Hindawi
Journal of Food Quality
Volume 2021, Article ID 5536645, 10 pages
https://doi.org/10.1155/2021/5536645

Research Article

Analysis of Volatile Organic Compounds by HS-GC-IMS in Powdered Yak Milk Processed under Different Sterilization Conditions

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Received 2 March 2021; Revised 25 May 2021; Accepted 18 June 2021; Published 30 June 2021

Academic Editor: Constantin Apetrei

Headspace-gas chromatography-ion mobility spectroscopy (HS-GC-IMS) was used to detect the volatile organic compounds (VOCs) of yak milk powders (YMPs) under ultra-high-pressure sterilization (UHPS) and thermization (TH) methods. The analyses led to the identification of several characteristic of compounds, therefore, exploitation and comparison of the different flavors. A total of 46 peaks were detected, and 17 compounds were identified, including 7 aldehydes, 5 ketones, 3 acids, 1 terpene, and 1 ester. Furthermore, principal component analysis (PCA) and fingerprint similarity analysis based on Euclidean distance compared the YMPs and found that the YMPs had certain differences, which can distinguish the YMPs with different sterilization methods. In conclusion, different sterilization methods possibly affect the flavor of YMPs, and UHPS is bettedslfr than TH. Also, aldehydes were mainly be detected in UHPS groups, whereas the ketones and acids mostly appeared in TH groups. Most importantly, UHPS can retain the original flavor of yak milk to a greater extent.

1. Introduction

Yak milk is an important food and dairy processing raw material for people of all ethnic groups on the Tibetan Plateau because of the abundant nutrition and a long history. It is rich in nutritional components, such as protein ($5.06 \pm 0.24\%$), fat ($7.14 \pm 0.31\%$), lactose ($5.00 \pm 0.32\%$), dry matter ($18.45 \pm 0.65\%$), and ash ($0.81 \pm 0.03\%$) [1]. Yak milk contains many unsaturated fatty acids including pentadecenoic acid, eicosapentaenoic acid, and docosahexaenoic acid that are not present in other milk [2], in addition to vitamin A (44.4583 μg/100 mL), vitamin E (98.5271 μg/100 mL) [3], vitamin B1 (34.705 μg/100 mL), vitamin B2 (179.963 μg/100 mL), vitamin B3 (345.5886 μg/100 mL), vitamin B5 (84.834 μg/100 mL), vitamin B6 (47.481 μg/100 mL), vitamin B11 (4.8157 μg/100 mL), and vitamin C (34.46 μg/mL) [4, 5]. However, due to the special geographical conditions, transportation, deep processing, and storage of yak milk have become a challenge; therefore, the production and processing of yak milk powder (YMP) has solved this problem.

Sterilization is an important step in the milk manufacturing processes, which plays a critical role in food safety and extends the shelf life. It inactivates microorganisms and enzymes during the sterilization process and has a certain impact on the flavor [6]. The sterilization of yak milk includes high-temperature instantaneous sterilization, ultra-high-pressure sterilization, pasteurization, microwave sterilization, and thermization, and different sterilization methods may lead to different flavors. For example, high pressure and high temperature will promote the increase of ketones and aldehydes [7, 8]; heat treatment will also increase the acid content [9], and ultrasonic treatment will increase the hexanal content [10]. Moreover, the secondary metabolites of food microorganisms have a certain impact on the unique flavor of yak milk [11]. Jiang et al. [12] found

that fermented yak milk contains 14 volatile substances including 6 acids, 4 ketones, 1 aldehyde, 1 alcohol, 1 ester, and 1 ether, which may be affected by microorganisms and fermentation conditions. Chi et al. [13] found 21 volatile substances by gas chromatography-mass spectrometry (GC-MS) and gas chromatography-olfactory-mass spectrometry (GC-O-MS) detection, including ketones, aldehydes, alkenes, alcohols, heterocycles, phenols, and ethers. In addition, 37 volatile compounds were identified by mass spectrometry (MS) and retention index (RI), including acids, ketones, alkanes, aldehydes, lipids, aromatics, and terpenes [14]. The production of milk taint is directly related to factors such as the activity of lipase in raw milk and the total number of bacteria.

To judge whether a new technology can be applied in food industry, firstly, it must effectively kill microorganisms in food, secondly, it must preserve the natural characteristics of food to the greatest extent, and finally, it must provides consumers with a safe and nutritious product. Ultra-high-pressure sterilization (UHPS) can achieve the effect of sterilization and enzyme elimination at room temperature. It is very important that the pressure does not break up the covalent bonds of food components, thereby reducing the loss of nutrients and the deterioration of color and flavor caused by high temperature [15]. Thermization (TH) destroys some heat-sensitive nutrients and flavor substances, reduces the nutritional value of food, and changes the original flavor of food. The protein itself has a weak flavor, but it can affect the flavor by binding or adsorbing flavor substances. Heat treatment has a great impact on the structure and functional properties of the protein. Also, with the extension of heating time, the protein binding constant decreases and the number of binding sites increases, which makes the sample flavor change to a certain extent [16]. However, Thermization is the most simple and common way of sterilization with low cost, which can reduce the cost for future industrial production. So, we considered comparing these two methods of sterilization.

