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Application of isotope ratio mass spectrometry (IRMS) in the geographical determination of selected herbs: A review

Long Chen [a,b], Luana Bontempo [a,*]

[a] Research and Innovation Center, Fondazione Edmund Mach, Via E. Mach 1, 38098, San Michele all'Adige, Italy
[b] Center Agriculture Food Environment, University of Trento, Via E. Mach 1, 38098, San Michele all'Adige, Italy

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ABSTRACT

Herbs have been consumed for their health benefits for centuries and are still attracting increasingly more attention. Their quality is prone to changes in climatic and geo−chemical conditions. Local cultivation patterns also impact the quality of herbs. Therefore, geographical origin is often regarded as an indicator of quality. However, profit−motivated fraud and adulterations degraded the quality of relevant products, and also destroyed the consumers' health and trust. Isotope ratio mass spectrometry (IRMS) is particularly useful in verifying the origin of herbs as the isotopic composition of several light elements (C, H, O, N and S) contain information about the geographical locations. Changes in the isotopic composition cannot be identified by other techniques but may be detected using IRMS. In this review, current applications of IRMS in tracing ginseng, saffron, chrysanthemum flos and goji berries were discussed and future development was envisaged.

1. Introduction

1.1. Herbs

Since thousands of years ago, herbs have been experiencing daily use as food supplements for imparting colors, aromas, flavors as well as for health management [1,2] because of their rich content of natural antioxidants and their antibacterial and anti−inflammatory effects [3,4]. In addition, several studies even reported the anticancer potential of herbs [5,6]. Across various cultures, herbs are consumed in different ways, individually or in combinations [7], but typically they are taken as herbal infusions for their medicinal effects but with less caffeine and theine with respect to traditional tea and coffee [1]. In addition to these advantages, herbs may also offer the possibility and capability to deal with diseases which may have afflicted humans for a long time, such as *Artemisia annua* L. that contains artemisinin for treating malaria [8–10].

Herbs usually command a high price and are sold as dried plant parts, such as flowers, roots and rhizomes [1]. The quality of herbs is affected by factors such as plant species, cultivation areas, cultivation conditions, processing methods and storage conditions and therefore, geographical origin is often regarded as an indicator of quality. Herbs also have a long and complex supply chain and each link of it might give rise to quality and safety matters [4]. Some unscrupulous producers sell unauthentic materials that are labeled as authentic ones to gain even more profits. Indeed, supply chains in the herbs sector tend to be long, complex and can pass through many countries with the presence of many intermediaries in the supply chain offering opportunities for malpractices and/or fraudulent practices. At the consumer level, it may not be feasible to visually identify characteristics of herbs and it may even be totally impossible to identify the plant origin when they are crushed or ground. All these elements generate a high probability of malpractices, some of them with important risks for public health (e.g. substitution of the named herb/spice with an allergenic product and/or color enhancement by non−authorized dyes) [11–13]. To avoid or detect malpractices in the field of herb production and distribution, it is, therefore, necessary to check the geographical origins of the herbs. To evaluate the quality of the herbs, physical, chemical and sensory analysis can be performed. Chemical analysis usually consists of methods based on e.g. chromatography, mass spectrometry, spectrophotometry, inductively coupled plasma and nuclear magnetic resonance spectroscopy (NMR) [4,14]. In Table 1, some of the most utilized methods and techniques used for the geographical traceability of herbs are summarized.

* Corresponding author.
E-mail address: luana.bontempo@fmach.it (L. Bontempo).

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Table 1
Overview of major analytical instruments and methods mentioned in this work to check the geographical traceability of herbs (IRMS not included).

Analytical methods	Advantages	Limitations	References
Chromatography (Liquid and Gas Cromatography -LC and GC)	LC: – Ability of separating both volatile and non−volatile compounds −Ability of identifying less stable molecules because of non−heating samples and columns GC: −Better resolution and peak separation −Especially suitable for highly volatile molecules	−Time consuming sample preparation −Use of organic solvents	[15]
Diode Array Detector (DAD)	−Simultaneous multiwavelength analysis −Peak measurements in all wavelengths −Quick determination of the correct wavelength	−Lower sensitivity and selectivity −Baseline noise at low concentration	[16,17]
Flame Ionization Detector (FID)	−High sensitivity −Simple to operate	−Inaccurate identification of active compounds	[18]
Mass Spectrometry	−Higher sensitivity and selectivity −Greater structural determination capabilities	−Maintenance needed −Method developing required −High cost of instrument purchase	[19–21]
Ion Mobility Spectrometry (IMS)	−Fast screening capabilities −High sensitivity −Portable devices available	−Low resolving power −Limited selectivity −Influenced by environment and sample matrix	[22,23]
Inductively Coupled Plasma (ICP) − MS	−Multielement analysis at the same time −Short analysis time −Simple sample preparation −Low detection limit	−High cost of equipment −Argon consumption −Laboratory set−up costs	[24]
Near−Infrared Spectroscopy	−Speed and efficiency −Easy to handle −Highly reproducible −Versatility and flexibility	−Low precision −Rigorous calibration needed −Low spatial resolution −Reference data required for quantitative analysis	[25–28]
UV−VIS Spectroscopy	−Easy and quick analysis −Low noise −Robustness and low cost −Simultaneous and multi−wavelength data acquisition	−Unselective −Difficult direct measurement of analytes at low concentration in complex sample −Sample preparation required for better selectivity and sensitivity	[29]
Raman Spectroscopy	−Both qualitative and quantitative −Independent on wavelength of incident radiation −Simple solvents (e.g. water) needed −Simple spectra −Highly specific (fingerprint of molecules) −Nondestructive −possibly without sample preparation	−Low sensitivity −High cost of instruments −Influence from fluorescence −Low probability of Raman scattering	[30]
E−sensors	−Rapid analysis −Low cost −Simple to use −Able to detect complex odors and volatiles −Holistic information about samples' volatile	−Prone to sample preparation and sampling −Sensitive to environmental conditions −Not suitable for open−field or mobile sensing −Training and validation with large number of samples for each type of sample −Not portable because of high energy demands	[31,32]
Transmission Electron Microscope (TEM)	−Capability to observe both electron microscope images and diffraction patterns −Able to study much smaller objects −Great sensitivity to small structural deviations	−High vacuum needed −Restricted to sample immobilization −Experienced and skilled staff required	[33,34]
Fluorescence Spectroscopy	−Nondestructive −Rapid analysis −Easy to use and relatively cheap −Small amounts of reagents required	−Short lifespan of fluorophore −Susceptible to interference due to pH changes and oxygen levels −Susceptible to autofluorescence −Limitations associated with photostability and loss of recognition capability	[35,36]

1.2. Stable isotope ratio analysis

Stable Isotope Ratio Analysis (SIRA) involves measuring the relative abundance of different stable isotopes within a sample. The isotopic composition of different elements may tell us information about the botanic classification, growing methods and growing regions of the plants or plant products in question. In particular, the delta value of carbon ($\delta^{13}C$) is closely related to the photosynthesis of the plant. According to the biological pathway of carbon fixation used by the plants, they can be divided into three types: C3, C4 and CAM; the nitrogen delta value ($\delta^{15}N$) indicates the nutritive values of soil, kind of fertilizers used and nitrogen fixation pathway; the delta values of hydrogen ($\delta^{2}H$) and oxygen ($\delta^{18}O$) reflect the local natural conditions of the place where the plants were harvested such as the precipitation, distance from the sea, altitude and latitude [12,37]; the sulfur delta value ($\delta^{34}S$) is affected by the geology of the area and agricultural practice so the $\delta^{34}S$ value may reflect information of the soil or fertilizer used during cultivation [1].

The results of the stable isotope analysis are usually expressed as per mil (‰)using delta notion (δ) with respect to a certain international standard, for instance, VPDB (−Vienna Peedee belemnite) for $\delta^{13}C$, VSMOW (ViennaStandard Mean Ocean Water) for $\delta^{2}H$ and $\delta^{18}O$, and Air−N_2 (atmospheric N_2) for $\delta^{15}N$, VCDT (ViennaCanyon Diablo Troilite) for $\delta^{34}S$ following Equation:

$$\delta^{i}E_{sample/standard} = \frac{R\left({}^{i}E/{}^{j}E\right)_{sample}}{R\left({}^{i}E/{}^{j}E\right)_{standard}} - 1$$

where the $R({}^{i}E/{}^{j}E)_{sample}$ is the ratio of the number of atoms of heavier isotope to the number of lighter isotopes in the sample and $R({}^{i}E/{}^{j}E)_{standard}$ is the ratio of the number of atoms of heavier isotope to the

number of lighter isotopes in the standard material.

1.3. Analytical methods

Based on whether sample separation is necessary before the proper analysis, the techniques used for stable isotope analysis could be categorized into two types i.e. compound−specific isotope analysis and bulk stable isotope analysis [38–40]. Although there have already been quite a few studies on the geographical traceability of herbs using stable isotope ratio analysis [41–48], yet in this review work, we will mainly focus on the application of BSIA in tracing the selected herbs which are ginseng, saffron, chrysanthemum flos and goji. They have been the more investigated ones with the isotopic approach, in particular in the cases of ginseng and saffron.

1.3.1. Isotope ratio mass spectrometry (IRMS)

Isotope ratio mass spectrometry (IRMS) exploits the magnetic sector mass analyzer of a mass spectrometer to obtain highly precise stable isotope ratios of light elements in a sample. Typical measurements target hydrogen, carbon, nitrogen, sulfur and oxygen analyses. Samples are previously converted to simple gases (i.e. hydrogen to H_2, carbon to CO_2, nitrogen to N_2, oxygen to CO and sulfur to SO_2) then introduced to the IRMS. It has been used for determining the origin (geographical, botanical, natural-synthetic) of food products for decades (e.g. vanilla [49] and wines [50]). Stable isotopes may reflect the growing environment of the plants and, with respect to the previously listed techniques, IRMS is able to reveal this information through the delta values of different stable isotopes [51].

1.3.2. Compound−Specific isotope analysis (CSIA)

CSIA consists of a variety of techniques that allow to examine simultaneously a number of molecules and their delta values. In compound−specific analysis, a preparatory step in which the components of the samples are separated is conducted prior to isotope ratio mass spectrometry. The separation may be achieved through gas chromatography (GC) or liquid chromatography (LC) according to the volatility and polarity of the targeted components. Particularly, GC can be used to separate volatile organic compounds (VOCs) in various types of samples like essential oils [52,53], white spirits [54], and foods and beverages [55–57]. Meanwhile, LC can be put to use for separating less volatile compounds or polar molecules in samples such as essential oils [58,59], herbal extracts [60], human serum [61,62] and foods and beverages [63,64].

