peptide identifiers, the other three species may produce ricotta cheese only as little as 0.5% as bovine whey [100]. Many milk water and proteins isolated from unadulterated milk that came from Australia and New Zealand, Australia, France, Germany, China and the USA in order to pinpoint the location of the milk's origin. Next, element analyzer-isotope ratio mass spectrometry (EA-IRMS) was used to determine the δ13C and δ15N values of the isolated proteins and the δ2H and δ18O values of milk water [101]. The findings suggested that utilising the analytes δ13C, δ15N, δ2H, and δ18O will enable distinguishing pure milk from these areas. It is now possible to determine whether expensive milk, such as buffalo milk, has been compromised with less expensive cow milk thanks to the identification of species-specific protein marker molecules in milk by LC-MS [102]. Additionally, protein markers specific to honey have been discovered. These markers can be utilised independently or in combination with those identified by GC-MS to determine whether the honey has been tampered with [103].

Vitamins

Vitamins are mostly found in food and are necessary for preserving and enhancing human health [104]. It is crucial to measure the percentage of vitamins soluble in water that are present in common food items in order to comprehend the effects of vitamin consumption on the health of people and to give regulators the details they need to set appropriate measures [105]. There are many methods in the literature for analysing water-soluble vitamins based on LC and MS, however most of them only allow the detection of one vitamin or concentrate on fortified foods or dietary supplements [106]. The quantitative amount of minerals in food is estimated using vitamin and mineral analysis. According to solubility extent, vitamins are classified into two: fat-soluble and water-soluble [107]. Technologies such as chromatography, electrophoresis, immunology, spectrophotometry, fluorometry, and microbiology are frequently employed for vitamin analysis in food and they are thus employed because of their good selectivity, simplicity, rapid response and specificity [108].

Chromatographic method

Several chromatographic procedures; comprising liquid chromatography (LC), gas chromatography (GC), ultra high performance liquid chromatography (UHPLC) and high performance liquid chromatography (HPLC) have been employed for the analysis of vitamins. Numerous detectors also, such as mass spectrometry (MS), fluorescence (FL), electrochemical (EL), ultraviolet/visible (UV/Vis), and fluorescence (FL), can be combined with these chromatographic procedures [109]. Adapting chromatographic procedures gives several options for operating food vitamin characterization.

Electrophoresis method

Using CE technique, a variety of water-soluble vitamins found in food and drink can be identified and separated. The method shortens the time needed to prepare samples and lowers reagent prices. Micellar electrokinetic capillary chromatography (MEKC) and capillary zone electrophoresis (CZE) are the two most often utilised CE techniques in food analysis [110].

Immunoassay method

The examination of vitamins B12 and D has been done using immunoassays, such as the enzyme-linked immunosorbant assay, which is a dependable technique for measuring vitamins [111].

Spectrophotometric assay

A vitamin's ability to react with a chromogen to change colour is the basis of the spectrophotometric assay. A spectrophotometer can detect the intensity of colour, which is proportionate to the content of vitamins [112]. Determining vitamin C is the primary function of the spectrophotometric assay.

Florometric test

The foundation of the fluorometric test is in the fact that some vitamins can react with a fluorophore to produce fluorescence, and that the amount of fluorescence produced is directly correlated with the concentration of the vitamin [113].

Microbiology method

The concentration of particular microbes like *Lactobacillus plantoides* and *Lactobacillus casel* which grow based on certain vitamins, can be measured using microbiological methods. Normally, a negative control with no vitamins at all is utilized. Microbiological tests have a high degree of specificity and sensitivity. They are frequently used when analysing vitamins that are soluble in water.

Since it is not constrained by the majority of the issues that immunoassays have, LC-MS/MS is regarded as the gold standard for measuring vitamin D metabolites [114]. Moreover, LC-MS/MS has the benefit of measuring many metabolites at once. Though LC-MS/MS technologies have many benefits, there are analytical problems also. Ion suppression, sample type, protein precipitation, analyte extraction, derivatization, chromatographic separation, ionisation, and mass spectrometer capabilities. Other significant factors influencing the accuracy of data are calibration, standardisation, and the application of internal standards [115].

