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Review Article

Food adulteration and traceability tests using stable carbon isotope technologies

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Abstract

Due to the fractionation of stable carbon isotopes in plant photosynthesis, bio-decomposition processes, environmental factors, plant physiology, geographical factors, climatic conditions and agricultural practices, different foods exhibit significant differences in stable carbon isotope ratios. Therefore, stable carbon isotope ratio analysis (SCIRA) presents an effective tool for detecting food adulteration and food traceability control. In addition, stable carbon isotopes can frequently be used as markers to identify veterinary drug residues, pesticide residues and toxic substances remaining in foods by isotope dilution mass spectrometry (IDMS). The emphasis of this review, which will help readers to modify stable carbon isotope technologies more easily and extend their application in adulteration and traceability for foods, is on the characteristics of various instruments and the data processing methods in SCIRA and IDMS technologies. The latest research is also reviewed and highlighted. This paper reviews potential applications of these technologies to improve current food detection and protect consumers' rights.

Keywords: *Food adulteration, Traceability, Stable isotopes, Stable carbon isotope ratio analysis, Isotope dilution mass spectrometry*

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INTRODUCTION

Food authenticity and traceability have become important subjects in food testing. Trace contaminants such as pesticides, veterinary drugs, bio-toxins and other environmental contaminants remaining in food, also lead to decreased food safety [1-3]. Owing to the fractionation effects among or within molecules during biochemical or biophysical processes, stable isotope analysis has been developed and applied to food adulteration and traceability [4]. Stable isotopes can identify adulterants with chemical structures similar to authentic components [6]. Among all common stable isotopes (e.g., hydrogen, carbon, oxygen and nitrogen isotopes) used in food detection, stable carbon isotope has been the most widely applied in terms of food detection [7].

In this paper, the latest research regarding stable carbon isotopes in food detection is reviewed, specifically highlighting potential applications for improving current food detection techniques. In addition, differences among instruments and data processing methods in the use of stable

carbon isotope ratio analysis (SCIRA, mainly reflected by $\delta^{13}C$ values), and isotope dilution mass spectrometry (IDMS) to detect trace hazardous substances, are extensively discussed in this paper.

SCIRA

Principles

In the 1970s, Smith and Epst5ein found that photosynthetic fractionation led to different $\delta^{13}C$ values in different plants [9] (Figure 1). Gradually, stable carbon isotope ratio analysis (SCIRA) was applied to distinguish the adulterants in plant foods with different $\delta^{13}C$ values. While within the same plant species, the $\delta^{13}C$ values also change with the physiological properties of the plants, geographical factors, climate conditions (including CO_2 concentrations in the local atmosphere and drought stress) and even the mode of cultivation [8,9]. These factors indicated that SCIRA could be applied to trace the geographic origin of plant foods. In addition, foods sourced from animals that were fed with natural feed vs artificial diets) can be discriminated [4,10]. Recent studies have shown that combining $\delta^{13}C$ values with other parameters (e.g., other stable isotopes including $\delta^{15}N$, $\delta^{18}O$ and $\delta^{2}H$ or trace elements such as S, Cl, Fe, and Cu) into suitable models including linear discriminant analysis (LDA) and principal component analysis (PCA) could also provide information on geographical origin, cultivar type and duration of cultivation [11] (Figure 2).

Common SCIRA instruments

Dual-inlet isotope ratio mass spectrometry (DI-IRMS) was developed in the 1940s and 1950s and was initially used in the field of geosciences. At 1970s, this technique began to spread in food detection after the recognition of stable isotope fractionation in plants [13]. Currently, continuous flow isotope ratio mass spectrometry (CF-IRMS), that provides fully automated $\delta^{13}C$ values with comparable precision to that of DI-IRMS, is widely applied [12,14]. In addition, interfaces with other preparative techniques, including elemental analysis (EA-IRMS), liquid chromatography (LC-IRMS) and gas chromatography with a combustion chamber (GC-C-IRMS) have been developed to satisfy various testing requests, such as bulk sample (analyzed by EA-IRMS) and compound-specific isotope analyses (CSIA, including GC-C-IRMS and LC-IRMS) [14]. As the means of adulteration became increasingly sophisticated, the detection of isotope fractionation at the intra-molecular level became increasingly important [15]. This level of precision can be achieved through site-specific natural isotope fractionation nuclear magnetic resonance (SNIF-NMR) [15]. (Table 1).