1.3.3. Bulk stable isotope analysis (BSIA)

The bulk isotope analysis involves the detection of the isotopic composition of samples that are analyzed as a whole. In this case, the researchers may obtain the isotope information about the samples as the average of all the components present in the sample. In the bulk isotope analysis, two main configurations may be employed: elemental analyzer (EA) and high temperature conversion elemental analyzer (TC/EA). The former one is used to determine the delta values of carbon, nitrogen and sulfur while the later one serves for analyzing the delta values of hydrogen and oxygen.

1.3.4. Comparison between CSIA and bulk analysis

Bulk stable isotope analysis is attractive because of various reasons including easy sample preparation, cost-efficient and shorter analysis time. Sample preparation could be as easy as a simple homogenization or grinding and then weighing into suitable capsules. The analysis time for each run might be reduced to several minutes. However, it still presents limitations. Since it measures the bulk tissue, it is unable to differentiate between isotopic signatures of individual compounds from the same sample, losing detailed information that may affect the final result. Probable overlaps in isotope ratios of samples from similar environmental conditions make it sometimes impossible to distinguish samples from different locations. The variability of isotope values in time and space induced by environmental changes is another principal limitation of this method. Compound specific isotope analysis, in contrast, can provide additional isotopic information about a series of compounds directly linked to metabolic pathways. With CSIA, both on-line and off-line isolation of compounds can be employed. Yet CSIA usually requires relatively larger sample sizes, and more complex sample preparation, which is also more time-consuming. Higher cost of instrumental investment is an important limitation as well [65–67].

1.3.5. Geographical differentiation capability

1.3.5.1. Carbon. Plants are classified into three categories based on their photosynthetic pathways: C3, C4, and CAM. The fundamental process of photosynthesis distinguishes between isotopes of carbon, specifically ^{13}C and ^{12}C. The variation in carbon isotopic composition among different plant types results from a combination of CO_2 diffusion and enzymatic activities occurring during photosynthesis [68–70]. C4 plants typically display more positive $\delta^{13}C$ values compared to C3 plants, while CAM plants tend to exhibit intermediate $\delta^{13}C$ values. C3 plants primarily follow the Calvin cycle in their metabolism. C3 plants comprise flowering plants, trees, shrubs and fruits and they thrive in moist, moderate to cold temperature [71]. These plants show carbon delta values ranging from approximately −30 ‰ to −22 ‰. C4 plants, found in both tropical and temperate regions, utilize the Hatch–Slack metabolism, resulting in carbon stable isotope compositions typically ranging from −14 ‰ to −8 ‰. CAM plant species, which adopt Crassulacean acid metabolism, are often found in arid regions and have carbon stable isotope compositions that fall between those of C3 and C4 plants [70]. In addition to plant type, other factors may influence the $\delta^{13}C$ values as well, among which there are temperature, water availability and anthropogenic activities. Particularly, the isotopic fractionation of carbon is affected by temperature due to its impact on the activity and stomatal conductance, as well as the CO_2 uptake rate of plants [72]. It has also been reported that high $\delta^{13}C$ values were observed under conditions of low humidity due to high temperature or low precipitation.

Meanwhile, CO_2 emitted by anthropogenic activities can lead to more negative delta values of carbon. However, carbon isotopic compositions in plants are well known to be derived from atmospheric CO_2 and primarily reflect the metabolic activity of the plant rather than the growth environment, making depletion in heavier carbon stable isotope content due to anthropogenic effects typical fluctuations within a certain range, without exceeding the extent of the plants' category [70,72,73].

1.3.5.2. Hydrogen and oxygen. Generally, plants in coastal areas or hot and dry regions show more positive hydrogen and oxygen delta values compared with plants from inland areas or cool and wet regions. Although metabolic dissimilarities in plants may lead to different delta values of hydrogen and oxygen within plant tissues and sap, they are more likely to be impacted by the geo−climatic conditions of the cultivation regions, especially the precipitation. Other parameters include temperature, altitude, water sources and distance from the sea. The growth of agricultural plants relies on soil water or groundwater which comes from precipitation and therefore reflects the isotopic composition of the rainfall. Generally, an increased quantity of heavier water isotopomers is observed in precipitation around the coastal regions and precipitation depleted in deuterium or ^{18}O is expected in inland areas. Seawater, enriched in hydrogen and oxygen stable isotopes, produces clouds. With the clouds moving, heavier isotopes (deuterium and ^{18}O) favorably drop in areas around the seaside leading to precipitation more enriched in lighter isotopes in inland regions [70,73].

1.3.5.3. Nitrogen. It is commonly known that the delta value of nitrogen is closely associated with the agricultural practices employed in the cultivation regions, especially the type (organic/synthetic), the chemical composition, the quantity, and timing of the different nitrogen−containing fertilizers used for growing the plants. The magnitudes of this value may also reflect the soil nutrition and isotopic fractionation by nitrification/denitrification of the surroundings where the plants were grown. Typically, plants treated with organic fertilizers exhibit greater nitrogen delta values than plants treated with synthetic fertilizers. In particular, the synthetic fertilizers are ideally expected to show $\delta^{15}N$ values close to 0 ‰ (range between −4 ‰ and +4 ‰), because the atmospheric N_2 is the main source of N for producing them; organic fertilizers such as green manures and animal waste, however, have a broader range of $\delta^{15}N$ values which may range from 2 ‰ to 30 ‰ or even higher due to their different origins. An interesting phenomenon was found that the $\delta^{15}N$ values of the same nitrogen−based fertilizers could fluctuate considerably because of the different producing processes employed by different manufacturers [68–70,72,73].

Variations of $\delta^{15}N$ can be expected between different harvest years [32,74]. Samples from the same country but collected in different years may result in a wide range of $\delta^{15}N$ causing the overlaps with samples from other countries and thus reducing the differentiation capability of this parameter [32].

Comparisons between ginseng grown in various soil types were also mentioned in a previous study [69]. Compared with upland fields (an elevated land area typically above the floodplain, characterized by its drier conditions compared to lowland or riparian zones), paddy converted fields (areas where traditional paddy (rice-flooded) fields are transformed into other land-use types) often show slower decomposition of organic materials. In addition, since the paddy converted fields are frequently reconditioned (oxidation/reduction processes) by floods and drainage, the soil of such kinds shows different properties from upland fields. Additionally, because of the presence of lower quantities of ready−to−use nitrogen, manures and composts have to be mineralized into suitable forms. The N isotopic fractionation typically occurs during the mineralization process, influenced by soil type and conditions, with manures being particularly susceptible [69]. Furthermore, it was also noticed that the nitrate contents in water supply, isotopic fractionation in soil, and fertilizer provision would impact the $\delta^{15}N$ measured.

1.3.5.4. Sulfur. The significance of variations in $\delta^{34}S$ among agricultural plants is still not as clearly understood as in the cases of the elements previously discussed. Isotopic fractionation of sulfur is generally considered to be associated with physical processes and the $\delta^{34}S$ value relies more on geological parameters than biological properties of the soil. Subsequently, the S isotopic composition of the plants is influenced by the soil and the delta value of sulfur may reflect the information about geographical origin. The variation of $\delta^{34}S$ is also connected with the distance between coast and cultivation areas. The $\delta^{34}S$ values are widely variable from human septic sludge and sewage sludge to animal manures, and from liquid synthesized fertilizers to solid ones. The reduction and oxidation processes play important roles in these S−containing substances when isotope composition of sulfur is to be considered. Particularly, during the abiotic or bacterial reduction step, greater isotopic fractionation is observed than during oxidation steps. Another factor that may impact $\delta^{34}S$ values is anthropogenic emission of SO_2 [69,73].

1.3.6. Statistical tools for data analysis

Statistics and machine learning have been proved to be powerful for drawing useful information from the experimental data. As well as in the studies of the herbs reviewed in this work, statistical tools, alongside the instrumental analysis, were intensively employed for data analysis, among which (orthogonal) partial least squares discriminant analysis ((O)PLS−DA), linear discriminant analysis (LDA), random forest (RF), principal component analysis (PCA), K−nearest neighbors (KNN), analysis of variance (ANOVA), and artificial neural network (ANN) are several important approaches applied for exploratory analysis and classifications [35,75–84].

IRMS has already proved to be capable of tracing geographical origins of herbs. In quite a few studies it was used to classify, for instance, *Atractylodes macrocephala Koidz.* [48], ginger [47], and *Codonopsis pilosula Franch.* [41,42]. In this review, the current application of IRMS in the geographical traceability of herbs was investigated, focusing on the selected herbs: ginseng, saffron, goji berries and chrysanthemum flos, among which ginseng and saffron are more intensively investigated by means of IRMS with respect to the others. At the end, an outlook into the future possibility of expanding the application of this particularly important and helpful technique in tracing plant products was discussed.

2. Ginseng

Ginseng is a highly valued medicinal herb that has been used for thousands of years in east Asia [85]. Within the Panax genus, there are around 10 species and three of them are of medicinal importance: *Panax ginseng M.*(Korean ginseng), *Panax notoginseng C.* (Chinese ginseng) and *Panax quinquefolius* L. (American ginseng) [86,87]. Amounts of research have revealed their medical effects such as enhancing the immune system, controlling blood pressure, strengthening the cardiovascular system [88], treating digestive problems and even hemorrhage [85] which may be related to the bioactive components contained. Among these bioactive components, the most important ones are polyacetylenes, sesquiterpenes, polysaccharides, peptidoglycans, vitamins and ginsenosides [69,89,90].

Although ginseng is now cultivated in farms to meet the increasing demand, the wildly grown ginseng is still considered as being of superior quality because of higher contents of ginsenoside and triterpene saponins [91,92]. According to the growing environment, the farmed ginseng can be subdivided into garden ginseng and mountain cultivated ginseng. The former one is cultivated in gardens or farms with intensive anthropogenic care and is generally harvested after 4−6 years; while the later one is grown by sowing the seeds in the mountain woods without artificial interference and is collected after 10−20 years [91]. As reported in other studies, ginseng quality may rely on the age of the plants and older ginseng contains higher quantities of active compounds and commands a higher price [91,93,94].

Some of the major producers of ginseng are China, Korea, and North America. There is evidence that quality of ginseng may vary according to the geographical origin since the chemical contents, especially the bioactive compounds in ginseng remarkably depend on the physical, chemical and microbial properties of the soil in the region where it grows. As a consequence, the geographical origin is considered as a key factor that determines the quality and the price of ginseng [69,73,89]. On account of the enormous demand around the world, ginseng and ginseng-based products have long been subject of adulteration in terms of geographical origin leading to illegal economic incomes. Consequently, meticulous discrimination between ginseng harvested in different regions is of particular importance for both consumers and scrupulous producers. Another purpose of identifying the origins of ginseng, mainly American ginseng in this case, is due to the fact that the American ginseng is classified as endangered and trading is illegal in some countries [69].