Sterols

Sterols are a significant class of chemical compounds that are present in fungi, plants, and animals with the most well-known animal sterol been cholesterol [116]. Plant-derived phytosterols, also referred to as phytosterols, have been demonstrated in clinical trials to inhibit the intestinal sites where cholesterol is absorbed and lower the plasma cholesterol level linked to low-density lipoproteins (LDL), both of which contribute to the reduction of cholesterol in humans [117]. Certain research indicates that they possess anti-inflammatory, anti-cancer, and antithrombotic properties. The US Food and Drug Administration has authorised its usage as a food additive due to these reasons. Numerous classes of vegetable oils, including Indian rice bran, sunflower, olive, and other plants have had sterol analysis done on them [118]. Using an optimised GC-MS approach, it was possible to find phytosterols in enriched milk and yoghurt [119]. Meanwhile, GC-FID and GC-MS were used to assess the total, free and esterified phytosterols in tetraploid and hexaploid wheat [120]. GC was also used to analyse the lipid content of Italian walnuts and to chemically characterise the lipids from crustaceans that have the potential to be used for skin care, including burns and inflammations [121].

Applications of mass spectrometry in the analysis of endogenous food toxins and exogenous food contaminants

Toxic substances that are naturally created by living things are known as natural poisons. The organisms themselves are not harmed by these toxins, but when consumed by other animals, including people, they may be poisonous. These chemical compounds vary in toxicity and biological function, and they have a variety of structures. Certain toxins are naturally created by plants as a defence against insects, predators, or microbes. They can also be produced as a result of a mould infestation or as a reaction to other environmental stresses like drought or excessive humidity [122]. Natural poisons derived from plants include lectins, furocoumarins, pyrrolizidine alkaloids, cyanogenic glycosides, and glycoalkaloids. These naturally occurring toxins of plant origin are extremely dangerous to animals and humans as they can have a wide range of negative health impacts [123]. Chemical compounds found in food are frequently analysed using GC-MS and HPLC-MS techniques. Volatile organic molecules, such as vitamins, amino acids, and fatty acids, are frequently used after derivatization with particular reagents, GC-MS is utilised to detect and identify these compounds [48]. It is also critical to keep an eye out for endogenous food toxins or exogenous toxic element contamination in order to maintain food safety and quality requirements and this is achieved by the use of HPLC-MS for the toxic analysis. Green potatoes for instance naturally contain solanaceous glycoalkaloids, α-solanine and α-chaconine toxins which give the potatoes their bitter flavour. Food poisoning may result from consuming green potatoes that contain these poisons [124]. used MALDI-MSI to show that these compounds are localised in the periderm, germ's centre and periphery, but not in the tuber or close to the cambium following bud break. Furthermore, unwanted chemicals for human consumption can build in grains and vegetables during production. Arsenic as another example is a poisonous substance that exists naturally in the environment and can get into the soil, water, or air and then into planted food sources so that consuming specific foods like wheat, rice, maize e.t.c might result in major health issues. The FDA therefore keeps an eye on and controls the amounts of arsenic in these foods. With the aid of mass spectrometry imaging (SIMS-MSI), [125] were able to show the subcellular distribution of arsenic in rice seeds and wheat grains, revealing that the endosperm's subaleurone cell protein matrix contains a higher concentration of arsenic. These instances of MSI technology in action show how effective and specialised the platform can be in determining the distribution of harmful compounds in food. Food hygiene includes the identification of pathogens, poisons, and byproducts in food that has been spoiled by microbes. It has been possible to identify volatile molecules connected to a specific microbial infection by profiling phytochemicals from food products using GC-MS. According to [126] volatiles that were exclusively produced in the presence of a specific microbe were found in infected beef samples following the application of this metabolomic technique. Among the many tainted meat samples, more than 100 metabolites were accurately identified, and their linkages were examined. It was discovered that the volatile component profile of the contaminated and control meat samples differed considerably. This fundamental method can also be used in conjunction with chemometric techniques to accurately interpret the outcomes of the metabolic profiling. Indeed, [127] employed