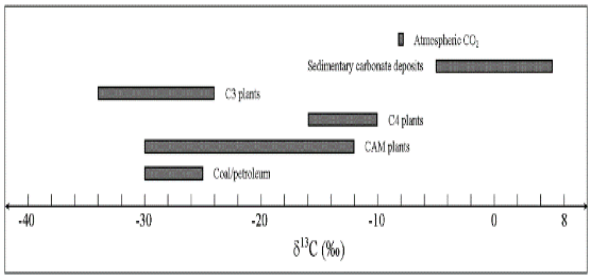

Figure 1: Carbon isotope ratio abundance ranges [15]

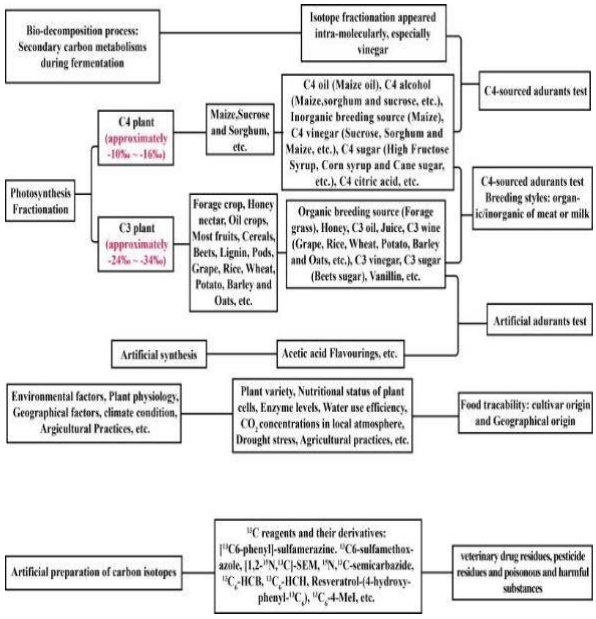

Figure 2: Applications of stable carbon isotopes technologies (based on various literature data presented in this review)

Elemental analysis isotope ratio mass spectrometry (EA-IRMS), which utilizes helium (He) gas as a carrier and provides faster and simpler analysis of a wider range of sample types than IRMS, can enhance the ability to acquire stable isotopic data from large sample quantities. ^{15}N and ^{34}S, which can also be analysed by EA-IRMS, are often used together with ^{13}C to strengthen the validity of traceability [16]. Furthermore, ^{18}O and D isotopes, that cannot be directly analysed via EA-IRMS, are often measured using a reverse-plumbed thermal conversion elemental analyser (TC/EA-IRMS) to provide supplemental information together with carbon isotopes [17,18]. However, due to the total combustion of the bulk sample in EA-IRMS, compound-specific data on individual components within the sample are lost [19].

Gas chromatography combustion isotope ratio mass spectrometry (GC-C-IRMS) is a widely used CSIA method that can separately determine the $\delta^{13}C$ values of different compounds and supply more detailed information on the tested sample. Aside from carbon isotopes, other stable isotopes such as oxygen, hydrogen, and nitrogen isotopes can be determined by GC-C-IRMS [19]. The principles of this technique have been fully reviewed by Katryna *et al* [19]. Recently, highly specific sample preparation has become increasingly necessary, and correspondingly, new sample pretreatment equipment is being developed and coupled with this technique. For example, by coupling with head-space solid-phase microextraction (HS-SPME), GC-C-IRMS enables the detection of $\delta^{13}C$ values of acetic acid in vinegar.

Liquid chromatography isotope ratio mass spectrometry (LC-IRMS) enables the $\delta^{13}C$ analysis of non-volatile and aqueous soluble compounds from detecting foods. In the 1980s, coupling liquid chromatography (LC) with mass spectrometry (LC/MS) was met with difficulty because the deficiencies of ion sources to deal with the continuous flow of LC eluents [7]. In the 1990s, this difficulty was overcome through innovations such as the moving-belt interface, and this technique was eventually commercialized in 2004 [20]. Subsequently, the combination of LC and IRMS was achieved due to the emergence of thermospray ionization [21]. Liquid chromatography isotope ratio mass spectrometry realizes the directly detection on the $\delta^{13}C$ values of the different saccharides in honey without additional pre-separation [22]. However, until recently, LC-IRMS was limited to SCIRA, and other related isotopes could not be measured via this technique [7].

Site-specific natural isotope fractionation nuclear magnetic resonance (SNIF-NMR) is specifically used in the measurement of isotope fractionation within a single molecule. In the 1980s, SNIF-NMR was initially applied in hydrogen isotope detection and performed powerful services in food authentication [23]. Later, the site-specific isotopic ratios ($^{13}C/^{12}C$) of the compounds became realizable through ^{13}C NMR spectroscopy, and the ratios in naturally sourced ethanol, acetic acid, and vanillin were presenting strongly correlation with different origins [15]. Afterwards, SNIF-NMR for carbon isotopes was gradually promoted in food detection, though the lower accuracy of carbon isotope analysis compared with that of hydrogen isotopes remains a challenge [23].

DETAILS OF STABLE CARBON ISOTOPE TECHNOLOGY IN FOOD ADULTERATION AND GEOGRAPHIC TRACTABILITY

Plant-sourced foods

Juice

Stable carbon isotope ratio analysis (SCIRA) was initially applied to juice adulteration in the 1970s. Doner *et al* [18] tested the $\delta^{13}C$ values of 40 apple juice samples and found that the average was -25.4‰ ± 1.2 ‰ and suggested that adulteration of high-fructose corn syrup with a $\delta^{13}C$ value of -9.7 ‰ can be preliminarily determined by testing the $\delta^{13}C$ value of apple juice. Although they found no significant variation in $\delta^{13}C$ with the variety of apple and geographical origin in their initial study, they established a linear relationship between $\delta^{13}C$ values in the tested apple juice and different levels of adulterated high-fructose syrup and noted in further studies that samples with $\delta^{13}C$ values above -20.2 ‰ could be highly suspected as adulterated [19].