Ion mobility spectroscopy (IMS) is an analytical technique that characterizes chemical ionic substances based on the difference in the migration speed of different gas phase ions in an electric field [17]. Since the poor resolution of IMS leads to false positives, the combination with highly selective Gas chromatography (GC) is a commonly used analytical method. Headspace-GC-IMS (HS-GC-IMS) is fast (3–10 min), has high sensitivity (detection limit as low as ppb_v level), high selectivity, simple operation (automated analysis), and fast response speed (normal pressure work), stable detection equipment does not need to preprocess the sample, and it can directly inject the sample in the headspace. It can perform a qualitative analysis of a single compound and can also perform rapid and result-oriented analysis of the GC-IMS two-dimensional spectrum of the sample. GC-IMS can detect a variety of substances such as ketones, aldehydes, alcohols, amines, halogenated substances, and esters [18]. In recent years, there are few articles about HS-GC-IMS used in food industry applications, and they mainly focus on medical metabolites, edible oil, meat and egg products, wine, traditional Chinese medicine, food, fruits, and vegetables, etc., for dairy product process testing less. Feng et al. [19] used HS-GC-IMS to detect the difference of YMP with different drying methods. But as far as we know, this is the one of the first examples to compare the VOCs differences of YMP under different sterilization methods. So, we thought about whether different sterilization methods could affect the flavor of YMP, analyzed exactly which class of volatile substances played a major role in YMP, and provided a theoretical basis for the extended processing of YMP.

This study compared the difference in flavor compounds of YMP after UHPS and TH processes by using HS-GC-IMS, compared the differences between the PCA and cluster analysis based on Euclidean distance, and analyzed the main flavor effects of volatile compounds with different methods of sterilization. In addition, the determination of the main volatile organic compounds (VOCs) of YMP aims to provide theoretical data for the industrial development of YMP.

2. Materials and Methods

2.1. Samples and Instruments. Yak milk was provided by Gansu Hualing Dairy Co., Ltd. (Lanzhou, Gansu Province). A GC-IMS Flavor analyzer (FlavourSpec®, G.A.S. Department of Shandong Hai Neng Science Instrument Co., Ltd., Shandong, China), ultra-high-pressure sterilizer (SYZT 30L-600MPA), water bath (HHS-21-4), freeze dryer (CHRIST ALPHA 1–2 LD plus freeze dryer), and spray dryer (Buchi Mini Spray Dryer B-290 spray dryer) were used.

2.2. Preparation of Yak Milk Powder. According to Feng et al. [19], the raw milk stored at −18°C was thawed to 0–4°C, and 1 L was taken separately under the high-speed shearing mixer of 2000 rpm, for 10 min, and then stored in container prior to the sterilization process. Then, UHPS (room temperature, 600 MPa, 10 min) and TH (85°C, 5 min in a water bath) were used. Finally, the yak milk after sterilization was further processed with freeze-drying (FD) and spray-drying (SD), respectively. To make the water content of yak milk powder reach 5%–6%, the samples were stored in a dry box before analysis.

2.3. HS-GC-IMS System. 2.0 g sample was placed in a 20 mL headspace bottle and incubated at 80°C for 20 min. The centrifuge speed was 500 rpm, the temperature of the inject needle was 85°C, and 500 μL sample was injected. Then, the gas chromatographic preseparation was performed on an FS-SE-54-CB-1 (15 $m \times 0.53$ mm, the film thickness 1.0 μm) capillary column at 60°C, the analysis time was 30 min, the carrier gas was N_2 (purity ≥99.999%), and the flow rate was 0–2 min–2 mL/min, 2–10 min–2–10 mL/min, 10–20 min–10–100 mL/min, and 20–30 min–100–150 mL/min. Finally, the temperature of the IMS ionization chamber was 45°C, the drift gas was N_2 (purity ≥99.999%), and the flow rate was set to 150 mL/min.

2.4. Statistic Data Analysis. Statistical data analysis was performed by Laboratory Analytical Viewer (LAV) and GC-IMS Library Search software from different angles. The data and diagram were created using Excel and Origin 8.0 (Microcal Software, Inc., Northampton, USA).

3. Results and Discussion

3.1. Identification of Volatile Components from YMP Processed by Different Sterilization Methods. There were few studies focused on the differences of YMP caused by different sterilization methods, especially in flavor volatile compounds. In the study of Yu et al. [20], 44 compounds in white yak milk were detected by GC-MS: 7 flavor substances with frankincense flavor were only detected in white yak milk, including 3-hydroxy-2-butanone, p-cymene, acetone, 2,3-butanedione, ethylacetate, and hexanal, 2-ethyl-1-hexanol. Furthermore, Chi et al. [13] used GC-MS to identify 24 compounds, including 9 ketones, 3 aldehydes, 3 terpenes, 2 alcohols, 2 phenols, 2 esters, 2 heterocycles, and 1 ether. In this study, the differences of flavor compounds in YMP were compared between UHPS and TH. As shown in Figure 1, the drift time was 1.0–1.7 ms set by normalization relative to the position of the reaction ion peak (RIP), and the effective retention time was 100–900 s. We found that 17 compounds were qualified by Retention Index (RI) and IMS databases. Table 1 lists the qualitative results, including the compound name, CAS number, Molecular Weight (MW), the Retention Index (RI), the Retention Time (RT), and the Drift Time (DT). Moreover, the counts in Table 1 were corresponding to the numbers in Figure 1.

