Electrostatic Spray Ionization-Mass Spectrometry for Direct and Fast Wine Characterization

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Supporting Information

ABSTRACT: Due to the globally existed and economically motivated adulteration including mislabeling and/or blending, fast wine characterization is important in wine industry. Herein, we developed an electrostatic spray ionization-mass spectrometry (ESTASI-MS)-based method to distinguish wines. Wine samples were directly analyzed by ESTASI-MS without any pretreatment. Microdroplets of wine were deposited on a plastic plate for analysis. The collection of each mass spectrometric datum can be accomplished in 1–2 min without any need of pretreatment to the sample, followed by principle component analysis to discriminate wines with different labels and vintages. Long-term storage of wine was simulated and characterized by utilizing the method. High-performance liquid chromatography-mass spectrometry-MS was further applied to identify the distinctive compounds in wines to indicate their difference. We found that the method can offer a strategy for quick wine analysis, which is of practical value in wine industry for wine classification and aging control.

1. INTRODUCTION

Wine, a type of alcoholic beverage made from grapes, is among the most popular drinks in the world. The wine consumption worldwide in 2016 was estimated to reach 242 million hectoliters.1 Due to the high profit and huge market, wine fraud exists in wine market, such as wine adulteration and/or mislabeling the origin and/or quality of wines, which may bring enormous problem to the wine market and possibly create serious threats to the health of wine consumers. Wine identification is of great importance for consumers’ finance and safety concerns.

The quality of wine is commonly discerned by color, flavor profile, degree of sweetness, and dryness. Judgment of wines’ quality traditionally considers the combined opinion from a group of experienced palates (also known as wine experts) for several aspects, e.g., complexity, aftertaste, etc. Nevertheless, judgment made by people can be emotional and subjective, which may not be considered as a systematic method of choice for product quality control. It is highly desirable to study wine from molecule level to establish an evaluation method.

All wines can vest in five fundamental groups, including red wine, white wine, rosé wine, sparkling wine, and fortified wine. Within each group, there are hundreds of different grape varieties and also different vinification styles. It has been reported that there are acetaldehyde, glycerol, alcohols, sorbitol, mannitol, sulﬁtes, acid, amino acid, esters, minerals, phenols, sugar, etc. in red wine.2 It is a huge project to systematically study the molecular components of different wines. Thus it is practically important to develop approaches with minimal time consumption and suitable to identify ambiguous wines.

Wine has been studied using instrument techniques such as high-performance liquid chromatography (HPLC), HPLC-diode array detector (HPLC-DAD), ultraviolet–visible (UV-vis) spectroscopy, proton nuclear magnetic resonance (H NMR) spectroscopy, isotoperatio mass spectrometry, and emission–excitation fluorescence spectroscopy.3 Among various analytical methods, mass spectrometry (MS) shows distinctive advantages in wine analysis because of its outstanding ability of molecule identiﬁcation, high sensitivity, high throughput, and high resolving power, especially in combination with chromatographic techniques.4 Gas chromatography (GC)-MS has been widely used to analyze volatile compounds in wines,5 while liquid chromatography (LC)-MS has been used to study nonvolatile ones.6 However, sample pretreatment, choice of columns, optimization of experimental conditions, and data interpretation make GC-MS- and LC-MS-based wine analysis approaches relatively complex.7 It is
desirable to develop fast and facile strategies for wine analysis, with the purpose of quality control and identification of adulterate and/or mislabeled products in wine market, by skipping or greatly simplifying pretreatment procedures.14

Ambient ionization techniques have been well developed during the last years for fast analysis by MS. The techniques normally hold the characteristics of direct ionization from original sample with minimal pretreatment, ionization under ambient condition, and little effect on the sample during ionization.9 Yong et al. proposed an analytical method based on ambient MS for direct and rapid analysis of pesticides in wine using the direct analysis in real-time (DART) MS technique.10 By virtue of adding an isotope-labeled internal standard, Di Donna et al. reported paper spray ionization MS for rapid quantification of resveratrol in red wine, which is a phenolic compound beneficial for health by scavenging reactive oxygen species.11 In addition to DART ion source and paper spray ionization, common ambient ionization techniques also include desorption electrospray ionization12 and electrostatic spray ionization (ESTASI).13 The ESTASI method was developed by Girault’s group in 2012 that can in situ generate molecular ions from untreated samples on an insulating surface.14 ESTASI-MS has been employed for many applications like perfume fingerprinting,15 enzyme assay screening,16 and caffeine analysis in drinks.16