However, adulterants containing beet sugar, which is a C3 sugar, cannot be discriminated. Subsequently, Martin et al [20] found that combining SCIRA with stable hydrogen isotope techniques improved the reliability of fruit juice authentication methods, including for added C3 sugars. Moreover, Jamin *et al* [21] used ISCIRA to analyse the relationship between the $\delta^{13}C$ values of sugar and organic acids in apple juice and found isotope correlations between these two compounds, suggesting a criterion for authenticity assessment. Furthermore, a significant correlation among the $\delta^{13}C$ values of sugar, citric acid and malic acid in apple juice was observed and applied to the detection of adulterants with sugar from C3 plants (such as beet) [23]. The limit of detection (LOD) can be controlled to 10% or even 5% using ISCIRA, which is significantly lower than applying traditional 13C methods (often >20%) on bulk juice [26]. Advances in SCIRA research have been extended to various juices, including pomegranate [22], citrus [27], lemon [23], and pineapple juice [21].

Although botanical origin (cultivar) and geographical origin have obvious influences on $\delta^{13}C$ values, these properties partially overlap among juices of various origin [8,9]. Therefore, determining cultivar or geographical origin based solely on SCIRA is not possible.

Table 1: Characteristics and applications of stable carbon isotopes techniques

Stable carbon isotopes techniques	Characteristics	Application
SCIRA: EA-IRMS [28, 32]	1. Fast and simplified in detection 2. High-precision and widely application 3. Entire sample is combusted and compound-specific data of single components within the sample are lost.	Analyse for bulk sample, almost samples including honey, wine and meat etc.
SCIRA: GC-C-IRMS [61, 67]	1. Provide isotope ratio details of volatile compounds in samples with excellent precision; 2. A stringent running conditions limits the precision and accuracy; 3. Carryover effects causing significant differences for the detection.	Including volatile or derivable compounds such as in oils, vinegar, aroma in fruit, acetic acid and glycerol in vinegar, vanillin, carbon dioxide in carbonated beverages etc.
SCIRA: HPLC-IRMS, LC-IRMS [29, 32]	1. Provide macro molecules in CSIA that cannot be analyzed online by GC-C-IRMS and EA-IRMS; 2. Filament lifetime is severely shortened; 3. Excellent precision and accuracy for small molecules.	Including nonvolatile, aqueous soluble compounds from complex mixtures, such as the protein and individual sugar insides the honey, and glucose, fructose, glycerol and ethanol in wine.
SNIF-NMR [20, 23]	1. The most sophisticated and the most specific method for the determination of food product authenticity; 2. Develops with the research of metabolomics and fermentation mechanism; 3. Still in need for a database for comparison purposes; 4. Accessing SCIRA with a suitable degree of accuracy has proved to be challenging.	Be applicable in any food product, currently used in wine and acetic acid in SCIRA.
IDMS [68] (ID-GC-IRMS, ID-LC-IRMS)	1. Absolute measurement properties; 2. Without strict separation sample preparation; 3. High measurement precision and accuracy, wide linear range; 4. Isotopic spikes should be added in the sample preparation process.	Be applicable in veterinary drug residues, pesticide residue and poisonous substances in food.

However, this task can be solved by incorporating other isotopic and/or non-isotopic techniques. Kornexl *et al* [24] first extended multi-isotope analysis (combining $\delta^{13}C$ and $\delta^{15}N$) to clarify characteristic clusters and differentiate the regional origin of citrus juices. Rummel *et al* [27] employed variables such as δD, $\delta^{13}C$, $\delta^{15}N$, $\delta^{34}S$ and $\delta^{87}Sr$ measured in pulp to discriminate authentic orange juices collected worldwide.

Recent results showed that an LDA model, in which $\delta^{13}C$ is employed with other related factors such as other isotopes and concentrations of trace elements in food, is effective in discriminating botanical, geographical and production origin. Furthermore, LDA analysis combining $\delta^{15}N$ values in proteins and pulp, $\delta^{13}C$ values in proteins and antioxidant activity can be important for differentiating between organically and conventionally grown fruits [29]. Nowadays, LDA analysis became the most successful approach for the regional discrimination of juice samples, with an overall prediction ability of 83.9 % [9], through considering multiple indexes including the values of $\delta^{2}H$, $\delta^{18}O$, $\delta^{15}N$, $\delta^{13}C$, D, and the concentrations of sulfur, chlorine, iron, copper, zinc and strontium.

Among the above detection factors, the factors that were most effective in distinguishing the different kinds of species were δD and $\delta^{18}O$ content in the water of fruit juice; the ratios of $\delta^{13}C$ and D/H of ethanol; and the concentrations of sulfur, magnesium, potassium, copper, and titanium. Taking into account these ten factors, the prediction ability can reach 75.8 % [9]. In this regard, juice is influenced by various factors. A suitable model with enough relevant parameters might enhance the sensitivity of adulteration detection and traceability.