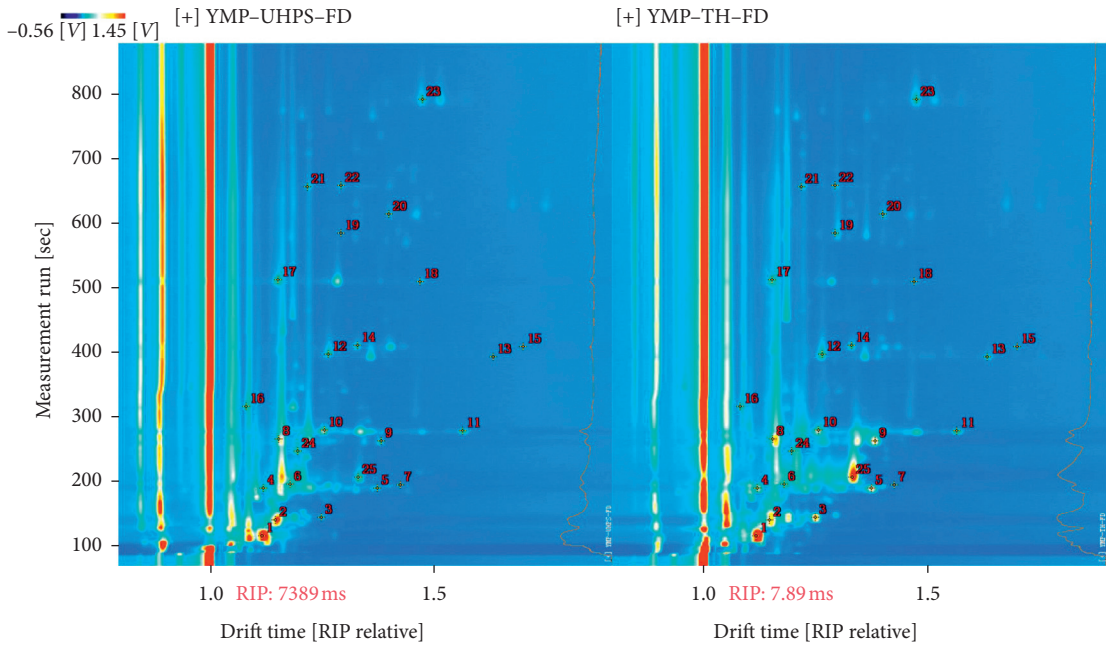
In Figure 1(a), when the drift time was around 0.95 ms, the VOCs' contents of YMP-UHPS-FD were higher than YMP-TH-FD. When the drift time was around 1.05 ms, the latter was higher than the former. However, in Figure 1(b), the differences of YMP-UHPS-SD and YMP-TH-SD were not observed intuitively. From Figure 1(a), it can be clearly seen that the concentration of acetoin in YMP-TH-FD was higher, probably due to the conversion of 2-butanone during heat treatment. As can be seen from Table 1, 17 volatile organic compounds included 7 aldehydes, 5 ketones, 3 acids, 1 terpene, and 1 ester. Among them, some compounds of YMP had the forms of monomers and dimers. The aromatic components of milk powder were affected significantly during the processing. For example, the higher the temperature, the higher the content of 2-heptanone [21, 22]; the high pressure will also increase the aldehyde compounds [23]. In addition, it was found that 52 of the 70 volatile compounds were greatly affected by high pressure in the cheese after ultra-high-pressure treatment, and the content of ketones, aldehydes, alkanes, and sulfur compounds was usually higher than that of unprocessed cheese [7].

In order to compare the volatile substances of YMP under different sterilization methods more significantly, Origin software was used to make a histogram of peak volume. The value of peak volume (equivalent to peak intensity) was proportional to the content of VOCs.