In the year of 2018, the global production of ginseng was 86223 tons based on fresh ginseng of which China produced 50164 tons (58.2 %), South Korea 23265 tons (27.0 %), Canada 11367 tons (13.2 %), United States 1285 tons (1.5 %) and others 142 tons (0.1 %). China and South Korea are also the two biggest markets (China 2870 million USD and South Korea 2489 million USD) [95]. The global ginseng market size is estimated to reach US$ 786.5 million in 2024. It will likely exhibit a Compounded Average Growth Rate - CAGR of 4.3 % during the assessment period, with an overall market valuation totaling US$ 1262.3

million by 2034 [96].

2.1. Techniques for geographical differentiation

Traditionally the recognition of a certain type of ginseng was based on morphological inspections [73,97], while modern techniques focus mainly on its chemical compositions using spectrophotometric methods [85,90,98], multielement analysis [99,100] or chromatography combined with mass spectrometry [89,91]. Zheng and colleagues [101] conducted a review on distinguishing *P. ginseng* from counterfeits using single nucleotide polymorphism, with a focus on the characteristic three genomes present in plants (chloroplast DNA, mitochondrial DNA, and nuclear DNA). Their conclusion highlights the effectiveness of utilizing single nucleotide polymorphism from these typical plant genomes for reliable discrimination of P. ginseng. Several studies focused on the stable isotope ratio of strontium ($^{87}Sr/^{86}Sr$) because it can reflect geochemical characteristics of the soil where the plant grows [93,100]. As previously mentioned, IRMS has been successfully applied in traceability of quite a few foods and beverages. Several studies were performed to discriminate *P. ginseng* and *P. quinquefolius* from different geographical origins by means of IRMS [68–70,72,73,90,92].

2.2. Sample treatment for isotope ratio analysis

Two principal methods for sample treatment before IRMS analysis were reported. The first one consists of removing the superficial soil from the roots, drying the roots under 60 °C in an oven until the moisture is totally removed, and finally grounding the samples into fine powders [70]. The second one begins with lyophilizing the collected ginseng roots at low temperatures (e.g. ⩽−40 °C) for at least 3 days, then the samples were pulverized, stored at −70 °C and were relyophilized before isotope ratio analysis [69,73].

2.3. Geographical differentiation capability

Studies focusing on the stable isotope analysis of light elements have been conducted to classify the geographical origins of Korean ginseng and American ginseng. The samples of American ginseng were collected from Shandong Province (China), Northeast China, Beijing (China), Canada and US, while the Korean ginseng samples were obtained from different regions in Korea. The cross−region range of the carbon delta value varies between −31.9 ‰ and −22.2 ‰ for American ginseng and between −29.0 ‰ and −22.7 ‰ for Korean ginseng. These findings agree with the fact that ginseng is a member of C3 plants. The overall delta value of hydrogen lies in the interval from −90.6 ‰ to −37.4 ‰ for American ginseng and from −69.2 ‰ to −30.6 ‰ for Korean ginseng. At the same time relevant variances in hydrogen delta value could be observed between regions. Oxygen, another commonly used indicator of geographical origins, showed significant differences between ginseng collected from different locations and the delta value varies from 18.3 ‰ to 30.5 ‰ for American ginseng and from 28.1 ‰ to 41.4 ‰ for Korean ginseng. Nitrogen delta value is usually considered to provide information about the nutritive values of the soil and the fertilizers used during the cultivation and stands a range from −2.7 ‰ to 3.6 ‰ for American ginseng and from −1.6 ‰ to 9.0 ‰ for Korean ginseng. The delta value of sulfur plays an important role in indicating the soil conditions and, the same as nitrogen, the type of fertilizer used. This value was determined only for Korean ginseng and ranged between 1.4 ‰ and 8.5 ‰ (See Table 2 and Table 3).

Although it is known that the isotopic compositions of ginseng are affected not only by geographical origins but also the ages, study showed that the values of $\delta^{13}C$, $\delta^{2}H$, $\delta^{18}O$ and $\delta^{15}N$ were not significantly different among different ages for ginseng samples older than 3 years [90]. In view of this, in this discussion part we are talking only about the influences brought by geographical parameters.

2.3.1. Carbon

The isotopic composition of carbon ($\delta^{13}C$) can effectively distinguish American ginseng grown in Beijing from those grown in other Chinese regions. This difference is likely because Beijing, one of China's most arid regions, has lower annual precipitation, leading to more positive $\delta^{13}C$ values due to water scarcity [68]. Conversely, Chung et al. [70] reported that densely populated areas with more industrial activity tend to show more negative $\delta^{13}C$ values. However, in the case of Beijing, natural factors seem to influence $\delta^{13}C$ more strongly than human activities. In contrast to Beijing's example, Korean ginseng samples from Gimpo-si, a sparsely populated coastal area, exhibit less negative $\delta^{13}C$ values. This is attributed to lower CO_2 emissions and strong sea winds, which promote air circulation [70]. Meanwhile, Canadian American ginseng displays slightly more negative $\delta^{13}C$ values on average, though the difference is not significant. This may be because all these samples from different growing locations were cultivated under controlled conditions and harvested in October, minimizing the impact of regional climate differences on $\delta^{13}C$ values [72].

Consequently, relying solely on $\delta^{13}C$ values is insufficient for clearly distinguishing the geographical origins of ginseng samples; however, $\delta^{13}C$ can still serve as a useful supplementary tool in origin identification [70,72,73].

2.3.2. Hydrogen and oxygen

Because of the continental effect, ginseng harvested from coastal areas presented more positive delta values of deuterium and ^{18}O than those from inland areas, resulting in an obvious classification of ginseng samples between Korea and China, as well as among different cultivation regions within Korea itself. The samples from Ganghwa Island in Korea, for instance, showed much more positive delta values of deuterium and ^{18}O with respect to those from Yeongju and Chungju, both inland regions in Korea and both showed similarly more negative delta values [70]. These findings were coherent with those of Wang et al. [68]. In particular, the authors confirmed that the delta values of deuterium and ^{18}O are influenced by annual average temperature, latitudes and distance to the sea. The samples from Shandong Province, located by the Yellow Sea and enjoying the lowest latitudes and highest annual average temperature, showed much more positive values than the samples from other regions. However, a discrepancy was observed in the study of Chun et al. [73]. They found a positive correlation between ^{18}O delta values in ginseng roots and the distance between the growing region and the sea. This may be due to the local topographical characteristics, but it is still unclear which factor could be the determinant [73].

An earlier attempt was made by using 50 American ginseng samples as a training database to establish a model for geographical discrimination. An overall accuracy of 88 % was obtained based on the training database and the individual accuracies of various origins were at least 72.7 %. This model was then used to distinguish 25 raw American ginseng samples which were well divided into 5 groups by the developed model, with 3 of them being wrongly classified. This tentative model proved to be a potential tool for differentiating the geographical origins of raw American ginseng samples [90].

Drawing from the insights in the preceding discussions, it becomes evident that $\delta^{2}H$ and $\delta^{18}O$ values not only hold significant potential as reliable indicators for discerning the geographical origin of ginseng but also provide nuanced information regarding the geo-climatic conditions of the roots growth regions.

2.3.3. Nitrogen

The study of Chung et al. [73], reported a larger variation of $\delta^{15}N$ in ginseng with respect to other fruits and vegetables such as carrots, tomatoes and lettuce, even if the same type, brand and quantities of fertilizers were used. This may be caused by the fact that ginseng is a perennial plant and is cultivated for several years in the same location. They further explained that the lower $\delta^{15}N$ values observed in ginseng roots from Eumseong were anticipated due to variations in N-isotopic

Table 2
Delta values (‰) and sample information (including number of replicates, harvest year and plants age) of American ginseng samples from various studies [68,72,90].

Elements	Origin	Mean ± SD ‰	Sample information	Note
Carbon $\delta^{13}C_{VPDB}$/‰	Shandong (China)	−28.4 ± 1.1 to −25.9 ± 0.9	n = 12, harvested in 2019, 4–5 yrs [68] n = 38, 3 yrs [72] n = 9 [90]	Discrepancies in carbon delta values may depend on the cultivation methods, harvest times and other natural or artificial factors.
	Beijing (China)	−25.9 ± 1.5 to −25.0 ± 0.6	n = 8, harvested in 2019, 4–5 yrs [68] n = 11 [90]	
	Northeast of China	−28.7 ± 1.1 to −25.5 ± 0.8	n = 8, harvested in 2019, 4–5 yrs [68] n = 18, 3 yrs [72] n = 11 [90]	
	Canada	−28.9 ± 1.1 to −26.4 ± 0.9	n = 10, harvested in 2018, 5 yrs [68] n = 15, 3 yrs [72] n = 10 [90]	
	US	−28.7 ± 1.4 to −26.7 ± 0.5	n = 6, harvested in 2018, 5yrs [68] n = 10, 3yrs [72] n = 12 [90]	
Hydrogen $\delta^{2}H_{VSMOW}$/‰	Shandong (China)	−66.6 ± 5.0 to −42.7 ± 3.3	n = 12, harvested in 2019, 4–5 yrs [68] n = 38, 3 yrs [72] n = 9 [90]	Great variations within the same regions may be caused by conditions of the specific locations.
	Beijing (China)	−67.4 ± 7.1 to −60.0 ± 5.6	n = 8, harvested in 2019, 4–5 yrs [68] n = 11 [90]	
	Northeast of China	−84.2 ± 4.1 to −65.9 ± 10.5	n = 8, harvested in 2019, 4–5 yrs [68] n = 18, 3 yrs [72] n = 11 [90]	
	Canada	−76.6 ± 4.4 to −48.7 ± 4.7	n = 10, harvested in 2018, 5 yrs [68] n = 15, 3 yrs [72] n = 10 [90]	
	US	−64.1 ± 5.3 to −51.3 ± 1.0	n = 6, harvested in 2018, 5yrs [68] n = 10, 3yrs [72] n = 12 [90]	
Oxygen $\delta^{18}O_{VSMOW}$/‰	Shandong (China)	23.1 ± 0.3 to 23.1 ± 1.8	n = 12, harvested in 2019, 4–5 yrs [68] n = 38, 3 yrs [72] n = 9 [90]	Variations within the same regions may be determined by conditions of the locations.
	Beijing (China)	21.2 ± 0.4 to 22.5 ± 4.1	n = 8, harvested in 2019, 4–5 yrs [68] n = 11 [90]	
	Northeast of China	20.6 ± 0.4 to 23.2 ± 1.3	n = 8, harvested in 2019, 4–5 yrs [68] n = 18, 3 yrs [72] n = 11 [90]	
	Canada	21.7 ± 0.5 to 25.1 ± 3.3	n = 10, harvested in 2018, 5 yrs [68] n = 15, 3 yrs [72] n = 10 [90]	
	US	21.3 ± 0.1 to 21.8 ± 2.2	n = 6, harvested in 2018, 5yrs [68] n = 10, 3yrs [72] n = 12 [90]	
Nitrogen $\delta^{15}N_{Air-N2}$/‰	Shandong (China)	−0.5 ± 1.5 to 3.1 ± 2.2	n = 12, harvested in 2019, 4–5 yrs [68] n = 38, 3 yrs [72] n = 9 [90]	Differences depend on the fertilizers used during the cultivation process.
	Beijing (China)	−0.5 ± 0.6 to 1.4 ± 0.6	n = 8, harvested in 2019, 4–5 yrs [68] n = 11 [90]	
	Northeast of China	−1.0 ± 1.1 to 2.3 ± 1.1	n = 8, harvested in 2019, 4–5 yrs [68] n = 18, 3 yrs [72] n = 11 [90]	
	Canada	−2.7 ± 1.0 to 0.3 ± 1.2	n = 10, harvested in 2018, 5 yrs [68] n = 15, 3 yrs [72] n = 10 [90]	
	US	−0.9 ± 1.6 to 3.6 ± 0.8	n = 6, harvested in 2018, 5yrs [68] n = 10, 3yrs [72] n = 12 [90]	

Table 3
Delta values (‰) and sample information (including number of replicates, cultivar and plants age) of Korean ginseng samples from various studies [70,73].