Flavorings

Vanillin (Figure 3) is the primary natural flavouring originated from the orchid vanilla pods, which is an expensive tropic plant. Vanillin can also be obtained by refining the oil from guaiacol and some cheap lignins of C3 plants; thus, cases of artificial vanillin addition are common [5]. Scientists differentiate natural from falsified samples based on $\delta^{13}C$ values, which vary within a very narrow range of -18.2 ± 0.6‰ in different natural vanillins [26]. Using GC/C/IRMS, Geißler, *et al* [25] determined the $\delta^{13}C$ values of −21.0 to −19.3‰, −28.2‰ and −32.6 to −29.3‰ for natural vanillin extracts, vanillin ex-lignin, and synthetic vanillin samples, respectively. Furthermore, $\delta^{13}C$ values in ex-tannin samples (ranging from −29.5 to −26.7‰) presented significantly different ($p < 0.05$) between the vanillins of natural and synthetic. Similarly, Geißler *et al* [25] described a feature using the $\delta^{13}C$ and δD ratios of methoxy groups in a PCA model for the clear segregation of critical provenance clusters for vanillins, including eugenol-derived qualities (natural) from lignin- or curcumin-based products (synthetic).

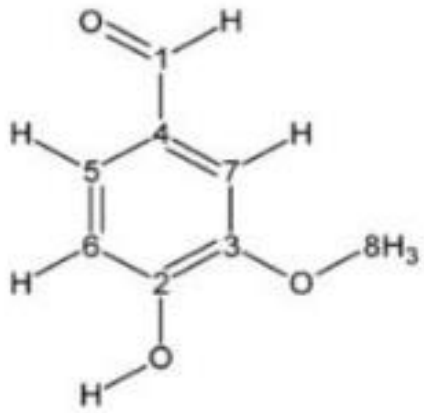

Figure 3: The structure of Vanillin molecule (the carbon sites were numbered presenting decreasing chemical shift.) [17]

However, endless fraud means enrich the $\delta^{13}C$ values of methoxy and aldehyde groups in artificial vanilla [5]. Accordingly, the $\delta^{13}C$ values of artificial and natural vanillin become equivalent, which indicates that measuring the $\delta^{13}C$ values of vanillin is insufficient to determine authenticity. Using SCIRA technology after chemical degradation was first introduced to solve this problem. To detect the fraudulent use of [methyl-13C] to adjust overall $\delta^{13}C$ vanillin values, a release and analysis of the C8 position was introduced. Site-specific natural isotope fractionation nuclear magnetic resonance (SNIF-NMR) makes it much easier to determine artificial addition of methyl-13C or carbonyl-13C. The traceability of vanillin can be achieved by calculating the δ^{13} value of each site (C1 - C8) in the same vanillin molecule through SNIF-NMR [23].

More recently, based on the combined determination of $\delta^{13}C$ and $\delta^{2}D$ values of bulk vanillin as well as the methoxyl groups, natural, synthetic, and semi-synthetic vanillins can be fully differentiated [32]. More recently, stable carbon isotope ratio analysis has also been used preliminarily for other flavouring [27] combined SCIRA with $\delta^{2}D$ values and $\delta^{15}N$ values of saffron samples to effectively differentiate geographical origin.

Animal-sourced food

Honey

In honey detection, stable carbon isotope ratio analysis (SCIRA) has been an important and essential technique for a long time (Table 2). Nearly all of the nectar-sourced plants are [13]. In the market, adulterated products typically contain added C4 sugars, such as sucrose and corn syrup, which can be easily detected using SCIRA techniques [34].

To increase the sensitivity of the technique, White and Doner established the ISCIRA method, which is based on the minimum stable delta $\delta^{13}C$ values of 0.1‰ between bulk honey and proteins in honey [28]. Using this method, as little as 7% of C4 adulterants in honey can be detected. Owing to its high efficiency and sensitivity, this procedure was validated and improved for worldwide application and was adopted in the AOAC for honey adulteration detection [29].

To discriminate C3 sugar adulterants, Cabañero *et al* [29] determined the $\delta^{13}C$ values of fructose, sucrose and glucose in 54 pure honey samples by HPLC-IRMS and established an identification method based on the correlation among these values, which was able to detect 10 % additional sugars, including beet sugar (C3 sugar). Elflein *et al* [16] determined $\delta^{13}C$ values for proteins and all the individual sugar components of 451 authentic honey samples by EA/LC-IRMS, and accordingly, the fingerprints of the 13C values of pure honey were established. Similar to juice, SCIRA can be utilized for tracing by coupling with other stable isotopes, especially $\delta^{15}N$ [10]. Recently, Dong *et al* [37] established a criterion based on the SCIRA of bulk honey and the main sugars for 53 pure honeys of various botanical and geographical origins to discriminate honeys which contained non-extractable proteins. The findings supplemented the AOAC 998.12 C4 sugar method. Until recently, the internal references were merely based on some sugars, acids and protein which exist inside honey, and in future research, various of other compounds can be developed for adulteration detection.