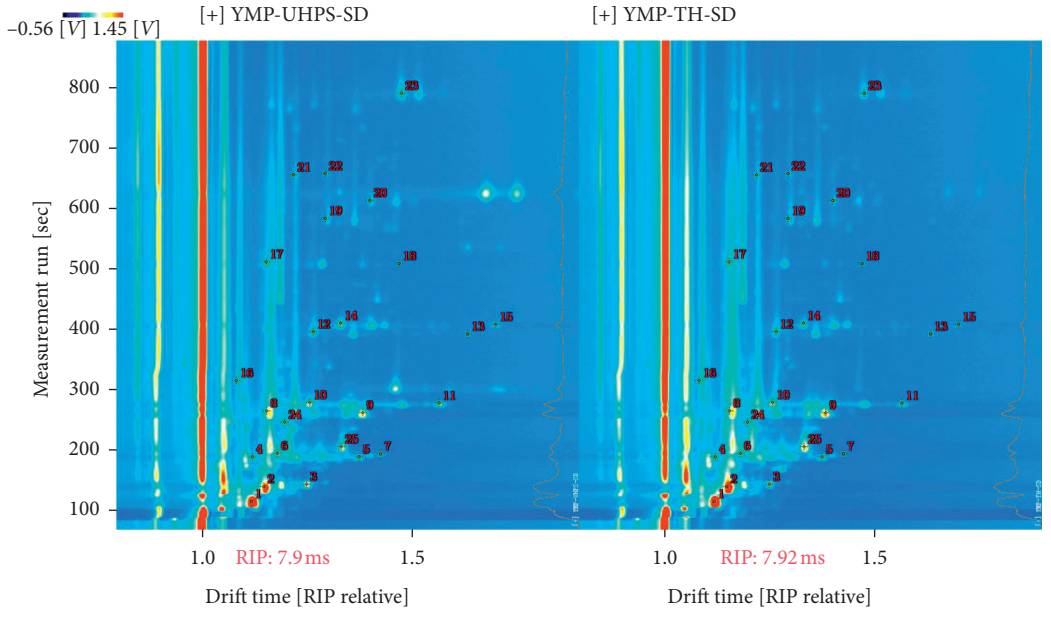
Figure 2 showed the content of ketones in the YMP-TH groups was higher than in YMP-UHPS groups, maybe due to the heat treatment caused by the oxidation reaction of YMP. For YMP-UHPS-SD and YMP-TH-SD, it may be that the hot-air drying affected the content of ketones between the two samples to result in an insignificant difference. In addition, it can be visibly seen the content of ketones was higher than aldehydes in all samples because aldehydes came from the auto-oxidation of lipid, while ketones were mainly derived from the thermal oxidation or degradation of unsaturated fatty acids [24]. Also, Yak milk contains many unsaturated fatty acids including pentadecenoic acid, eicosapentaenoic acid, and docosahexaenoic acid, so ketones would be higher than aldehydes. In this research, ethyl 2-methylpropanoate (boiling point: 110.1°C) was detected, and its content was higher in YMP-UHPS groups than in YMP-TH groups. It may be that the TH temperature (85°C) was not reaching the boiling point of ethyl 2-methylpropanoate not making it transform into volatile substances, causing a weaker gaseous escape of this VOC and then leading to its lower content. The esters formed by short-chain fatty acids had a fruity flavor, while those formed by long-chain acids had a slightly oily taste [24]. Moreover, it can be found that the acid content of YMP-TH groups was higher than that of YMP-UHPS groups, which may be due to the decomposition of nutrients in yak milk into small molecular peptides and organic acids [25]. The study had found that acids can coordinate the flavor of YMP and form the sample characteristics with aldehydes, ketones, and esters [11]. The acids contributed to fatty milky and rancid flavor [9]. Also, butanoic acid was the most important and obvious flavor substance [26]. Finally, limonene detected was mainly derived from yak feed and migrated into the milk through the rumen, and limonene had a lemon flavor [13].

3.2. Fingerprints of YMP with Different Sterilization Methods. In order to clearly compare the specific volatile substance differences in each group of YMP samples, all peaks are selected below for fingerprint comparison. Each row in the figure represents all the signal peaks selected in the sample, and each column represents the signal peak of the same VOC in different samples (Figure 3). The complete VOC information of each sample and the difference of VOCs between samples can be seen from the fingerprint (Figure 3). The individual dot represents a volatile substance, and the darker red color represents the higher content of the volatile substance in YMP. Also, the number represents unidentified substances. In this experiment, we used HS-GC-IMS to detect 46 peaks, and among them, 17 compounds were qualified.

The result showed the differences of VOCs of YMP with different sterilizations and marked the characteristic regions. 2-Heptanone, 2-pentanone, benzaldehyde, heptanal, hexanal, butanoic acid, limonene, and pentanal were detected by dimer and monomer signals at different drift times [27]. In Figure 3(a), it can be clearly observed that the characteristic area A of YMP-UHPS-FD contained pentanal, ethyl 2-methylpropanoate, benzaldehyde, acetic acid, hexanal, heptanal, and furfural. Also, the characteristic area B of YMP-TH-FD contained 2-heptanone, 2-pentanone, 2-



(a)



(b)

Figure 1: HS-GC-IMS spectra of YMP after different sterilization methods. The numbers are qualitative volatile components.

Table 1: Qualitative results of YMP with different sterilization methods.

Count	Compound	CAS#	Formula	MW	RI	Rt (sec)	Dt [RIPrel]	Comment
1	Acetone	C67641	C3H6O	58.1	527.7	114.536	1.11774	
2	Acetic acid	C64197	C2H4O2	60.1	583.3	139.507	1.14787	
3	2-Butanone	C78933	C4H8O	72.1	593.4	144.021	1.24942	
4	2-Pentanone	C107879	C5H10O	86.1	691.1	188.911	1.12085	Monomer
5	2-Pentanone	C107879	C5H10O	86.1	691.1	188.911	1.37427	Dimer
6	Pentanal	C110623	C5H10O	86.1	698.1	194.93	1.18048	Monomer
7	Pentanal	C110623	C5H10O	86.1	697.2	194.178	1.42552	Dimer
8	Butanoic acid	C107926	C4H8O2	88.1	779.4	264.738	1.15418	Monomer
9	Butanoic acid	C107926	C4H8O2	88.1	775.6	261.481	1.38374	Dimer

Table 1: Continued.