The present research aims at developing a fast and selective method for wine identification by ESTASI-MS. To explore the potential of ESTASI-MS for direct wine identification, red wines from different producers and regions were analyzed without any pretreatment. MS data were obtained using ESTASI in combination with a linear ion trap mass spectrometer (Thermo LTQ) directly from 2 μL of original wine samples, and then subjected to principal component analysis (PCA). The whole experimental procedure took only 1−2 min for each measurement without any sample pretreatment. It was found that different wines could be well differentiated using the method. The method can also well supervise wines stored under room temperature for a period of time. Peaks from the ESTASI-MS data that held large variable importance for the projection (VIP) values could be figured out for further HPLC-MS analysis of the components significantly different among different wines. The results show that the developed fast analysis method is promising to identify wines between labels that may show valuable applications in the wine industry.

2. RESULTS AND DISCUSSION

2.1. Direct Wine Analysis by ESTASI-MS. Wine samples were analyzed by ESTASI-MS without any pretreatment. As shown in Scheme 1, 2 μL of original wine sample was deposited on a polyimide (PI) target plate for MS analysis. Components inside the sample were ionized by ESTASI, and the detected MS data were processed by principle component analysis (PCA) to assist the classification of wines with different labels.

Table 1. Information of Red Wines Analyzed in the Present Study

| wine code | label | origin | vintage | main grape variety for wine production |
|-----------|-------|--------|---------|---------------------------------------|
| A1        | Jacob’s Creek/Shiraz Cabernet | Australia | 2015 | Shiraz and Cabernet Sauvignon          |
| F         | Bordeaux/Baron Philippe de Rothschild Rouge | France | 2015 | Merlot, Cabernet Sauvignon, and Cabernet Franc |
| C         | Zhangyu/Cabernet Gernischt dry red | China | 2015 | Cabernet Gernischt                    |
| AG        | Mendota/produced and bottled by Andean vineyards | Argentina | 2016 | Malbec                               |
| A2        | Jacob’s Creek/Merlot | Australia | 2015 | Merlot                               |
and total area normalization are two common methods.\textsuperscript{18} More information on the analyzed wine can refer to Table 1.

Figure 1. Mass spectra of wine with codes of A1, A2, AG, C, and F analyzed by electrostatic spray ionization-mass spectrometry (ESTASI-MS). Mass spectrum of blank was obtained under the same condition but using deionized water as analyst. The main peaks in the mass spectra were labeled with their corresponding \( m/z \) values. More information on the analyzed wine can refer to Table 1.

As shown in Figure 2, the plot of PCA scores indicates that four of the five analyzed wines can be distinctly separated into four units. The total variance of the data explained by two principal components (PCs) is 54.9\% (31.4\% from PC1 and 23.5\% from PC2). The color-covered area displays 95\% of confidence region. It can be observed that overlap exists for wines A1 and F on the PCA plots, which may be because an identical type of grape was used to produce these two wines, i.e., Cabernet Sauvignon, as listed in Table 1. The results in Figure 2 show that when analyzing the mass spectral data set by partial least-squares discriminant analysis (PLS-DA), these two wines can be clearly discriminated in the 95\% confidence level. Thus, PLS-DA modeling, which is a supervised method, is more powerful to discriminate two groups of data sets due to its regression algorithm.\textsuperscript{19} Based on the results, it is promising to build a spectral library for wine authentication.

To further demonstrate the reliability of the method, we conducted ESTASI-MS analysis on the same five wine brands but from different vintages. The information on the wine sample is listed in Table S1. Three bottles of each brand of wine were analyzed, and at least nine mass spectra were collected from nine times of independent sample injection to the ESTASI-MS for each bottle. As shown in Supporting Information Figure S1, wine samples from different bottles but with the same brand and vintage cannot be distinguished by the PCA plots. When all of the five brands were plotted together with three bottles for each brand, similar results to Figure 2 were observed, as shown in Supporting Information Figure S2, where the five different brands can be well distinguished, demonstrating the good reproducibility of the method. We have further studied the matrix effects from wine samples that may interfere the MS analysis.\textsuperscript{20,21} A group of selected compounds, including phenacetin, caffeine, and dextromethorphan, were spiked into the wine samples with codes A2, AG, and F, as explained in Table S1, and analyzed by ESTASI-MS. As shown in Figure S3, the analyzed wines showed similar matrix effects to the detection of the spiked compounds.