Meat

In the 21st century, stable isotopes techniques such as ^{13}C, ^{34}S, ^{15}N, ^{18}O and D were gradually developed to be applied to meat traceability. Among these isotopes, $\delta^{13}C$ values are the most widely used in discriminating breeding styles of meat [5]. Organic breeding usually adopts natural forage grass (C3 plant), while inorganic breeding adopts artificial fodder generally made of corn (C4 plant) and artificial nutrients, which can make beef cattle grow rapidly. The $\delta^{13}C$ values of meat and fat in cattle fed maize are higher than in those fed grass. Furthermore, the $\delta^{13}C$ values of fodder and animal tissues are slow to equilibrate, and the $\delta^{13}C$ values of meat and fat do not change significantly with even 230 days of feeding with fodder of different $\delta^{13}C$ values [40]. Similarly, solely using $\delta^{13}C$ values in muscle and lipid from steak can differentiate the dietary composition (grain or grass) of beef. Furthermore, both the $\delta^{13}C$ value and ^{14}C levels are higher in muscle tissue than in lipids [41].

Stable carbon isotopes can be used in meat traceability, especially in large reports on beef traceability [42]. Through comprehensively determining $\delta^{13}C$, $\delta^{15}N$, and 23 trace elements in defatted beef, Zhao *et al.* [35] correctly determined the origin of 60-80 % of samples coming from different Chinese regions. To obtain high accuracy, the authors emphasized the importance to collect the samples at the same time point to avoid seasonal differences. Similarly, Liu *et al* [36] sampled the tail hair of cattle to determine stable isotope ratios. In addition to beef, the use of SCIRA in the traceability of other meats or meat products is gradually increasing. Kim *et al* [37] found that combining $\delta^{13}C$ and $\delta^{15}N$ values helped to discretely identify the origin of commercial fish. The combined or individual use of SCIRA, other isotopes (N, H, O, S, B and Sr), and multi-element analyses to authenticate fishery and aquaculture products has been reviewed by Li *et al* [38].

Recently, Camin *et al* [39] also attempted to utilize SIR, including SCIRA, for the geographical traceability of Italian rainbow trout. Their results revealed that ^{13}C, ^{15}N, ^{36}S, δD and $\delta^{18}O$ could be used as the traceability markers. And through utilizing the tested PLS-LDA multi-class model, the authors obtained 91 % accuracy for the two Italian regions.

Furthermore, $\delta^{13}C$ values can also be used to detect dietary components in chicken and to identify the origins of pork and beef. Combining carbon isotopes into multi-isotopic ratios, Perini *et al* [39] used PCA models to authenticate Italian protected designation of origin (PDO) ham. Li *et al* [44] tested 99 samples of lamb tissue from different regions in China and obtained a total discriminating accuracy of 88.9 and 83.8 % by combining C, N and H isotopes from lamb muscle and wool.

Table 2: Application of stable carbon isotope technique in detection of adulteration in honey

Year	Instrument	Main contribution	References
1971	IRMS	Based on the fact that almost all the nectar sourced plants are C3 plants, SCIRA was initially established to detect adulteration in honey	[9]
1978	IRMS	Based on the fact that almost all the nectar sourced plants are C3 plants, SCIRA was initially established to detect adulteration in honey	[15]
1980	IRMS	Established the ISCIRA method which based on the stable delta $\delta^{13}C$ values between bulk honey and protein in honey was 0.13‰. Using this method, 7% of C4 adulterants in honey can be detected out.	[18]
1998	IRMS	Based on the ISCIRA, AOAC built the main method aiming to identify the C4 sugar adulteration of honey.	[56]
2006	HPLC-IRMS	Determined $\delta^{13}C$ values of fructose, sucrose and glucose in 54 pure honey and established identification method from the correlation among these values, which is able to detect 10% additional sugar including beet sugar (C3 sugar).	[29]
2008	EA/LC-IRMS	Determined $\delta^{13}C$ values in protein and all the individual sugar components of 451 authentic honey by EA/LC-IRMS, and accordingly the fingerprints of the ^{13}C values of pure honey were founded.	[16]
2010	IRMS	Combined SCIRA with $\delta^{15}N$ for adulteration detection, botanical and geographical tracebility in Slovene honey	[30]
2013	EA–IRMS	Evaluation of measurement uncertainty for determination of sugar from C4 plant content in adulterated honey.	[31]
2015	EA-IRMS HPLC-IRMS	A very strong correlation was observed between $\delta^{13}C$ honey and $\delta^{13}C$ protein of pure honey. Moreover, δD of honey samples have been developed to be combined with SCIRA to improve isotopic methods.	[32]
2018	EA-IRMS LC-IRMS	$\delta^{13}C$ bulk honey and $\delta^{13}C$main sugars were utilized to identify honeys with non-extractable proteins. The findings supplemented the AOAC 998.12 C4 sugar method, with regard to honeys from which protein cannot be extracted.	[37]

Similarly, Erasmus *et al* [40] tested stable carbon and nitrogen isotope ratios in lamb meat from South Africa. For lamb meat authentication, the differences of $\delta^{13}C$ and $\delta^{15}N$ showed promising results for the application of IRMS as a powerful analytical tool. The use of SCIRA has also been extended to identifying the geographical origins of sea cucumber [41]. Besides above-mentioned meat (fish, beef and mutton), stable carbon isotopes technologies can be applied in other various meat in future.