Count	Compound	CAS#	Formula	MW	RI	Rt (sec)	Dt [RIPrel]	Comment
10	Hexanal	C66251	C6H12O	100.2	792.2	278.489	1.25701	Monomer
11	Hexanal	C66251	C6H12O	100.2	791	277.042	1.56552	Dimer
12	2-Heptanone	C110430	C7H14O	114.2	889.5	395.992	1.26483	Monomer
13	2-Heptanone	C110430	C7H14O	114.2	886.1	391.847	1.63323	Dimer
14	Heptanal	C111717	C7H14O	114.2	897.6	409.116	1.33061	Monomer
15	Heptanal	C111717	C7H14O	114.2	896.8	407.734	1.70033	Dimer
16	Furfural	C98011	C5H4O2	96.1	822	314.445	1.08156	
17	Benzaldehyde	C100527	C7H6O	106.1	953.1	510.555	1.15344	Monomer
18	Benzaldehyde	C100527	C7H6O	106.1	951.9	508.438	1.47056	Dimer
19	Hexanoic acid	C142621	C6H12O2	116.2	992.7	582.96	1.29424	
20	Octanal	C124130	C8H16O	128.2	1008.2	612.734	1.40094	
21	Limonene	C138863	C10H16	136.2	1029.9	655.139	1.21883	Monomer
22	Limonene	C138863	C10H16	136.2	1030.5	656.492	1.29424	Dimer
23	n-Nonanal	C124196	C9H18O	142.2	1098.6	789.804	1.47543	
24	Ethyl 2-methylpropanoate	C97621	C6H12O2	116.2	757.8	246.223	1.19696	
25	Acetoin	C513860	C4H8O2	88.1	710.4	205.496	1.33213	

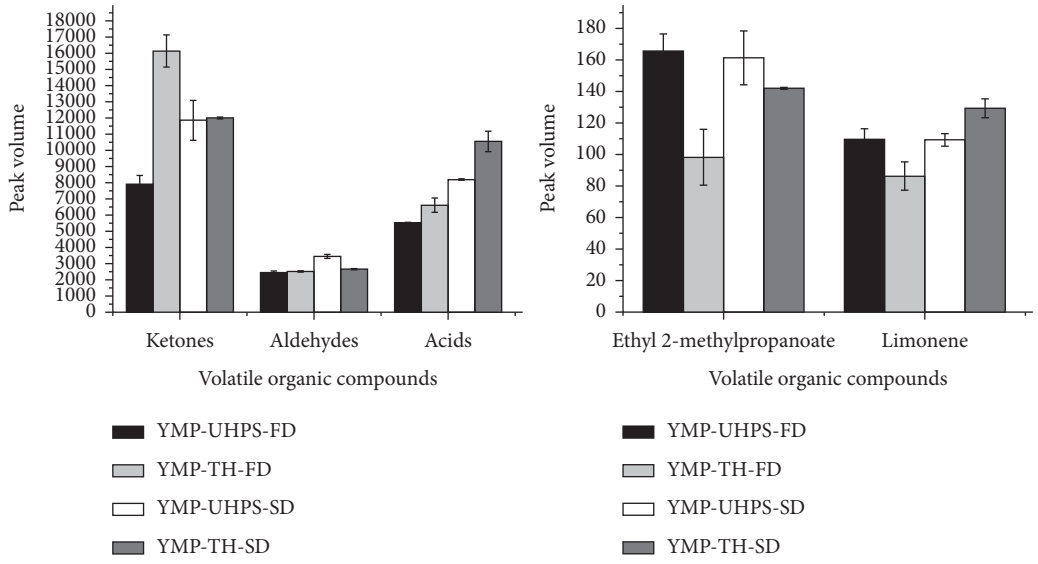
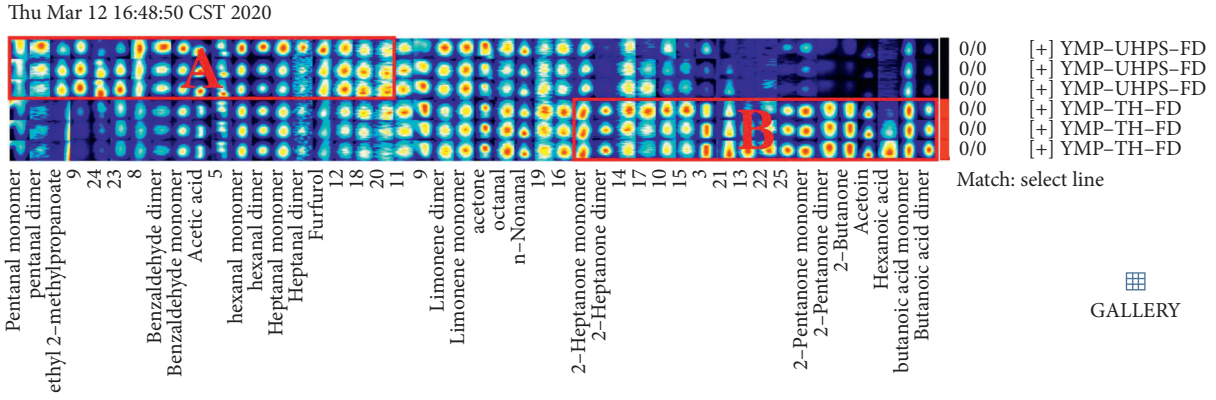
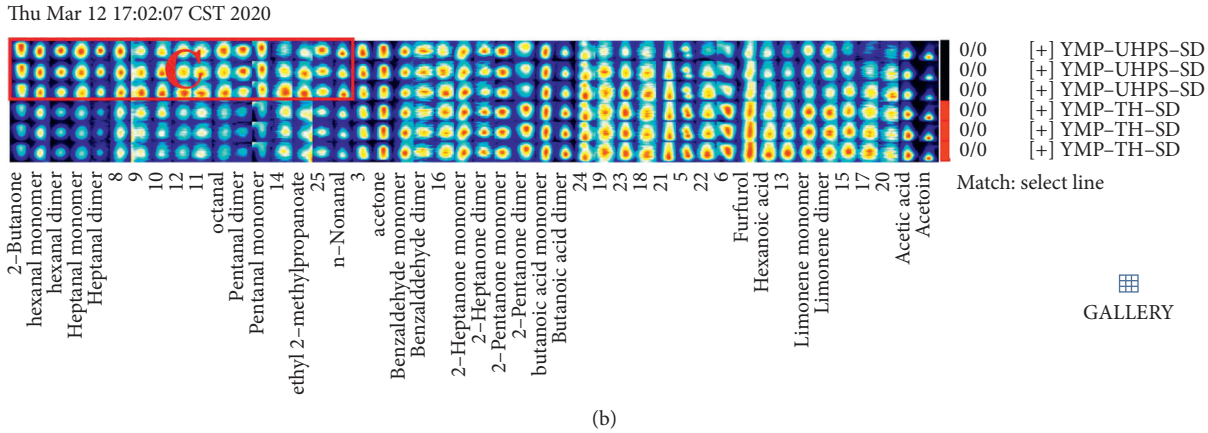