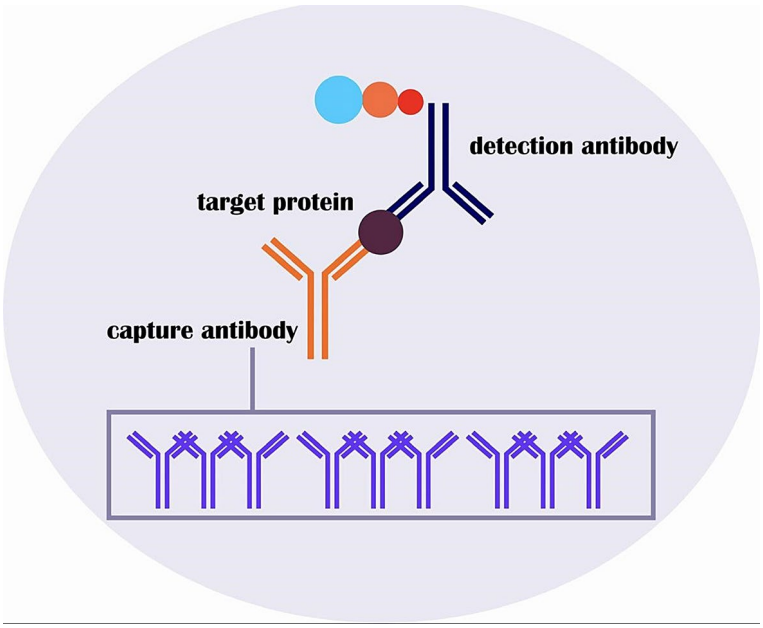

Fig. 5 Showcases the ELISA test used to detect antibodies or mycotoxins of food analysis in mass spectrometry

principal component analysis (PCA) to discern significant areas within the GC-MS chromatogram that ensued from the volatile organic chemical profile of naturally deteriorated pork and pork tainted with Salmonella typhimurium. Peak deconvolution was used to boost the peak's confidence after the crucial chromatogram regions had been identified.

Mycotoxins

Mycotoxins are toxic secondary metabolites that are often found in food and are created by fungi like *Fusarium*, *Penicillium*, and *Aspergillus*. The global concern is their presence in hot processed meals. These naturally occurring substances are extremely harmful to people and can cause hepatotoxicity, genotoxicity, immunosuppression, nephrotoxicity, teratogenicity, and cancer when they enter the body through the food chain [128]. Enzyme linked immunosorbent assay (ELISA) is an antibody based assay that is commonly used as a detector for mycotoxins in food analysis as seen in **(**Fig. 5**).** The application of MS to natural mycotoxin analysis in food is also outlined in **(**Table 2**).** Numerous agricultural goods, including grains and nuts, contain mycotoxins. As a result, mycotoxin analysis has received a lot of interest. There are various types of mycotoxins as demonstrated in **(**Fig. 6**)**. The current most popular method for detecting mycotoxins in food is LC-MS, particularly when examining grains and grain products, since it allows for more precise quantification of the toxins [129].

Similarly, quantitative analysis and mycotoxin screening are aided by GC-MS. The mycotoxin analysis was summarised and its properties were analysed by Singh et al. using both conventional (HPLC) and sophisticated (LC–MS

Table 2 The utilization of ms to natural mycotoxins analysis in food

Food stuffs	MS	Analytes	Sample preparation	LODs	References
Nuts	UHPLC-MS/MS	AFB1, AFB2, AFG1, AFG2, OTA	Grinding	-	[130]
Honey	HPLC,LC-MS/MS	DON, HT2, T2, OTA	Drying	0.0004-0.012ng/mL	[131]
Wheat flour, peanut, spice, chilli pepper	LC-MS/MS	AFB1, AFB2, AFG1, AFG2, OTA	homogenization	-	[132]
Cereal products	LC-MS	Mycotoxins	-	-	[133]
Table ready food	LC-MS/MS	Aflatoxin B1,B2, G1,G2, ochratoxin A	Homogenization	0.01-2. ug/kg	[134]
Soy-based burger	UHPLC-Q- Orbitrap HRMS	DON, 3-ADON, 15-ADON, DAS, HT-2, T-2, ZON, OTA, AFM1, AFB1, AFB2, AFG1, AFG2, FB1, FB2	-	21mycotoxins, 12 isoflavones	[135]