Dairy products

Like meat, milk is also classified as organic or inorganic based on the breeding method [42]. Chung *et al* [43] found that $\delta^{13}C$ values were lower in organic milk compared with commercial milk in Korea, indicating that stable carbon can be applied to control fraudulent organic milk labelling in Korea. In a study by Luo *et al* [44], the $\delta^{13}C$ and $\delta^{15}N$ values of extracted proteins and the δD and $\delta^{18}O$ values of milk water were determined by EA-IRMS. The 3D distribution of $\delta^{13}C$, $\delta^{15}N$, δD, and $\delta^{18}O$ could clearly presented regional concentration phenomena according to the producing regions of the milk samples.

Aside from combinations with other isotope technologies, stable carbon isotope techniques can also be combined with other non-isotopic technologies in the detection of milk. By testing 286 milk samples in Germany, Molkentin *et al* [52] found that the maximum $\delta^{13}C$ of organic milk was always below —26.5 ‰, and a negative correlation (r = —0.93) between the C18:3ω3 content and $\delta^{13}C$ value was observed in organic milk. Using multivariate analysis of $\delta^{13}C_{casein}$ combined with other stable isotopes ($\delta^{15}N_{casein}$ and $\delta^{18}O_{glycerol}$) and trace elements (Ba, Ca, K, Mg, and Rb), Bontempo *et al* [45] effectively classified 94 % of 109 samples especially effective for the samples from Fontina and Puzzone. In addition, $\delta^{13}C_{casein}$ and $\delta^{13}C_{glycerol}$ supplied an estimate of maize intake of dairy animal diets in their study. In addition to studies using SCIRA to test the contents of milk itself, work by Behkami *et al* [46] showed that SIR of cattle tail hair can be used for the geographical traceability of the milk. By measuring $\delta^{13}C$ and $\delta^{15}N$, they observed a significant positive correlation ($p < 0.0001$) (n = 54) between milk and that of the hair, indicating that these matrices can be used in traceability of animal products and the tissues [10]. Although this research is preliminary, it brings a new thinking that besides internal references, the stable isotopes of external matrix would also give us information for adulterants detection or traceability.

Other food products

Alcohol

Since 1990, the European Union (EU) has maintained a database of stable isotopes (^{13}C, D and ^{18}O) in wine from different producing areas. OIV (International Organization of Vine and Wine), CEN (Committee European for Normalization), and the AOAC (Association of Official Analytical Chemists) have also established alcohol testing standards using stable carbon isotopes techniques [5]. The MA-E-AS312-06-ETHANO official OIV method established in 2001 still uses $\delta^{13}C$ in wine determination. Oganesyants *et al* [47] found that the addition of exogenous alcohols derived from C4 plants produced an obvious increase and resulted in significant changes in the $\delta^{13}C$ values of ethanol in fruit wines, while adding sugars or alcohols from C3 plants leads to a slight change.

Combined with other isotopic or non-isotopic elements, Weber et al. [48] determined the $\delta^{13}C$ values of organic acids of wine and must producing from Rheinpfalz area, and observed the correlations with those of sugar and ethanol from 57 EU databank. Besides, a new constant correlation in wine for ethanol and citric acid ($\Delta\delta^{13}C = +2.4 \pm 0.4$ ‰) was discovered and the d-value between citric acid in wine and the fermented sugar can be deduced as +0.7±0.6 ‰ [55]. Francois *et al* [55] sampled sweet and semi-sweet wines (n = 20) produced in France, and determined ^{13}C isotope ratios of ethanol, glycerol, glucose, and fructose by using LC-TRMS. They found that the ratios were 1.00 ± 0.04, 1.02 ± 0.08, 1.15 ± 0.10, and 1.16 ± 0.08 for $R^{13}C_{glycerol/fructose}$, $R^{13}C_{glycerol/ethanol}$, $R^{13}C_{ethanol/Sugar}$ and $R^{13}C_{glycerol/Sugar}$, respectively.

Additional glucose, fructose or glycerol adulterated in pure wine would show an abnormal variation of the $R^{13}C$ value, and the LOD of the adulterants can be as low as 2.5 µg/mL [49]. The same method can also be applied to the authentication of grape juice. Zyakun *et al*. [50] found that the relative constant carbon isotope composition between ethanol and the dry residue remaining in the final product provided a basis for determining the authenticity of grape wines irrespective of natural factors. According to Roßmann *et al* [48], the determination of ^{13}C in wine ethanol offers an approach to roughly estimate the origin and authenticity of commercial wines, and the accuracy can be largely improved by combining $\delta^{13}C$ determination with D/H ratio and $\delta^{18}O$ in water.

Dutra *et al* [51] demonstrated that SCIRA can also be used in wine traceability when combined with $\delta^{18}O$ values in water and the content of minerals (Rb and Li) in DA models. In addition to wine, stable carbon isotope technologies can also be applied to the authentication of beers and spirits. $\delta^{13}C$ values can be used to distinguish beers fermented from barley malt from those with added C4 sugar, as well as whisky sourced from C3 plants (grape must, rice, wheat, potato, barley and oats, etc.) from those fermented from C4 plants (sucrose, sorghum and maize,) [51].