Figure 2: GC-IMS peak volume of different YMP samples.



(a)

Figure 3: Continued.



(b)

Figure 3: Fingerprint of volatile compounds of YMP.

butanone, acetoin, hexanoic acid, and butanoic acid. In Figure 3(b), the characteristic area C of YMP-UHPS-SD included 2-butanone, hexanal, heptanal, pentanal, ethyl 2-methylpropanoate, and N-nonanal compounds. However, for YMP-TH-SD, its characteristic area cannot be visually distinguished. Yu et al. [20] had found acetone, acetoin, and hexanal were the typical components of white yak milk flavor. When the samples were heated, the Strecker reaction may produce benzaldehyde or furfural be produced under acidic conditions in the intermediate stage of Maillard reaction [28]. The study found that the content of 2-heptanone in heated milk at 90°C for 15 minutes was higher than that in raw milk [29]. Also, it had been reported that 2-heptanone caused the cinnamon smell of milk [22], hexanal had an oily aroma [30], and acetic acid will make yak milk produce a rancid and stinky taste [9]. In addition, some saturated aldehydes in food were considered to be odor compounds [31]. UHPS was carried out at room temperature to avoid the adverse effects of heat treatment on yak milk. Therefore, the original taste, flavor, color, and nutrients of the sample were well maintained. According to some reports, 127 metabolites were detected in the metabonomic analysis of *Bacillus licheniformis*, including a large number of carbohydrates, amino acids, and organic acids, which produced furfural or benzaldehyde as reactants in the Maillard reaction [32].

3.3. PCA of YMP Samples. Principal component analysis (PCA) is a multivariate statistical method which can examine the correlation between multiple variables [19]. It constitutes a powerful visualization tool, provides a way to reduce the dimensionality of data, and can eliminate unnecessary information [33, 34]. In this study, we selected variables with compound list and peak volume. In order to analyze the problem comprehensively, the PCA is performed on these variables. Generally, when the cumulative contribution rate of PC1 and PC2 reaches 80%–85%, the PCA model is regarded as the preferred separation model [35]. Chen et al. [33] had used PCA to find the relationship between element distribution and milk types. Moreover, PCA was used to compare the volatile flavor components of yak milk in different ecoregions, which can determine a certain flavor substance contributed to flavors [36].

Figure 4 showed the difference in the contribution of different VOCs to different treatment of YMP by PCA analysis. In general, if the samples are similar, the difference is small; otherwise, the difference is significant. In Figure 4(a), the cumulative contribution rates of PC1 and PC2 were 79% and 17%, respectively. In Figure 4(b), PC1 was 79% and PC2 19%. Therefore, the PCA model can be used to distinguish the samples. It can be seen from Figure 4 that there were obvious differences between the samples.

3.4. Fingerprint Similarity Analysis. Euclidean distance is a cluster analysis method based on distance discrimination. It is a commonly used distance definition, which refers to the true distance between two points in space or the natural length of the vector (the distance from the point to the origin) [37]. In addition, it is consistent with the two chemometric methods of the PCA method in terms of classification results, and when combined together, the two will play a complementary role [19]. Also, the similarity analysis of fingerprint based on Euclidean distance shows the difference and relationship between categories. The difference and connection of each other are more detailed than PCA. Similarity analysis based on Euclidean distance reflects the degree of intimacy between the research objects [38]. Tables 2 and 3 were the values of Euclidean distance between YMP-UHPS groups and YMP-TH groups.