2.3. Identification of Distinctive Compounds in Wines. PCA can discover similarities and differences between wine samples and find the specific components that lead to the differences among a set of mass spectral data of wines. The plot of loadings of PCA associated with Figure 2a shows the distribution of the variable mass spectral signals (labeled with \( m/z \) values in the figure), as shown in Figure 2c. In the loadings plot, the discrete dots were concerned rather than the gather dots. The plot of VIP scores was obtained from PLS-DA. High VIP scores usually indicate the significance of the corresponding mass spectrometric signals (labeled with \( m/z \) values on the figure) on the separation of different samples. A total of 10 MS signals with largest VIP are listed in Figure 2d.

The compounds associated with the MS signals with high VIP scores were further characterized by HPLC-MS/MS. MasterView software was used for qualitative analysis according to the MS and MS/MS information of the corresponding compounds. The ions and corresponding identified distinctive compounds in the wines are listed in Table 2. These compounds are significantly different in amounts among the wines, as shown by the color blocks in Figure 2d. The approach developed here shows that it is feasible to differentiate wines by ESTASI-MS with the assistance of PCA and to quickly profile the main MS signals for further identification of the distinctive compounds in the wines by HPLC-MS/MS.

2.4. Quality Control during Wine Storage. Quality control of wine during storage is an important concern for flavor and aroma. The aging of wine is necessary and can potentially improve the quality of wine. However, when wine is bottled, too long storage can lead to decrease of wine quality due to oxidation. Herein, ESTASI-MS was used to follow the change of wines during storage, which can be used to guide the consumption of wines before their quality is getting questionable. During the experiments, bottle-packed wines were opened, sealed with their original corks or caps, and stored in ambient condition. The introduction of air can fasten oxidation of wines, thereby to simulate in a short time the

Figure 2b show that when analyzing the mass spectral data set by partial least-squares discriminant analysis (PLS-DA), these two wines can be clearly discriminated in the 95\% confidence level. Thus, PLS-DA modeling, which is a supervised method, is more powerful to discriminate two groups of data sets due to its regression algorithm.\textsuperscript{19} Based on the results, it is promising to build a spectral library for wine authentication.

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long-term storage of bottled-wines in a sealed status. ESTASI-MS data were collected from three types of wines after different periods of storage. From the PCA results of the MS data shown in Figure 3, little change occurred within 24 h of storage, as indicated by the overlapping of the clustering units in the PCA plots. Significant differences were observed after 3 days of storage, indicating the potential content changes of the wines. Actually, very low sensory experience (tastes of the wines) was reported for the wines stored longer than 3 days compared to that in 1 day of storage. Therefore, it is possible to indicate significant changes of wines during storage with the developed method, and it is better to consume a wine before significant changes have been observed by ESTASI-MS. Figure 3 also plots 10 peaks with the highest VIP scores, indicating the most distinctive MS signals among the same sample after various storage times. Some identical signals have been observed among the three wines to change significantly, i.e., at m/z 409, 350, 294, 191, 119, 87, 65, and 147. According to the HPLC-MS/MS identification results in Table 2, the signals can be originated from coumarin, succinic acid, glycerol, and diethyl dicarbonate, which experienced changes possibly due to the volatilization, fermentation, and oxidation of the wine samples.

3. CONCLUSIONS

A strategy based on ESTASI-MS was developed to distinguish wines with different labels. Different wines can be directly analyzed by ESTASI-MS without any pretreatment. Each ESTASI-MS detection of wine can be accomplished in 1–2 min without any sample pretreatment, followed by multivariate statistical analysis for wine identification. On the basis of the information of the distinctive MS signals indicated by PCA and PLS-DA models, the compounds in the wine can be further identified with HPLC-MS. It is promising to apply the developed approach to wine quality control during wine production and wine storage.