Elements	Origin	Mean ± SD	Sample information	Notes
Carbon $\delta^{13}C_{VPDB}$/‰	Yeongju−si	−27.2 ± 0.9 to −25.8 ± 0.9	n = 4–6 [70]	Differences observed in the samples from the same region rely on the farms where the ginseng grew
	Chungju−si	−26.9 ± 1.4 to −25.7 ± 1.8	n = 4–6 [70]	
	Hwacheon−gun	−26.1 ± 0.7 to −24.9 ± 1.5	n = 4–6 [70]	
	Ganghwa−gun	−24.3 ± 0.6 to −23.4 ± 1.4	n = 4–6 [70]	
	Gimpo−si	−27.8 ± 1.0 to −24.8 ± 0.3	n = 4–6 [70]	
	Paju−si	−25.3 ± 1.3 to −23.6 ± 1.0	n = 4–6 [70]	
	Eumseong	−28.4 ± 0.05 to −23.7 ± 0.11	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	Variances of delta values in the same region depend on the cultivars of ginseng analyzed
	Jinan	−26.3 ± 0.04 to −25.0 ± 0.10	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Cheorwon	−26.9 ± 0.07 to −23.6 ± 0.00	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Pyeongchang	−25.6 ± 0.01 to −22.0 ± 0.06	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Punggi	−25.8 ± 0.01 to −22.8 ± 0.05	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
Hydrogen $\delta^{2}H_{VSMOW}$/‰	Yeongju−si	−67.4 ± 1.3 to −56.3 ± 6.3	n = 4–6 [70]	Differences observed in the samples from the same region rely on the farms where the ginseng grew
	Chungju−si	−64.5 ± 2.1 to −58.6 ± 1.6	n = 4–6 [70]	
	Hwacheon−gun	−54.7 ± 2.6 to −54.3 ± 0.7	n = 4–6 [70]	
	Ganghwa−gun	−42.9 ± 2.6 to −40.1 ± 6.8	n = 4–6 [70]	
	Gimpo−si	−52.7 ± 2.3 to −52.7 ± 1.9	n = 4–6 [70]	
	Paju−si	−56.2 ± 1.7 to −49.8 ± 4.9	n = 4–6 [70]	
Oxygen $\delta^{18}O_{VSMOW}$/‰	Yeongju−si	28.5 ± 0.4 to 33.6 ± 1.1	n = 4–6 [70]	Differences observed in the samples from the same region rely on the farms where the ginseng grew
	Chungju−si	31.4 ± 0.5 to 31.9 ± 01.1	n = 4–6 [70]	
	Hwacheon−gun	30.1 ± 1.2 to 32.3 ± 1.6	n = 4–6 [70]	
	Ganghwa−gun	38.4 ± 0.8 to 39.7 ± 1.8	n = 4–6 [70]	
	Gimpo−si	31.5 ± 0.7 to 32.1 ± 1.4	n = 4–6 [70]	
	Paju−si	31.5 ± 2.1 to 34.6 ± 1.4	n = 4–6 [70]	
	Eumseong	26.3 ± 0.34 to 28.0 ± 0.21	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	Variances of delta values in the same region depend on the cultivars of ginseng analyzed
	Jinan	25.2 ± 0.03 to 25.8 ± 0.37	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Cheorwon	26.9 ± 0.38 to 28.0 ± 0.27	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Pyeongchang	25.3 ± 0.19 to 26.9 ± 0.24	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Punggi	26.1 ± 0.58 to 27.4 ± 0.24	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs	

(*continued on next page*)

Table 3 (*continued*)

Elements	Origin	Mean ± SD	Sample information	Notes
			Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
Nitrogen $\delta^{15}N_{Air-N2}$/‰	Yeongju−si	−0.82 ± 0.3 to 6.8 ± 1.2	n = 4–6 [70]	Differences observed in the samples from the same region rely on the farms where the ginseng grew
	Chungju−si	6.4 ± 0.9 to 7.6 ± 1.2	n = 4–6 [70]	
	Hwacheon−gun	−1.6 ± 0.7 to 7.7 ± 2.3	n = 4–6 [70]	
	Ganghwa−gun	4.9 ± 1.3 to 9.0 ± 1.2	n = 4–6 [70]	
	Gimpo−si	2.6 ± 1.7 to 8.8 ± 1.9	n = 4–6 [70]	
	Paju−si	5.9 ± 0.9 to 6.9 ± 3.4	n = 4–6 [70]	
	Eumseong	0.7 ± 0.01 to 2.1 ± 0.07	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	Variances of delta values in the same region depend on the cultivars of ginseng analyzed
	Jinan	7.5 ± 0.03 to 9.0 ± 0.05	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Cheorwon	1.9 ± 0.03 to 3.7 ± 0.12	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Pyeongchang	2.4 ± 0.10 to 4.6 ± 0.08	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Punggi	2.5 ± 0.02 to 5.7 ± 0.04	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
Sulfur $\delta^{34}S_{VCDT}$/‰	Eumseong	3.1 ± 0.1 to 6.7 ± 2.4	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	Variances of delta values in the same region depend on the cultivars of ginseng analyzed
	Jinan	3.4 ± 0.1 to 6.3 ± 0.6	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Cheorwon	2.6 ± 0.3 to 3.9 ± 0.5	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Pyeongchang	1.4 ± 0.2 to 8.5 ± 1.7	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	
	Punggi	3.5 ± 0.1 to 4.4 ± 0.5	Gopung, n = 3, 3 yrs Geumpung, n = 3, 3 yrs Sunwoon, n = 3, 3 yrs Yeonpung, n = 3, 3 yrs Cheonpung, n = 3, 3 yrs K−1, n = 3, 3 yrs [73]	

fractionation and the availability of fertilizers. These factors, in turn, are influenced by the soil's physical, chemical, and microbial properties, rather than solely by the use of chemical nitrogen-based fertilizers. Other studies also confirmed the influence of fertilizers, soil conditions on delta values of nitrogen [68,72]. At the same time, the $\delta^{15}N$ values could also be influenced by climatic factors such as air temperature and

sunshine hours [72]. The growing regions of American ginseng in the US and Canada belong to continental climate while Shandong Province and Northeast China belong to subtropical monsoon regions. The samples growing in these two types of climate show significant differences in $\delta^{15}N$ values while those from the same climatic conditions didn't show much difference.

Based on the aforementioned discussion, $\delta^{15}N$ values may serve as a reliable indicator of ginseng growth location. However, when multiple farms within a given area utilize identical fertilizers, distinguishing the origins solely based on nitrogen delta values becomes challenging [70,72].

2.3.4. Sulfur

No data on sulfur delta values are reported in literature for American ginseng according to our best knowledge. The $\delta^{34}S$ level reported for Korean ginseng displays a negative correlation with the distance between growing location and the coast. The $\delta^{34}S$ value varies also according to type of fertilizers used for cultivation and may be used as a potential marker for verifying the authentication of ginseng. As a result, $\delta^{34}S$ values could have the potential to help with distinguishing ginseng from different cultivation regions [69,73].

3. Saffron

Saffron, the dried stigma of *Crocus sativus L.* flowers, is known to be the most expensive spice in the world [102–105]. It is a bulbous perennial stem−less plant [106]. Its main producing countries include Iran, Spain, Greece and Italy. It is often used as a food supplement for its particular color and flavor as well as its medicinal properties such as anti−asthma, anti−inflammatory, antioxidant, antitumor, cardio−protective, antidepressant, antibacterial and anti−Alzheimer [15,35,78,106–109]. Since ancient times, saffron has been used as traditional medicine for treating diseases including depression, cardiovascular disease, menstruation disorders, asthma, insomnia, digestive ailments and some others [106,110–113]. Several studies have already revealed the chemical compositions of saffron which contains more than 300 volatile and non−volatile compounds [106] and about 150 of these compounds are volatile or aroma−yielding terpenes, terpene alcohols and esters [32]. Among all these chemicals, crocin, picrocrocin and safranal are more important than the others. The characteristic color of saffron is mainly due to the presence of crocetin esters, also known as crocins, a family of water soluble mono and dyglucosyl esters; while picrocrocin (glucoside of safranal) is responsible for the slightly bitter flavor of saffron; and safranal is the principal contributor of the distinctive saffron aroma [15,78,105,108,109]. Besides the three major components, lycopene, beta−carotene, as well as vitamins like riboflavin and thiamin are also found in Saffron [15] and the bioactive properties of saffron, although mainly due to the presence of crocin picrocrocin and safranal, but also to the synergistic activity of other compounds discovered in this spice [114].

The quality of saffron may be influenced by several parameters during the process of harvesting, dehydration and storage, or simply by the actions adopted by the producers or dealers [102]. The high price and limited production of saffron determine that it is one of the most frequently adulterated spices [115]. In the review work of Kumari and colleagues [105], the authors summarized the adulteration and main types of adulterants found in saffron. Briefly, the adulterants may be classified into two categories which are nature based or biological adulterants (butterfly bush, safflower and wild carrot etc.), and artificial or chemical based or synthetical adulterants (inorganic salts, liquid glycerin, and various types of dyes etc.). Natural materials may be present unintentionally due to different production processes and are able to produce good color and quality of food, yet artificial materials are added for more vibrant and various colors.

The global saffron market was estimated at USD 602.2 million in 2023 and is expected to grow at a CAGR of 7.1 % from 2024 to 2030 [116]. It was estimated that the global production of saffron in 2018 was 418 tons of which 90 % was produced in Iran [117]. In Figs. 1 and 2, the percentage of export and import by countries in the year 2022 were shown.