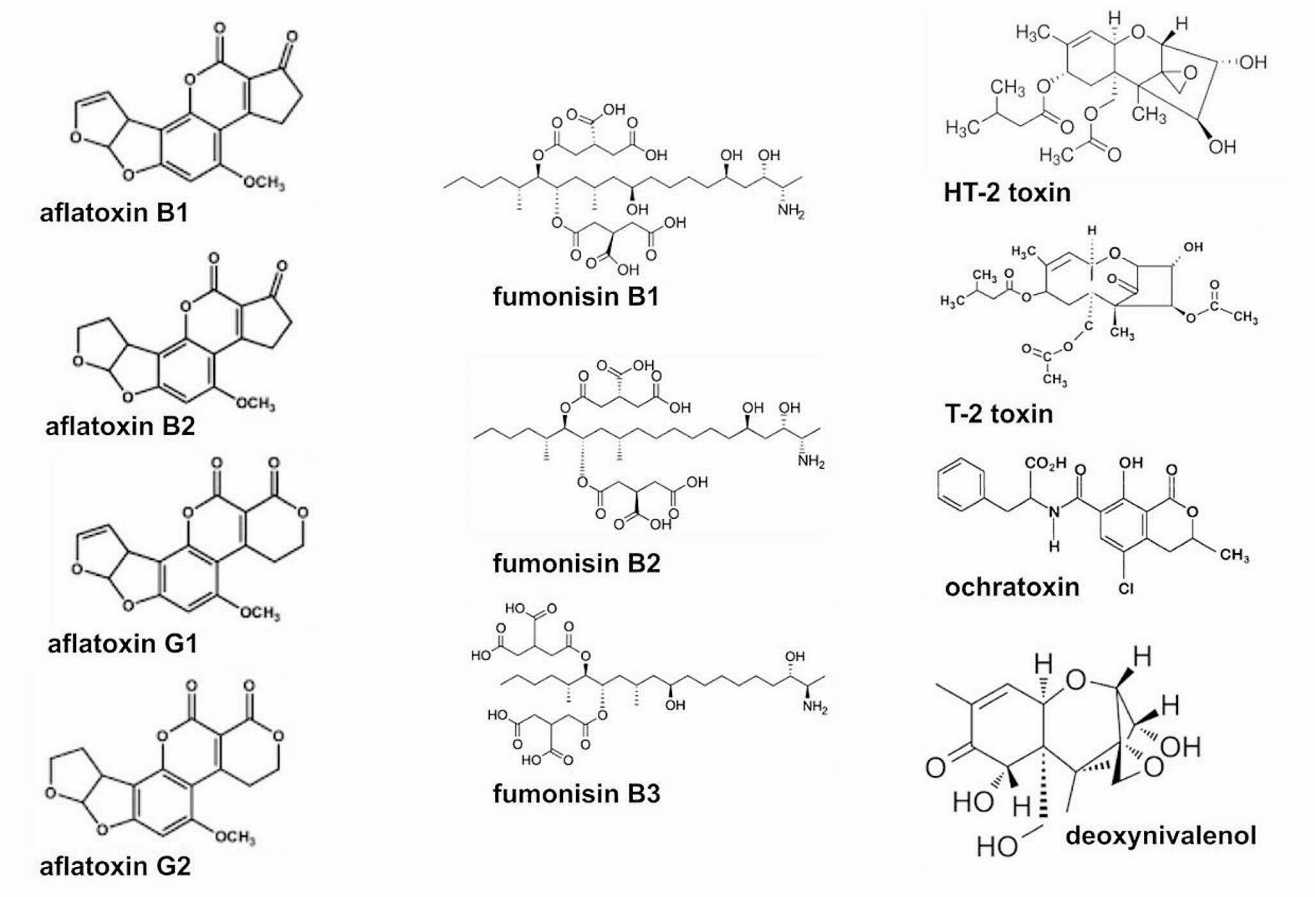

Fig. 6 Illustrates the different types of mycotoxins [136]

and GC–MS) methods. The outcome demonstrated the superior sensitivity of LC-MS and GC-MS over traditional techniques. Mycotoxins in cereal products were covered in another study, which also provided a summary of the most often used detection methods, such as LC-ESI-MS. QuEChERS, a minimal clean-up technique that is fast, easy, cheap, systematic, long-lasting, and certain was used for sample pre-treatment [137]. Cereals > cornflakes > bread > breakfast > wheat > baby products > pasta > other products was the order in which the number of trials for cereal products was determined in this work [138]. This suggests that there has been a lot of interest in the research on mycotoxins in cereal products. Research has indicated that the LC-MS/MS technology has been utilized to analyse 120 food matrices for mycotoxins [139]. LC-MS/MS was utilized by a researcher to concurrently identify mycotoxins in samples of pepper, wheat flour, pistachios, peanuts, raisins, and spices. The Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) was used for sample pretreatment, and recoveries ranged from 81.94 to 101.67% [140]. Similarly obtained satisfactory findings from their analysis of several mycotoxins in finished food products using stable isotope dilution and LC–MS/MS. Additionally it was found in bee products are which are crucial components of diets for both adults and children and help strengthen immunity mycotoxin. In healthy people, the potential health consequences of bee products tainted with mycotoxins remain unknown.

In current times, focus on food safety and quality has increased among the general public. As a result, there is a growing need for the creation and use of more effective and potent instruments to assess food pollutants of chemical or microbiological origin. There are several food-borne pathogens and residues related to food safety which are present today. These include pesticides, veterinary medications, ecological pollutants, growth-promoting chemicals, impurities that arise while at food processing, and others from the materials for packaging.