From Figure 5 and Tables 2 and 3, the similarity of fingerprints of VOCs in YMP can be concluded according to the distance. The Euclidean distance average of YMP-UHPS-FD and YMP-TH-FD was 3714546.193, which was larger than the values of YMP-UHPS-SD and YMP-TH-SD with 872315.65. Therefore, the YMP-UHPS-SD and YMP-TH-SD were close to each other, so their differences were not significant and they had obvious similarity of fingerprints.

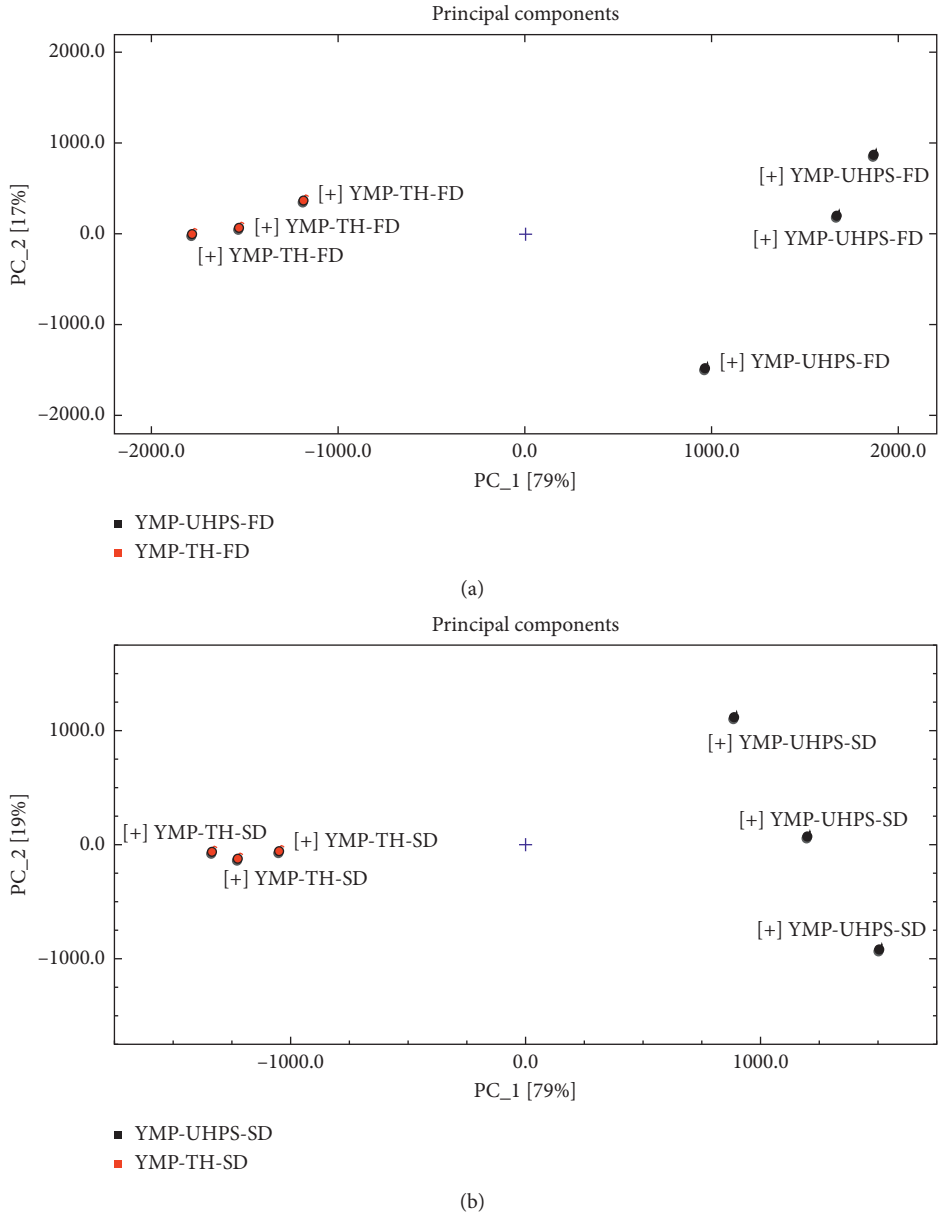


Figure 4: PCA of YMP with different sterilization methods.

Table 2: Euclidean distances of YMP-UHPS-FD and YMP-TH-FD.

	Full distance matrix					
	YMP-UHPS-FD	YMP-UHPS-FD	YMP-UHPS-FD	YMP-TH-FD	YMP-TH-FD	YMP-TH-FD
YMP-UHPS-FD	0	663570.25	1257752.404	2443268.364	2869713.167	3376552.448
YMP-UHPS-FD	663570.25	0	105320.2595	3157390.93	3888051.7	4547590.055
YMP-UHPS-FD	1257752.404	105320.2595	0	3601039.491	4424322.922	5122986.664
YMP-TH-FD	2443268.364	3157390.93	3601039.491	0	128068.5946	348570.4775
YMP-TH-FD	2869713.167	3888051.7	4424322.922	128068.5946	0	65324.54767
YMP-TH-FD	3376552.448	4547590.055	5122986.664	348570.4775	65324.54767	0

Table 3: Euclidean distances of YMP-UHPS-SD and YMP-TH-SD.