3.1. Techniques for geographical differentiation

A few studies have reviewed techniques and methods for detecting adulterants in saffron [15,108,109]. The same techniques can also be employed in geographical classification of saffron from different production regions. The available methods cover a wide range of different techniques or their combinations. Inductively coupled plasma−mass spectrometry (ICP−MS) was applied to investigate elemental composition contained in saffron [105,118], near−infrared (NIR) spectroscopic fingerprints of saffron samples were recorded and compared with pure standards to identify differences [102], UV–Vis spectra of aqueous saffron extracts were recorded for geographical classification [104], chromatographic methods combined with different detectors were used to quantify various compounds in saffron [103,119–121]. ^{1}H NMR was used to obtain the metabolite fingerprints of saffron [115,122] and fluorescence intensities were used to create excitation and emission matrix to differentiate saffron from different countries [35]. More recently, new techniques have been emerging to verify the genuineness of saffron such as Time of Flight−Secondary Ion Mass Spectrometry (ToF−SIMS) [123], hyperspectral imaging [124] and optical-nose based on fluorescent nanomaterials sensor array [125]. These new techniques emerged because of their outstanding performance in food analysis. ToF-SIMS is renowned for its molecular specificity and high sensitivity. Usually, it is considered non-destructive for the quantity of sample required at microscale. Moreover, it can work without extraction making it an eco-friendly technique [123]. Hyperspectral imaging is a relatively fast and non-destructive technique for investigating food authenticity. The most important advantage is that it can also provide valuable spatial information about the positions of the components in the samples [124]. Aggregating non-specific sensor responses enables efficient design and construction of sensor arrays for analyte detection, where fluorescent probes offer a sensitive and simple method for analyzing complex mixtures [125].

IRMS, on the other hand, as a particularly interesting technique, has risen to be an important and pretty widespread way to determine the provenance of saffron. Compared to the other techniques, IRMS not only reveals regional signatures and verifies saffron authenticity but also provides environmental and agricultural insights, such as the growing conditions and types of fertilizers used [74,126].

3.2. Sample treatment for isotope ratio analysis

3.2.1. Drying and grinding

Saffron samples that contained excess humidity had to be dried. Drying procedure could be carried out using an electric oven, sun−-drying, microwave assisted drying, or lyophilization [32,126,127]. The dried samples were ground into fine and homogeneous powder to be more suitable for further steps such as bulk analysis and extraction.

3.2.2. Extraction

Extraction might be performed in various ways. Maggi and colleagues [74], for instance, conducted ultrasonic bath assisted extraction followed by centrifuge to obtain defatted dried matter (DDM), i.e. carbohydrates and proteins. In another work, both water−soluble and triacylglycerol fractions were extracted following different procedures [110]. Other extraction methods were also carried out by the researchers [128,129].

3.3. Geographical differentiation capability

SIRA has been used for geographical origin differentiation of saffron

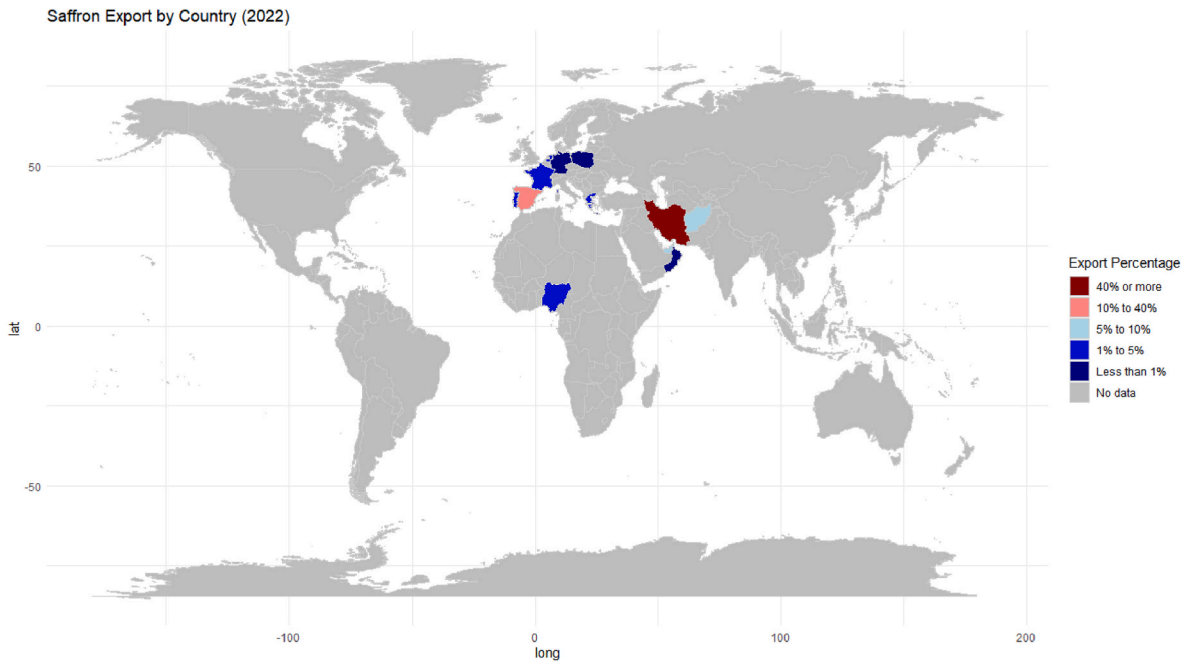

Fig. 1. Global export of saffron (generated by R version 4.4.1, data souce: https://oec.world/en/profile/hs/saffron).

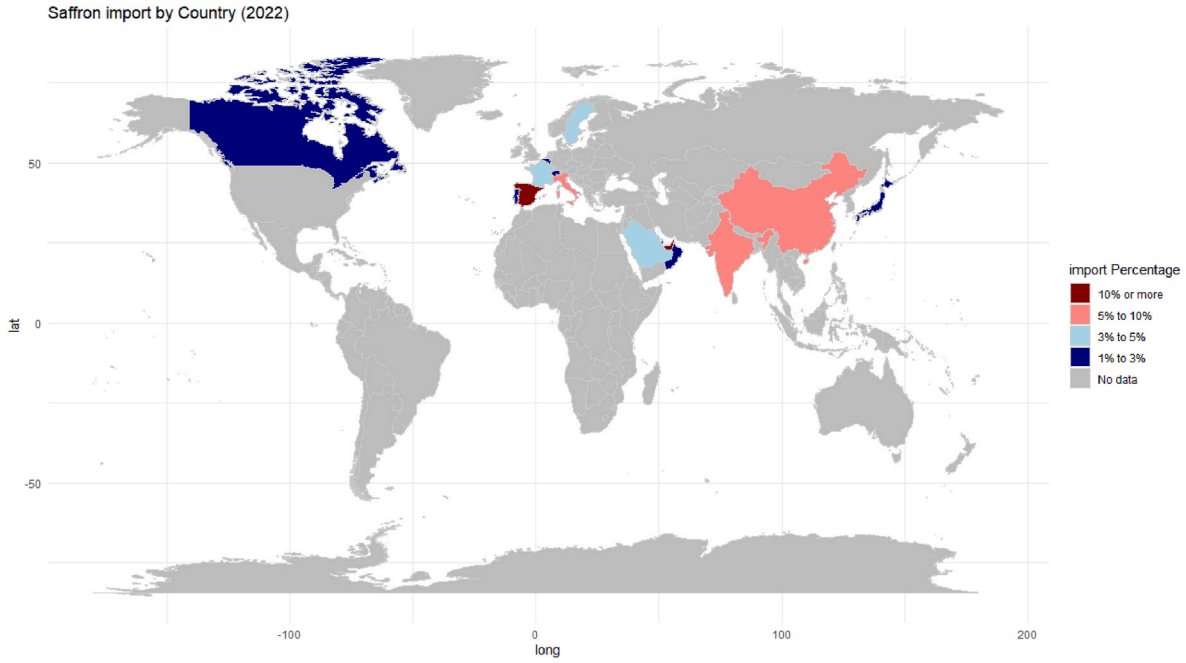

Fig. 2. Global import of saffron (generated by R version 4.4.1, data souce: https://oec.world/en/profile/hs/saffron).

spice since decades ago [74]. Quite a few studies [32,74,110,111, 126–129] showed that delta values of light elements (H, C, N, O and S), alone or in combination with other chemical information about the samples, had proved to be a powerful tool for classifying geographical origin and as well as verifying the authentication of saffron samples.

3.3.1. Carbon

Rocchi et al. [32] studied the delta values of carbon and nitrogen of Italian saffron samples and non-Italian ones. They found that these samples were classified mainly by $\delta^{13}C$ values (Italian samples ranged from −31.52 ‰ to −27.37 ‰ while non−Italian ones ranged from −27.10 ‰ to −25.19 ‰) instead of $\delta^{15}N$ values (between 0.55 ‰ and 5.14 ‰ for Italian samples and for others between 2.39 ‰ and 6.83 ‰). Meanwhile, the $\delta^{13}C$ values of defatted dry matter - DDM were discovered to be able to discriminate saffron from Italy (−26.6 ‰ ± 0.1 ‰) and Greece (−26.6 ± 0.2 ‰) against those from Iran (−24.5 ± 0.2 ‰) and Spain (−24.5 ± 0.4 ‰) [74]. Similar results were also observed by another group of researchers [110] who discovered that carbon isotope ratio was the principal factor that determined the differentiation of saffron samples from Iran (−25.3 ± 0.5 ‰) and Greece (−27.5 ± 0.4 ‰). Nie et al. [126] and Liu et al. [127] studied saffron grown in China and in other countries (Iran and Spain). Their studies also showed the potential of carbon isotope ratio as a marker of geographical provenance in cases of saffron, and even for distinguishing saffron from western

(Tibet, −25.7 ± 0.1 ‰ and Xinjiang, −25.9 ± 0.5 ‰) and eastern (Shanghai, −26.7 ± 0.2 ‰ and Zhejiang, −26.6 ± 0.7 ‰) China.

Compound specific isotope analysis focused on safranal was carried out by Moras and colleagues [129] and showed the potential of combining $\delta^{13}C$ and $\delta^{2}H$ for the authentication of saffron products from Iran. With respect to saffron samples from Spain, Greece, France, Morocco and Italy, Iranian saffron has more positive $\delta^{13}C$ values.