The quality of food refers to the properties of food, including constituents like fats, proteins, carbohydrates, vitamins, and carbohydrates, as well as additions like flavouring, colour, and odorants, preservatives, and antioxidants. Food quality and safety are strongly intertwined, particularly when it comes to some potentially food borne illnesses that may arise from consuming particular foods. The governing authorities of several nations expanded the quantity of pertinent regulations and requests for the

authentication of food as a result of their increased global attention. Because of its benefits of high throughput, high sensitivity and selectivity, MS is been regarded as one of the techniques most suited and is frequently employed quality analysis for food-safety [141]. MS can now analyse hazardous or harmful substances in food at extremely low quantities more precisely, quickly, and accurately thanks to recent advancements in the field. Methods that combine MS with separation techniques, like GC-MS and liquid chromatography LC-MS, have demonstrated excellent automation ease and food analysis appropriateness. For the purposes of analyte screening, identification, and structural elucidation, a variety of mass analyzers are employed in conjunction with GC and LC. Excellent-resolution mass spectrometry (HRMS), while potentially more expensive to acquire and maintain, provides excellent selectivity and sensitivity for the analysis of complicated materials as well as the potential identification of unknown chemicals. HRMS enhances detection and identification through precise mass measurements. HR tandem MS, also known as MS/MS or MSn, offers a wealth of structural information with fewer extraction or separation processes needed [142]. Emerging MS methodologies and omics applications (proteomics, lipidomics and metabolomics) have been developed as a result of enhanced technique and equipment performance. Direct food analysis, ambient-ionization MS, and MALDI-TOF-MS imaging and profiling are other recent advances in MS.

Pesticides

GC-MS is one of the most widely used analytical tools for determining the presence of pesticides in food. Using this method, distinct chemical components in a sample can be identified and separated. Pesticides can be found even at low quantities thanks to the excellent sensitivity of GC-MS. It can also determine the precise kind of pesticide that is contained in a sample. GC-MS, however, takes a lot of time and requires knowledgeable operators to accurately interpret the results. LC-MS is another widely used analytical tool. This technique uses liquid chromatography, which divides a sample's constituent parts according to their chemical makeup, to separate and identify pesticides [143]. A large variety of pesticides can be detected by the extremely sensitive LC-MS method but it can be costly, need sophisticated tools, and call for skilled operators. There are several other techniques for determining the presence of pesticides in food in addition to these analytical tools, QuEChERS approach is one of the most popular ones. Using a mixture of solvents and salts, pesticides are extracted from a food sample in this process. GC-MS or LC-MS are then used to evaluate the pesticides that were extracted. The QuEChERS method is a well-liked option for routine pesticide analysis since it is easy to use, quick, and affordable. Other additional techniques for examining pesticides in food include biosensors, which employ biological components to identify pesticides, and ELISA which utilise antibodies to identify certain pesticides [144].

Food adulteration

The falsification of food has been a persistent topic of research for scientific communities worldwide [145]. In milk, water is a popular and easy adulterant. The addition of water to milk can alter its colour, flavour, and nutritional value. It is possible to duplicate natural milk by adding other potentially toxic adulterants, such as melamine, which poses a major risk to human health. In order to maintain the original lipid and carbohydrate composition while also making the milk more viscous, melamine is usually added. Milk adulteration with soybean, pea, and whey protein isolates at 0.5,1,3,5, and 10% levels have also been detected using flow injection mass spectrometry (FIMS) in conjunction with chemometrics [146]. The detection period was one minute, and the detection limits of 0.5% were met. Ambient mass spectrometry generally needs little to no sample preparation while in operation. Adulterants have been found in fruits, vegetables, fish, meat, dairy products, cheese, butter, and vegetable oils when analysed using this technique. According to certain research, AMS is susceptible to changes in the sample matrix, if chromatographic separation is not used. Numerous studies have demonstrated that qualitative analysis yields greater effectiveness than AMS-based quantification of adulteration [147].

Conclusion

MS is a fundamental contributing technology used in food evaluation. Different types of MS like LC-MS, MAT-MS and HRMS have been used for their powerful molecular analytical capacity and numerous features and have been applied in the analysis of food nutrients, the detection of harmful substances, public health-related food safety studies, etc. Studies pertaining to the precise authentication, quantization, and transformation of components of food are essential since modern food processing innovations have produced food items with more complex and diversified components. MS is thus really considered an essential tool for monitoring food contamination. Given these considerations, the technique should be employed in food monitoring and general food safety in both research laboratories and routine analysis.

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