In 2017, Akamatsu *et al* [53] found that $\delta^{13}C$ values can be used to to determine adulterated citric acid from C4 plants in Japanese apricot liqueur. Furthermore, a scatter plot applying $\delta^{13}C$ and δD could be used to determine the mixed citric acid originating from C3 and C4 plants in Japanese apricot liqueur [53]. Similar to juice, alcohol is directly made from natural plants. In this regard, migration correlation method from juice might improve the detection efficiency, for example, select internal references such as sugar and acids molecules.

$\delta^{13}C$ values can also be applied to discriminate the natural fermented vinegar and the chemical synthesized vinegar. According to Armin, the $\delta^{13}C$ values of vinegar fermented from C3-plants are clearly lower than those from pure C4-plants (-11 ‰) but are still much higher than that of chemically synthesized acetic acid (-34 ‰) [54]. Applying head-space solid-phase microextraction (HS-SPME) combined with gas chromatography−high temperature conversion or combustion-isotope ratio mass spectrometry (GC-TC/C-IRMS), Hattori *et al* [54] tested $\delta^{13}C$acetic acid values in 14 vinegar samples and observed greater depletion in methyl carbon than in carbonyl carbon.

Furthermore, isotopic differences ($\delta^{13}C$carboxyl-methyl) in acetic acid varied in different plants, among which the delta values of C3, C4 and CAM plants were 2.1 ‰ ~ 6.7, 11.6 and 18.2‰, respectively [55]. Using GC-C-IRMS, Sighinolfi *et al* [55] were recently the first to measure the $\delta^{13}C$ values of glycerol in balsamic vinegars and suggested $\delta^{13}C_{glycerol}$ as an additional authentication tool, because the isotope ratio is completely dependent on the chemical composition of glucose in the substrate and the metabolic pathway. Due to the effects of natural, seasonal and regional factors, the use of other molecules, such as acetic acid, was proposed to enhance the diagnostic accuracy of isotopic approaches.

Edible oils and volatile matters

Stable carbon isotope ratio analysis (SCIRA) is extensively used as a promising tool to detect adulteration in oil. Woodbury *et al* [56] demonstrated the feasibility of discriminating corn oil (C4 plants) adulterants from C3 vegetable oils through stable carbon isotope techniques and established the carbon isotope indexes of various vegetable oils for discrimination. Kelly *et al [*27] showed that the $\delta^{13}C$ values of individual fatty acids in oil might provide an additional indication of authenticity of oils produced from C3 plants.

Woodbury *et al* [56] measured the $\delta^{13}C$ values of major fatty acids in several commercial vegetable oils by GC-C-IRMS and found that this approach might be applied to traceability. They also observed a slight difference in $\delta^{13}C$ values between fatty acids and bulk oil. To further clarify this difference, they acquired pure fatty acids by hydrolysing triglycerides with trypsin and the measured $\delta^{13}C$ values of the 1-, 2-, and 3-positions of fatty acids. This analysis revealed that quantitative differences in the $\delta^{13}C$ values between fatty acids at the 2-position and that of bulk oil might be a useful criterion for assessing the purity of edible oil. Subsequently, Angerosa *et al* established a stable carbon isotope identification standard for Mediterranean olive oil [57].

Liu *et al* [58] successfully identified the $\delta^{13}C$ values and relative fatty acid abundance of swill-cooked oils (recycled oil). Both isotope values (both total organic and compound-specific carbon) and fatty acid ratios (C14/C18) presented significant differences between recycled oil refined from C3 plants (-35.7 to -27.0 % and 0 to 0.15, respectively) and animal oils (-28.3 to -14.3 % and 0.1 to 0.6, respectively) [59]. Combination with other isotopes such as oxygen and or hydrogen with carbon also contributes to oil detection. Indeed, stable isotope fractionation of carbon and oxygen occurs following both biotic and abiotic processes. Thus, these isotope patterns might reflect producing area, harvest year, and climatic conditions[57] built a dual-isotope conceptual model and identified a positive relationship between $\delta^{13}C$ and $\delta^{18}O$ owing to the open and the close states of olive leaf stomata, which can influence the fractionation of $\delta^{13}C$ and $\delta^{18}O$ (driven by gain and loss of carbon dioxide and water, respectively). Inspired by this finding, Portarena *et al* [60] plotted $\delta^{13}C$ versus $\delta^{18}O$ values of olive oil, and the results present a strong correlation with those indexes, including latitude, temperature, rain and xerothermic climate.

In addition to oil, abundant organic matter, especially volatile compounds, widely and naturally exist in food products. These carbon-based components are influenced by photosynthesis, and SCIRA thus provides a robust tool for identifying natural volatiles from synthetics, especially those extracted from fruits such as pears, strawberries, apples, and bananas [61]. Supplemental isotopes can include δ^2D or/and $\delta^{18}O$ which have been used in the discrimination of natural volatile compounds. This approach was described in detail in a review of GC-C-IRMS applications by Leeuwen [61].