3.3.2. Hydrogen and oxygen

Unlike what has been seen in the cases of ginseng, it is interesting to note that the study of Maggi et al. [74] revealed the highest hydrogen isotope ratio in saffron samples from Khorasan Province, Iran (in average −67.8 ‰) than the samples from Sardinia in Italy (averaging −72.4 ‰), La Mancha in Spain (averaging −75.1 ‰) and Western Macedonia in Greece which presented the lowest hydrogen isotope ratio (in average −84.7 ‰). The continental effects usually determine more negative hydrogen isotope ratios inland than near the ocean. The authors concluded that Khorasan, even though far away from the ocean, experiences high temperatures, low precipitation and humidity. These factors lead to the fact that the relevantly higher rate of evapo−tranpiration caused the enrichment of heavier hydrogen isotope within the plant tissue. At the same time, Western Macedonia enjoys much higher humidity that contributed to a depletion in deuterium. In contrast, the saffron samples from Tibet, China followed the continental effects and showed much lower $\delta^{2}H$ (−112.5 ± 0.8 ‰ for Tibet and −85.0 ± 0.8 ‰ for Shanghai) and $\delta^{18}O$ (21.7 ± 0.1 ‰ for Tibet and 26.4 ± 1.0 ‰ for Shanghai) values than samples from other provinces of the same country [126,127] but between China (−95.9 ± 11.2 ‰) and Iran (−95.1 ± 2.4 ‰) no significant distinction in $\delta^{2}H$ values was observed [126]. Perini and colleagues examined the correlation between $\delta^{2}H$ and $\delta^{18}O$ values and the production region. They found clear discrimination between Italian samples and Iranian ones but only partial classification between Italian and Moroccan ones. They also observed a better correlation between delta values and local natural conditions for hydrogen than oxygen because hydrogen can be absorbed only from roots when oxygen can also be uptaken by stomata in the form of CO_2 and O_2 [111].

3.3.3. Nitrogen

Rocchi et al. [32] pointed out that $\delta^{15}N$ did not lead to statistical differences between Italian saffron and non−Italian saffrons. Similar results were obtained also by Liu et al. in their investigation of saffron in the Chinese market [127]. Only the samples from Tibet show much more positive $\delta^{15}N$ values than the samples from other provinces in China and from Iran and Spain. When comparing the overall values of the three countries, although the average value of Iranian saffron is significantly more negative than those of Chinese and Spanish samples, yet the ranges overlapped. So, it is not sufficient to distinguish saffron samples in the China market by their origin using only the $\delta^{15}N$ value. In another study, however, it was found that $\delta^{15}N$ of the DDM could clearly differentiate saffron from Italy and Greece, and the saffron from Iran and Spain [74].

3.3.4. Sulfur

Few studies reported $\delta^{34}S$ values of saffron samples. Notable differences in $\delta^{34}S$ were discerned between saffron from different places in China, from westernmost (e.g 1.3 ± 0.2 ‰, Tibet) to easternmost (e.g 5.7 ± 0.9 ‰, Shanghai). This classification may be the result of the difference in the distances from the ocean of the farmlands, which indicates that $\delta^{34}S$ could be a valuable parameter for verifying saffron spice from locations impacted by the ocean or not [127]. The geographical differentiation capability of $\delta^{34}S$ was also confirmed by Perini et al., but because of the large numbers of factors which could impact this parameter, considerations about these values are difficult to be carried out [111].

4. Chrysanthemum flos

Chrysanthemum Flos, the dried flowering head of *Chrysanthemum morifolium (Ramat) H.*, has been long known to contain components that are good for health in the petals and has been used as an important traditional edible and medicinal herb in China, especially as flower infusion for healthcare by infusing dried chrysanthemum into hot water, which is one of the most popular drinks consumed in China [130–133]. Modern pharmacological studies showed that the chrysanthemum has extensive biological activities ranging from anticancer and anti−inflammatory effects to antioxidative and antidiabetic effects [134]. Investigation on chemical constituents shows that chrysanthemum contains significant amounts of bioactive compounds including flavonoids, phenolic acids, volatile oils, polysaccharides, nucleosides and amino acids [135–139] of which the former three types are considered as principal components and are believed to be responsible for the activities previously mentioned [140]. Recent research identified, in total, more than 200 different types of compounds from different cultivars of chrysanthemum morifolium of which more than 40 flavonoids, about 160 lipid molecular species, 40 nucleobases, nucleosides, nucleotides and amino acids and about 20 chlorogenic acids and other caffeic acid derivatives [139,141–143]. According to the Chinese Pharmacopoeia (2020 edition), the chrysanthemums are divided into five principal groups based on the regions of origin and processing methods, i.e. ‘Bo’ (Bozhou, Anhui Province), ‘Chu’ (Chuzhou, Anhui Province), ‘Gong’ (Huangshan, Anhui Province), ‘Hang’ (Tongxiang, Zhejiang Province), and ‘Huai’ (Jiaozuo, Henan Province) [80,144]. Although the evaluation criteria of different cultivars of chrysanthemums are the same in the Chinese Pharmacopoeia, chrysanthemums from different regions vary a lot in the market because of their differences in chemical compositions and quality as shown in other studies [80,131,145]. Besides the aforementioned cultivars, some other cultivars from other origins can also be seen in the market. These chrysanthemums available may have different medical effects but are almost identical in appearance and smell [146] and consequently consumers are unable to distinguish them and this leads to profit−motivated adulterations. Owing to what has been talked about, it is important and necessary to identify the cultivar of a certain chrysanthemum.

4.1. Techniques for geographical determination

Many techniques have been applied for this purpose. Chromatography combined with mass spectrometry is the most widely used one for determining and differentiating the cultivars and geographical origins of Chrysanthemum Flos. Lai and cooperators identified and characterized 23 flavonoids and caffeoylquinic acid derivatives from the flower and the leaf of Chrysanthemum morifolium [141]. During the following years, more studied have been carried out to verify the cultivars and geographical origins of Chrysanthemum morifolium samples using chromatography coupled with mass spectrometry and focusing on various compounds such as flavonoids, phenolic compounds, nucleobases, nucleotides, nucleosides, amino acids, lipids and multiple mineral elements [134,143,147–150]. Other analytical techniques such as fluorescence together with transmission electron microscopy (TEM) was used as a novel visual censoring method [146]; high performance thin layer chromatography (HPTLC) was used to compare the chemical profiles of chrysanthemum of different cultivars from various regions and inductively coupled plasma mass spectrometry (ICP−MS) was used to determine the heavy metal contaminations [151] and laser−induced breakdown spectrometry (LIBS) was applied to rapidly identify the origin of chrysanthemum [151,152].

In recent years, isotope ratio mass spectrometry has been increasingly widely used for authentication and traceability of plant products [52,153] but not many studies have been performed on chrysanthemums. Bai et al. [83], and Yao et al. [84], studied the origin traceability of the same cultivar of chrysanthemum Hangbaiju (HBJ) from different

regions and that of different cultivars: Hangbaiju (HBJ), Chuju (CJ), Gongju (GJ), Huaiju (HJ), Fubaiju (FBJ) and Qiju (QJ) from different regions, respectively, by means of isotope ratio mass spectrometry and multi−element analysis combined with chemometrics.

4.2. Sample treatment for isotope ratio analysis

Fresh flowers were collected from local farmers or planting bases in October and November 2020. After removing surface moisture, samples were oven-dried at 60 °C for 1−2 days, ground, sieved (50−mesh), labeled, and stored in a desiccator until analysis [83,84].

4.3. Geographical differentiation capability

In order to distinguish HBJ from different production origins, stable isotope ratio analysis (δ^{15}N, δ^{13}C, δ^{2}H and δ^{18}O) and multi−element analysis based on 44 elements were both performed [83]. In this study, δ^{13}C ranged between −29.0 ‰ and −26.6 ‰, which falls into the typical interval of a C3 plant. The slight difference in the δ^{13}C value might be the reflection of the climate information and may be related to the differences in latitude, longitude and altitude of the production regions. However, it is more likely that the variance of δ^{13}C is the result of the synergy of multiple climatic factors rather than only one of them. Huangtan and Jiangchang have lower latitude and show more positive δ^{2}H and δ^{18}O values with respect to Yancheng, Rudong and Tongxiang which have higher latitude and show more negative δ^{2}H and δ^{18}O values. Jinhua, having low latitude, showed more negative δ^{2}H and δ^{18}O values which may be caused by the higher altitude and higher annual precipitation than other regions. The results also showed that δ^{15}N of Rudong was notably higher than that of the other origins. Such differences were probably the consequence of the usage of fertilizers during planting. Notable differences in δ^{15}N values were observed by Mei et al. as well [51]. Samples were collected from 3 different regions in the same province (Zhejiang, China). The values indicated the use of synthetic fertilizers during the growing of the flowers. Significant differences might be the results of several compound fertilizer sources used across the regions, as supposed the authors. They also found more positive δ^{13}C (−27.8 ‰), δ^{2}H (−61.8 ‰) and δ^{18}O (25.8 ‰) values in the samples from Chun'an where there is longer sunshine duration. Different water sources and climatic conditions may also contribute to this result. In Mei's study on the Chrysanthemum [51], significant differences in delta values were also noticed in different plant tissues and during different growth stages. The results of these studies could be seen in Figs. 3 and 4.

Another study took into consideration different varieties of chrysanthemum from various regions. In general, δ^{2}H values vary between −90.9 ‰ (Jiaozuo) and −60.4 ‰ (Huangshan), while δ^{18}O values fall into the range between 20.8 ‰ (Jinhua) and 31.9 ‰ (Machang). GJ (Huangshan) showed the most positive δ^{13}C (−26.1 ‰) value which might be caused by the highest altitude and highest annual precipitation of Huangshan. The samples from Jiaozuo present the most negative δ^{2}H value and relatively negative δ^{18}O value. This may be explained by the fact that this city has the highest altitude which is, as stated by the authors, in agreement with the findings of other studies that the delta values of H and O are negatively related to altitude and longitude while those of carbon and nitrogen are positively related [84].

5. Goji

Goji berries, also known as wolfberries, are the fruits of two closely related species (*Lycium barbarum* L. and *Lycium chinense Mill.*) in the family Solanaceae. These fruits are orange red in color and sweet in taste. The commercial products are usually the sun−dried fruits after being harvested around late summer and early autumn [25,154].

Goji berries have been used as a traditional medicine in China for centuries and until today, they are still considered as functional food. Quite a few studies confirmed the pharmaceutical and medicinal properties of goji berries, such as ocular neuroprotection, glucose control, antioxidation, hepatic protection, immunomodulatory effects, antiaging, lowering blood lipid and cholesterol and even potential anticancer properties [25,31,81,82,154–156]. These functions are the results of the chemical compounds contained in the fruits. Up to now, many researchers have revealed the chemical components of goji berries: polysaccharides, simple sugars, phenols, carotenoids and carotenoid esters, vitamins, and trace elements. The principal soluble contents are saccharides and organic acids which determine the taste, ripeness of the fruits, and consumer acceptability. These are also important signs of the berries' quality. Another major group of metabolites in goji berries is carotenoids, which include zeaxanthin dipalmitate. Zeaxanthin is the most representative pigment in the macular zone of the human retina and is peculiarly helpful for protecting the macular from oxidative harms. The anti−cancer activity of goji berries may be related to the presence of Quercetin, kaempferol, and relative derivatives [81,154–158].