4. EXPERIMENTAL SECTION

4.1. Wines and Chemicals. Five red wines, Bordeaux (year 2015, France, made with Merlot, Cabernet Sauvignon and Cabernet Franc, coded as F), Mendoza (year 2016, Argentina, made with Malbec, coded as AG), Zhangyu (year
in the mass range of 50–100 μm. A stainless steel (316 L) was deposited on the PI sample target plate. The target plate was lifted slowly toward MS orifice until ESTASI happened. Usually, ESTASI happened when the distance between target plate and MS orifice was 2–3 mm. MS data were recorded until the complete consumption of the wine sample by ionization and evaporation. The PI foil was used as a disposable substrate and changed for each sample to avoid cross-contamination. For aging experiments, the bottles were sealed with their original caps and stored under room temperature in the dark.

### 4.3. Statistical Analyses

MS raw data were processed by an R package named MALDIquant.17 Peaks with signal-to-noise ratio (S/N) > 3 were extracted from the processed MS data with the information of m/z and relative intensity to form aligned matrices. Multivariable statistical analysis to the matrices was performed by using MetaboAnalyst 4.0 (http://www.metaboanalyst.ca).

#### 4.4. LC-MS Analyses

Wine samples were filtered by a 0.22 μm microporous membrane prior to high-performance liquid chromatography (HPLC)-MS analysis. The HPLC system (Shimadzu, Japan) used in this work consisted of two pumps, an autosampler, and a column thermostat. An Athena C18-WP column (100 Å, 2.1 × 150 mm², 3 μm) purchased from CNW technologies (Shanghai, China) was used. The mobile phase was composed of A (water with 0.1% formic acid) and B (acetonitrile), with gradient elution being optimized as 0–5 min (B, 0–20%), 5–14 min (B, 2–40%), 5–14 min (B, 40–80%), and 14–18 min (B, 80%). Flow rate was set as 0.2 mL/min. Column temperature was controlled at 25 °C. Sample injection volume was 2 μL.

A Q-TOF mass spectrometer (Triple TOF 4600, AB Sciei) was coupled with the HPLC system through an ESI source. Ionization was performed in positive mode. ESI high voltage was set as 5500 V. Ion source parameters were optimized as follows: gas 1, 45 psi; gas 2, 50 psi; curtain gas, 30 psi; source temperature, 500 °C. MS/MS data were acquired in information-dependent acquisition (IDA) mode with a maximum precursor ion number of 10 and mass range of 50–1000 m/z. MasterView (AB Sciei) and FooDB (http://foodb.ca) database were used to identify peaks from the LC-MS/MS data.

#### ASSOCIATED CONTENT

**Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b02259.

Plots of PCA for the ESTASI-MS data from three bottles of wine (Figure S1); reproducibility study of ESTASI-MS for wine identification by plotting PCA and PLS-DA of wines (Figure S2); evaluation of matrix effects in the ESTASI-MS analysis of wine by spiking phenacetin, caffeine, and dextromethorphan in wine samples (Figure S3).
Figure 3. Plots of principle component analysis (PCA) scores and variable importance for the projection (VIP) scores from partial least-squares discriminant analysis (PLS-DA) for the electrostatic spray ionization-mass spectrometry (ESTASI-MS) data from different wines during storage. Storage time is labeled in the inlet. h and d are short for hour and day, respectively. More information on the analyzed wine A1, A2, and AG in (a)−(c) can refer to Table 1.

S3); information of wine samples used to get the results in Figures S1−S3 (Table S1) (PDF)
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Notes
The authors declare no competing financial interest.

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ABBREVIATIONS
$M_w$, molecular weight; ESTASI-MS, electrostatic spray ionization-mass spectrometry; HPLC, high-performance liquid chromatography; DAD, diode array detector; UV–vis, ultraviolet–visible spectroscopy; H NMR, proton nuclear magnetic resonance spectroscopy; GC, gas chromatography; DART-MS, direct analysis in real-time mass spectrometry; ESTASI, electrostatic spray ionization; VIP, variable importance for the projection; S/N, signal-to-noise ratio; IDA, information-dependent acquisition; PI, polypeptide; PCA, principle component analysis; PLS-DA, partial least-squares discriminant analysis; PC, principal component; LC-MS/MS, liquid chromatography-tandem mass spectrometry

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