	Full distance matrix					
	YMP-UHPS-SD	YMP-UHPS-SD	YMP-UHPS-SD	YMP-TH-SD	YMP-TH-SD	YMP-TH-SD
YMP-UHPS-SD	0	127301.0841	377690.2796	1015777.871	1076173.411	1166654.665
YMP-UHPS-SD	127301.0841	0	80887.23678	758933.4931	820824.4263	887721.266
YMP-UHPS-SD	377690.2796	80887.23678	0	651218.8438	712469.4628	761067.4841
YMP-TH-SD	1015777.871	758933.4931	651218.8438	0	14019.44705	19230.69455
YMP-TH-SD	1076173.411	820824.4263	712469.4628	14019.44705	0	7734.811158
YMP-TH-SD	1166654.665	887721.266	761067.4841	19230.69455	7734.811158	0

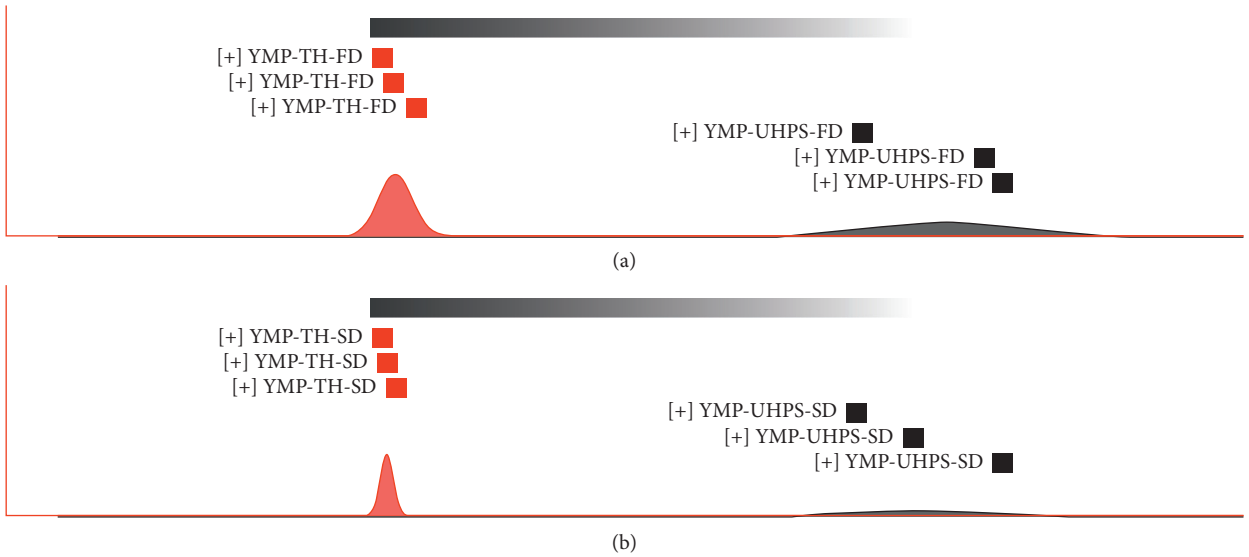


Figure 5: Similarity analysis of fingerprint based on the Euclidean distance of YMP.

4. Conclusions

With the development of society, industrialization and convenient transportation will make it more convenient for us to promote yak specialty food. Thus, we began to think whether it is possible to detect the differences of VOCs and flavor of YMP. Many volatile substances have a characteristic flavor; for example, acetone has a milky aroma, hexanal is green, fatty, and has a milky aroma, and 2-heptanone has cinnamon and a slightly spicy aroma [1, 13, 34]. It is noteworthy that the diversity of sterilization methods makes the samples have diversity and also leads to different volatile substances differences.

In this study, HS-GC-IMS was used to detect the flavor substances of YMP with different sterilization methods. A total of 46 peaks were detected, and 17 compounds were characterized, including 7 aldehydes, 5 ketones, 3 acids, 1 terpene, and 1 ester identified. However, GC-IMS cannot detect alkane compounds, and 21 peaks had not been qualitative analyzed. On this account, it is important to perform GC-MS or other qualitative methods. For YMP-UHPS-FD and YMP-TH-FD, the difference of VOCs was significant; while the difference between YMP-UHPS-SD and YMP-TH-SD was not obvious which maybe the spray-drying affected. Besides, aldehydes were mainly detected in UHPS groups, whereas the ketones and acids mostly appeared in TH groups. So, the study showed that YMP under UHPS had a better flavor than TH, which can retain the original flavor of yak milk to a greater extent. In addition, PCA and fingerprint similarity analysis also provided well-distinguished explanation for YMP with different sterilization methods. It is recommended that subsequent research studies investigate the quantification of VOCs and employ more different methods of sterilization and the potential mechanism for the difference in the flavor of YMP with different sterilization processes, to provide a variety of theoretical support for the intensive processing technology of YMP.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Duo Feng conducted investigation, wrote the original draft, and performed plot analysis. Jing Wang conducted formal

analysis and Visualization. Xiao-jiao Ji conducted investigation and provided validation. Wen-xiang Min collected resources. Wen-jie Yan reviewed and edited the manuscript, supervised the work, and acquired funding.

Acknowledgments

This work was supported by the Academic Research Projects of Beijing Union University (ZK70202004) and the National Key Research and Development Plan during 13th five-year plan period (Grant no. 2016YFD0401504).

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