Currently, the major global supplier of goji berries is China. Particularly, the primary production regions are Ningxia Hui Autonomous Region, Qinghai Province, Gansu Province, Tibet, Inner Mongolia, and Xinjiang Uyghur Autonomous Region [25,31,154]. With the increasing customer demand for this fruit and the related food products (such as supplements or capsules), some other countries also introduced goji berries. Several cultivars can be found in Europe, Mediterranean regions, South America, Australia and Africa [156,157,159]. Each geographical location possesses its proper climatic, geo−chemical and anthropogenic conditions such as temperature, sunshine intensity, precipitation, soil nutrients, and cultivation methods. These factors may lead to differences in the contents of functional components [25,31,154,160]. Certain regions, such as Zhongning County in Ningxia, enjoy a reputation for producing goji berries of high quality and are able to demand a relatively higher price than other regions [154]. Illegal dealers produce lower quality goji berries but label them as "Origin from Zhongning", for instance, to grab more economic profit and therefor, geographical authentication is needed to fight against counterfeit and guarantee the benefits of both consumers and legal producers and dealers worldwide [31,82,157,160].

In 2023, the total area of goji berries cultivation nationwide in China reached 1221 km^2, with a fresh fruit yield of 1.4 million tons. The processing conversion rate was close to 20 %, resulting in a dried fruit yield of 240,000 tons [161].

5.1. Techniques for geographical differentiation

Traditionally, identifying the origin of goji berries consists of observing the color, shape, and size, as well as flavor tasting. However, these methods are not sufficiently reliable and require that the identifiers be highly qualified and experienced and the result be subjective enough [31]. Modern methods, including mass spectrometry, chromatography, near infrared spectroscopy and other techniques, have been employed to obtain more accurate and more subjective results. Particularly, LC−qTOF−MS has been used to draw the metabolic profile of goji berry extracts [154], the total flavonoid and total phenolic content were determined by means of NIR [25,31] and HPLC [158], atomic absorption spectrometry (AAS), ICP−MS and UV–Vis were applied to identify and quantify mineral elements and polysaccharides [140], and holistic information about samples' volatiles can be obtained by E−nose [31] or HS−GC−IMS [159]. IRMS, as an emerging technique for tracing the geographical origin of various food samples [49,50], has also been applied to determine the provenance of goji berries [155,156,160].

5.2. Sample treatment for isotopic analysis

Samples may be naturally air−dried and ground into homogenous fine powder with the assistance of liquid nitrogen. Besides air−drying, other drying processes were also evaluated: heat drying, drying without

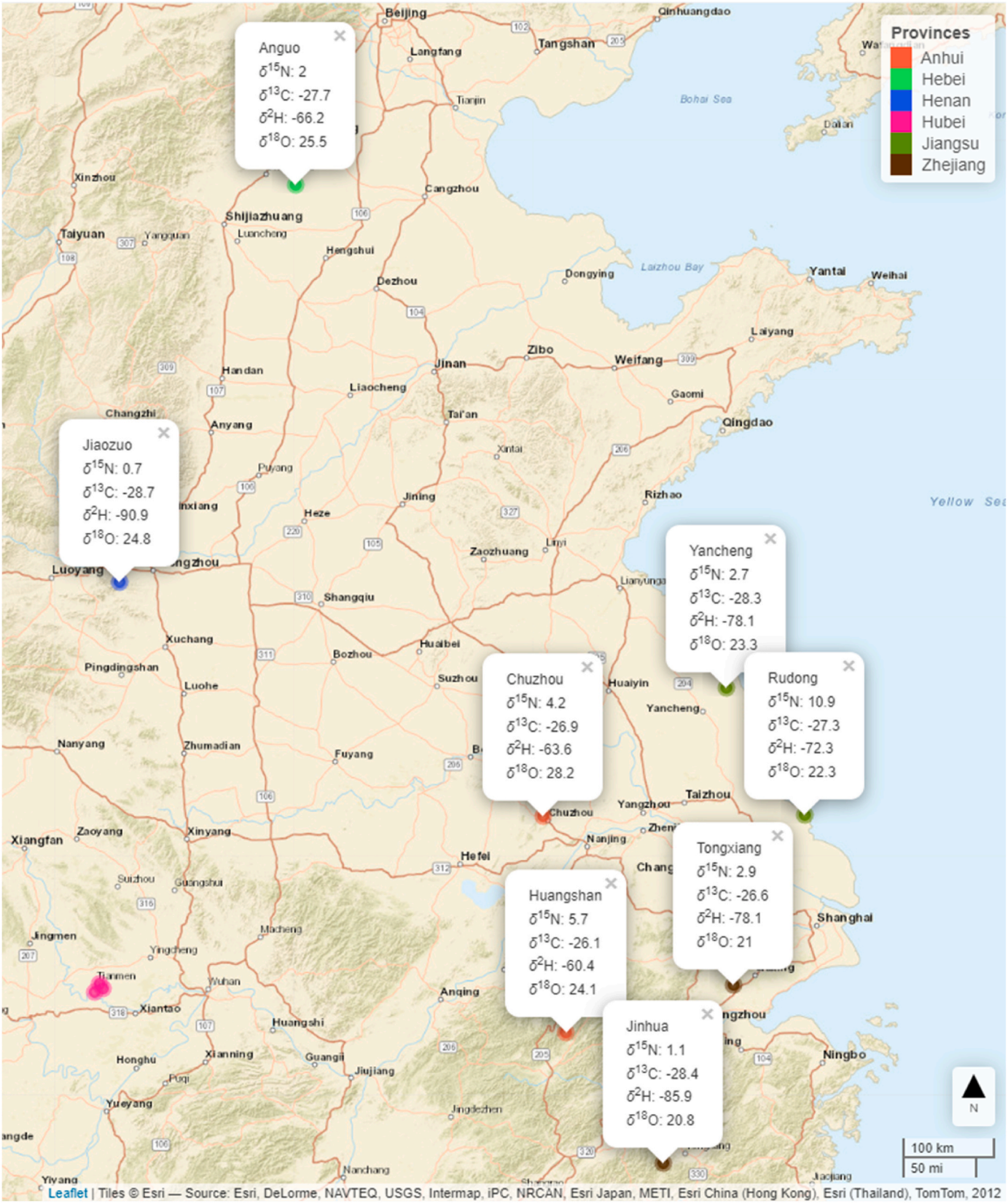

Fig. 3. Geographical distribution of Chrysanthemum samples (delta values expressed in ‰; generated by R, 4.4.1).

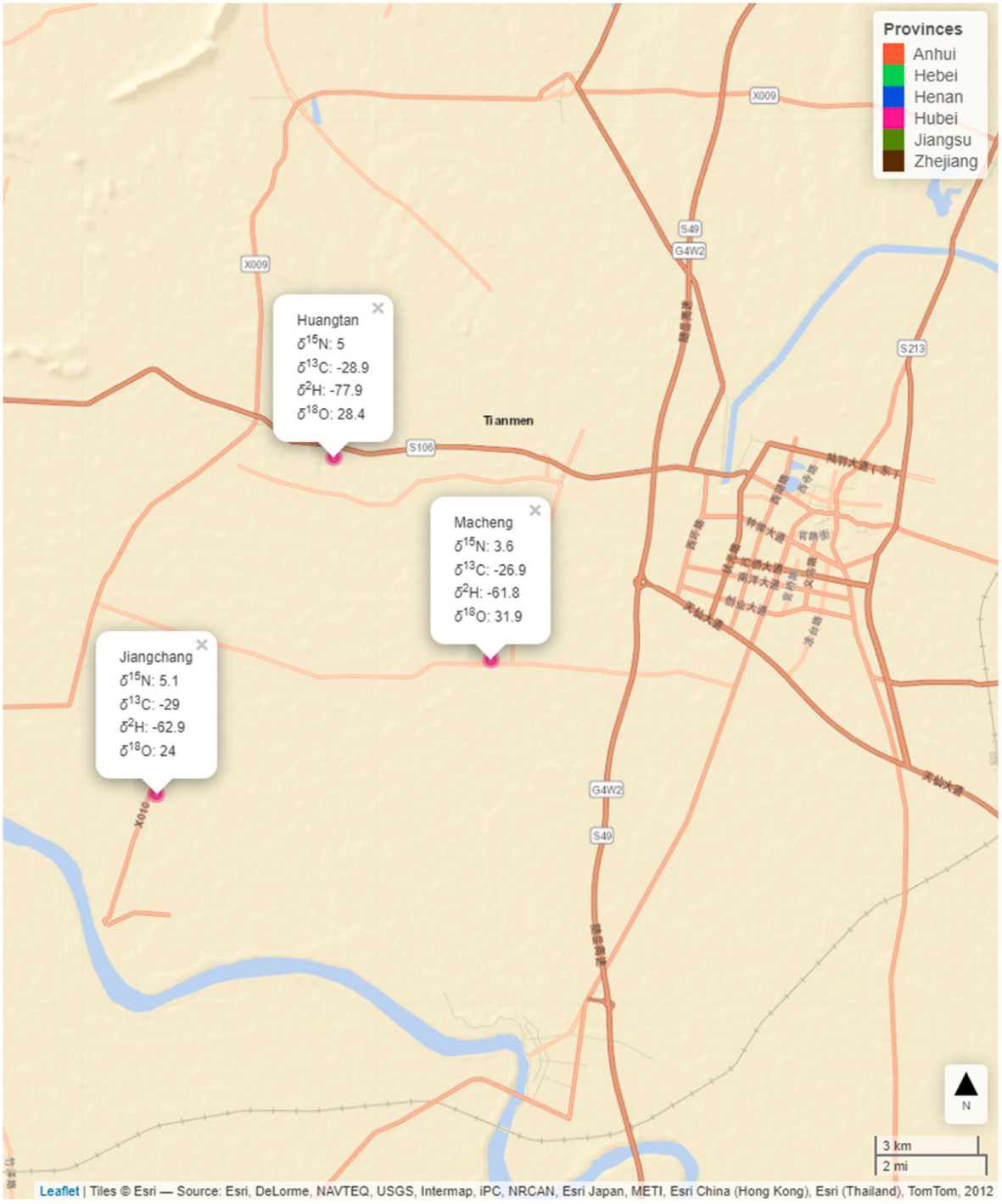

Fig. 4. Geographical distribution of Chrysanthemum samples (delta values expressed in ‰; generated by R, 4.4.1).

dewaxing, mechanical drying, and lyophilization. In all drying processes the samples were dewaxed by means of 15 % $NaHCO_3$, except for drying without dewaxing and lyophilization [156].