Isotope dilution mass spectrometry

Principles

In addition to the application of SCIRA based on the isotope fractionation effect, stable carbon isotopes can be internal markers in IDMS technology to detect veterinary drugs residues, pesticide residues and toxic substances remaining in food in trace amounts that could not be accurately sensed by other methods [2,62,63]. The principle for IDMS is straightforward: initially, known amounts of an isotopically labelled analogue are added into the sample and the blank. After equilibration, the ratios of the natural and labelled isotopes in both the sample and the calibration blends are measured, and the ^{13}C value of the target analyte in the sample can be subsequently derived [64]. Using internal reference isotopes in the detection of veterinary drug residues, pesticide residues and poisonous and harmful substances in food can effectively correct errors appearing in detection methods and significantly improve the sensitivity and stability of these methods [65].

Applications of stable carbon isotope IDMS in food detection

Owing to the methodological developments in the artificial preparation and separation of carbon isotopes, ^{13}C reagents and their derivatives are increasingly and widely used in the detection of various veterinary drug residues in food, including deoxynivalenol (DON), 15-acetyldeoxynivalenol (15-ADON), 1-aminohydantoin (AHD), HT2-toxin (HT2), semicarbazide (SEM), T2-toxin (T2), nitrofurans (NFs) and sulfonamides (SAs) [63,64]. Tamošiūnas and Padarauskas [64] selected [$^{13}C6$-phenyl]-sulfamerazine and $^{13}C6$-sulfamethoxazole as internal references to detect SA residue in honey and eggs by UPLC-MS and obtained more accurate results than merely using LC-MS without isotope-labelled internal markers. Combined with ^{15}N and ^{13}C labels, double-isotope standard compounds can be optimized to detect nitrofurans (NFs). For example, Effkemann and Feldhusen [65] selected [1.2-^{15}N, ^{13}C] -SEM as double internal references to test residual furan in animal tissues and eggs, with an LOD as low as 10 µg/kg. Metabolic products of furacillin in animal tissues can also be detected by IDMS using ^{15}N, ^{13}C-semicarbazide.

Stable carbon isotope dilution mass spectrometry can also be used to detect pesticide residues, especially organochlorine pesticides (OCPs), which include dichlorodiphenyltrichloroethane (DDT), cypermethrin, and endosulfan [66]. $^{13}C6$-hexachlorobenzene (HCB) and $^{13}C6$-hexachlorocyclohexanes (HCH) were used as standards to test HCB and HCH residues in Panax ginseng, and LODs and limits of quantitation (LOQ) were found to be approximately 0.5 µg/kg and 2.0 µg/kg, respectively [65]. Isotope dilution mass spectrometry (IDMS) can likewise be applied to detect microbial toxins such as aspergillus, versicolour, patulin and deoxynivalenol. Furthermore, increasingly abundant environmental pollutants such as bisphenol, dioxin-like compounds, which are enriched in foods through the trophic chain, can be sensitively determined with the development of ^{13}C IDMS [67,68].

Recently, Ansari and Häubl [69] using a fully carbon-13-labelled internal standard to compensate for matrix effects, developed and validated a simple and accurate method using LC-MS/MS for determining cyclopiazonic acid (CPA) in food and feed samples. Applying this optimized method, LODs and LOQ were achieved down to 0.2 lg/kg and to 0.5 lg/kg, respectively. Donna *et al* [70] selected resveratrol-(4-hydroxyphenyl-$^{13}C6$) as an internal reference to detect resveratrol in red wine through paper spray mass spectrometry (PS-MS) and multiple reaction monitoring with 100 % accuracy, low LOD (0.5 µg/mL)and LOQ (0.8 µg/mL) values, respectively.

Feng *et al* [71] utilized $^{13}C6$-4(5)-methylimidazole (4-MeI) as an isotope-labelled internal standard to determine trace levels of 4-MeI in beverages using dispersive liquid-liquid microextraction coupled with the electrospray ionization (ESI)-HPLC-MS/MS. The resulting method exhibited an excellent LOQ of 0.3 µg/L and good linearity (R^2 = 0.999). In addition, 4-MeI recovery in carbonated beverages ranged from 102.60 to 113.22 % and from 103.24 to 108.85 % in soft drinks [71].

CONCLUDING REMARKS

Almost all foods are derived from carbon-based organisms; hence, the potential for the development of carbon isotope technology is boundless. SCIRA is a powerful tool for detecting adulteration and for traceability in food. In addition to the aforementioned foods in this paper, the application of SCIRA has more recently extended to assessments of various foods. However, most of these studies remain preliminary and have yet to be cited in standards as recommended approaches. To improve the detection level of SCIRA, clarification of the detailed fractionation mechanisms of stable carbon isotopes (including artificial fractionation and separation as well as natural fractionation reactions such as plant breathing, physiological metabolism, and environmental factors) and their relationship with indicators are urgently needed to protect consumers' rights.

DECLARATIONS

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Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Dr Guo, Mr Mai and Ms Lai put forward the argument of this article, wrote the manuscript, and also contributed equally to the manuscript. Ms Sun and Ms Shao collected and analysed the materials. All authors have read and approved the manuscript for publication.

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