5.3. Geographical differentiation capability

Gong et al. [156] conducted a study on goji samples collected from five different provinces and autonomous regions (Inner Mongolia, Gansu, Xinjiang, Qinghai, and Ningxia) in China. They revealed that significant differences in $\delta^{13}C$ were observed among Ningxia (excluding Zhongning County, -26.2 ± 0.9 ‰), Qinghai (-25.3 ± 0.7 ‰) and Inner Mongolia (-27.0 ± 0.5 ‰) while $\delta^{15}N$ varied significantly among Ningxia (excluding Zhongning County, 4.2 ± 1.8 ‰), Inner Mongolia (6.3 ± 3.3 ‰) and Xinjiang (2.7 ± 3.5 ‰). The author confirmed that in their study, the compositions of earth element, free amino acids and saccharides are all influenced by cultivation regions. Combined with the chemical composition, stable isotope ratios of carbon and nitrogen showed potential to distinguish goji berries from various planting places.

A similar study was carried out to investigate the geographical classification of goji berries from Italy and Asian areas [155]. The delta values of carbon, hydrogen, oxygen, nitrogen, and sulfur were tested alongside 57 mineral elements and 14 carotenoids. The delta values of carbon fell into the interval between -28.2 ‰ and -24.3 ‰, in line with

the botanical origin of goji berries (C3 plant). The sample from Gobi Desert showed the most positive delta value because of the high temperature, low air humidity and high ground water deficit in this region. It is interesting to notice that the delta values of both O and H of Gobi samples are not correlated to the annual precipitation. This may be caused by the irrigation in this area for growing goji berries. Another interesting observation was that Asian samples demonstrated generally more positive $\delta^{34}S$ values (ranging from 4.2 ‰ to 11.5 ‰) than the Italian samples (ranging from 2.6 ‰ to 7.9 ‰). This phenomenon may be due to pedological characteristics of the soil. Particularly, samples from volcanic regions showed more positive $\delta^{34}S$ values. At the same time, the combustion of certain kinds of fossil fuels in the industrialized areas caused atmospheric pollution which may deposit on the soil and then lead to more positive $\delta^{34}S$ values. The $\delta^{34}S$ and $\delta^{15}N$ values of the samples are not correlated indicating different sources of the two elements: other than fertilization, pedological characteristics of the soil also play important roles. The t−test showed significant differences between Italian samples and non−Italian samples in $\delta^{34}S$, $\delta^{15}N$, concentrations of several elements like B, K, Cu, Al, As, Fe and some carotenoids.

A more detailed compound specific analysis was performed using GC−IRMS to investigate the carbon stable isotope ratio of several compounds (limonene, tetramethylpyrazine, safranal, geranylacetone, and β−ionone) contained in the goji berries (harvested in Qinghai, Gansu and Ningxia during Oct. 16–25, 2016) [160]. The results showed that the $\delta^{13}C$ values of tetramethylpyrazine and geranylacetone could be used to initially distinguish wolfberries from Qinghai compared to those from Gansu and Ningxia. Additionally, the $\delta^{13}C$ values of β−ionone provided further differentiation among all three regions. The larger $\delta^{13}C$ variation between Qinghai and the other two provinces is likely due to Qinghai's distinct high−altitude climate (above 2000 m), characterized by stronger sunlight and lower growing temperatures, which increases carbon isotope fractionation during the plant's growth.

6. Chemometric analysis

Multivariate analysis is a useful tool in data analysis for drawing information from the measurements. The most frequently used ones can be divided into two categories: unsupervised and supervised. In unsupervised methods, the goal is often to uncover previously unknown structures in the dataset, such as groups or clusters. In contrast, supervised methods assume these structures are already known and leverage this knowledge in the data analysis [162].

6.1. Principal component analysis (PCA)

PCA is a typical unsupervised multivariate analysis and is often used as the first step to reduce the size of the dataset to be analyzed while preserving most of the information for an inspection of the data distribution [72,73]. But it is not powerful enough when amounts of different factors are taken into consideration, as PCA was not able to distinguish, for instance, the American ginseng samples from Shandong (China), Northeast China, Canada and the US [72]. An insufficient separation of samples was also observed for both the domestic saffron and between Chinese and Iranian saffron in the China market [126]. The samples from four domestic regions were separated into three groups in the PCA plot. There were also slight overlaps between Chinese saffron and Iranian ones. Unlike in the studies of ginseng and saffron, the majority of the goji crops were correctly clustered by their origin using PCA. Goji from Zhongning County, Ningxia (-26.9 ± 1.0 ‰ for $\delta^{13}C$ and 2.4 ± 2.4 ‰ for $\delta^{15}N$), regarded as of premium quality, were discriminated against the fruits from the rest of Ningxia and the other four provinces in China using selected indices [156]. Bertoldi et al. [155] made attempts using PCA and cluster analysis based on the whole dataset showed satisfying results with one Italian sample being wrongly grouped with the Asian ones. This sample was wrongly grouped possibly due to its higher content of some trace metals and rare earth elements. A further statistical model based on selected parameters was built applying forward stepwise discriminant analysis. Using this model, all samples were correctly classified as of Asian or Italian origin.

6.2. Partial least squares − discriminant analysis (PLS−DA)

PLS−DA is a supervised model that is commonly used for authentication and botanical characterization [52]. To better discriminate the geographical origin of saffron, two PLS−DA models were established based on the chemical profile and isotopic compositions of the samples: a China−Iran model and a Chinese domestic model [126]. Although a fuzzy boundary was seen between Chinese and Iranian samples, yet the efficiency of separation was improved compared with PCA. In the domestic model, slight overlaps could still be observed between central and southwest regions. This unsatisfactory result could be due to the small sample sizes used for training and test sets. A 3D PLS−DA model was established to distinguish the same cultivar (HBJ) from different origins. The result showed a clear separation of Jinhua HBJ from the others, but insufficient distinction was observed for Yancheng, Rudong and Tongxiang; the same problem was also seen for Huangtan and Jiangchang. HJB from Tongxiang, being identified as a national geographical indication product (GI) [83], requires a more powerful model to further differentiate it. For this purpose, the authors also applied orthogonal partial least squares discriminant analysis (OPLS−DA) which, compared with PLS−DA, has a higher resolution and effectiveness. This model was also based on isotope ratio analysis and multi−element mineral analysis and proved to be able to clearly separate Tongxiang HBJ from the rest of the samples. The same attempts were made to classify six different cultivars of chrysanthemum from six different regions [84]. In the PLS−DA model, CJ, GJ and QG were not clearly separated among them while the other samples were obviously distinguished. At the same time, a parallel random forest model was applied and showed better classification. In order to promote the capability to verify the geographical origin of the samples, OPLS−DA models were employed to further classify the samples, and the results demonstrated a complete separation of the samples from different origins.

6.3. Linear discriminant analysis (LDA)

LDA is a supervised approach used in machine learning to solve multi−class classification problems. It was designed to increase the ratio of between−class variance to within−class variance for greatest separability [72]. A model based on LDA was established to discriminate between goji samples from three provinces (Qinghai, Ningxia and Gansu). Satisfying results were obtained in both the training groups and the testing groups, proving that a suitable LDA model based on $\delta^{13}C$ could be a potential method for origin traceability of goji fruits [160]. Another successful example of the application of LDA could be found in the study of Shuai et al. [72]. In this LDA model, ginseng samples from the four growing locations (Shandong Province, Northeast China, Canada and US) were successfully separated and a recognition rate of 96.3 % based on concentrations of various elements and the delta values of stable isotopes was achieved.

PCA, as an unsupervised method, is good for exploratory data analysis and it preserves most of the variance in the dataset which allows an efficient extraction of the feature. However, it doesn't consider the class labels but maximizes the variances so it may not be suitable for classification tasks. The sensitivity to the outliers affects the class separability of PCA. Another main limitation of PCA is that it is based on the linear correlation between two or more variables which may not exactly hold for the dataset to be analyzed [163]. LDA shares the same problem of working on linear correlation between variables and could not work on non−linear dataset. Like PCA, also LDA is sensitive to the presence of outliers because it works well on normalized datasets. At the same time,

LDA is a supervised method which is more suitable for classification tasks than PCA and provides results that are easier to interpret [164]. PLS−DA is a supervised model that is useful for both reducing dataset dimensions and classifying sample points. It can also handle multicollinear datasets. PLS−DA is effective when the dataset has a clustered distribution, but it provides nearly no insight into the data when the classes are featured by linear or nonlinear relationships [165].

7. Conclusion

Herbs, having various advantages, are consumed worldwide as food supplements and infusions for health management. The increasing consumers' demand of this premium and natural products and their relatively higher price led to frauds and adulterations which have brought great concerns about health of the public and harmed the economical profit of producers. Not only are traditional methods for geographical traceability not reliable or subjective enough, but they also require highly experienced testers. Modern methods that rely on chemical compositions and delta values emerged to provide more robust ways for tracing herbs and herbal products. Drawing from the discussions on the selected herbs in this review, isotope ratio mass spectrometry has proven to be a powerful tool for the aim of tracing the geographical origin of herbs and has been intensively applied in cases of ginseng and saffron, while in the studies of Chrysanthemum flos and goji berries, we may expect further applications. In general, we can look forward to a bright future of IRMS in geographical determination of herbs, since this method showed satisfying results and, even better classification when combined with chemical compositions like volatile compounds and mineral elements. A major part of the studies reviewed here focused on bulk stable isotope analysis for simpler sample preparation, sacrificing the detailed information provided by various compounds contained in the samples. The application of compound specific isotope analysis may be still less investigated, but it possesses the advantage of overcoming the limitations of not being able to detect differences in the isotopic composition of specific components in samples. Although it requires more complicated and more time−consuming sample treatment, yet the delta values of individual compounds will be a potent tool to fight against even more sophisticated food frauds and adulterations in herbs and herbal products. Thanks to recent technological advances, we are moving towards a future where we can determine isotopic compositions with increasing precision and efficiency. This includes not only bulk samples and individual compounds derived from them but also site-specific isotopic composition within single molecules, potentially uncovering new markers for traceability. Isotope ratio analysis remains one of the most promising, hypothesis-driven techniques for verifying the geographical origin of herbal products. However, certain limitations and considerations must be addressed to optimize its application.

First, complementary methods, including rapid profiling or screening techniques, should not be overlooked, as they often provide essential information for data interpretation or for preselecting samples for isotope analysis. Additionally, isotope analysis relies heavily on robust databases; an adequately comprehensive number of analyzed samples is necessary to accurately represent real-world conditions. Ensuring measurement accuracy and precision is also crucial to determine whether observed differences are statistically significant—especially when developing a global database to support regulatory enforcement and chemometric traceability models.

In the longer term, a deeper understanding of how meteorological and geochemical signatures are transferred to plant products could reduce the need for extensive, costly databases of authentic samples. Ultimately, this could lead to the development of isotopic 'maps' (known as isoscapes) for foods from different geographical regions, which could be integrated into traceability systems.

CRediT authorship contribution statement

Long Chen: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Data curation. **Luana Bontempo:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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