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Research Article

ENVIRONMENTAL CHEMICAL CONTAMINANTS

Determination of 19 Fragrance Allergens in Paper Household Goods by Solid-Liquid Extraction-Dispersive Liquid-Liquid Microextraction-GC-MS

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Abstract

Background: Fragrance allergens (FAs) refer to these volatile or semi-volatile fragrance compounds that can induce sensitization, and they are widely used in household goods.
Objective: In this work, a method combining solid-liquid extraction (SLE) and dispersive liquid-liquid microextraction (DLLME) with gas chromatography-mass spectrometry (GC-MS) has been developed and applied in the analysis of 19 FAs (including hydrocarbons, alcohols, aldehydes, esters, and phenols) in paper household goods.
Method: The samples (infant or personal paper hygiene products) were cut into small pieces and underwent SLE with methanol as solvent. The supernatant was taken, and ultrapure water, sodium chloride, and trichloromethane (extractant) were added, which was mixed with vortex. After centrifugation, the bottom chloroform layer was taken for GC-MS detection.
Results: Under optimized conditions, a good linearity was achieved ($r \geq 0.9985$) in the range of 0.01–128.0 mg/kg with relative standard deviations lower than 15%. The method showed limits of detection (LODs) within the range of 0.96–12.0 μg/kg and recoveries from 70.6% to 128.9%, except furfuryl alcohol with low recoveries (53.8–64.6%). Twenty kinds of paper household goods samples were analyzed by this method; nine FAs were detected. The linalool detected in one sample was more than 10 mg/kg, and the contents of other analytes in this sample and all analytes in other samples were less than 10 mg/kg.
Conclusions: The performance evaluation of the method met the requirements of the analysis of trace components. The established method was successfully applied to the detection of FAs in paper household goods samples. The proposed method could provide a basis for the establishment of relevant detection standards in the future.
Highlights: The LODs were found between 0.96 and 12.0 μg/kg. A simple, economical, and sensitive method was established for the determination of 19 FAs in paper household goods.

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Fragrance allergens (FAs) have been widely used in skin care products, cosmetics, wipes, and other household goods. However, they have been reported to have irritative or other adverse effects on human skin, eyes, respiratory tract, etc., which can cause lung disease, dermatitis, migraine, and even endocrine diseases (1–3). Since the skin and mucous membranes of infants and women are sensitive, the concentration of FAs that causes irritation and negative reactions for these people may be very low. Therefore, the composition and concentration of common FAs in household goods, especially these directly contacting with skin and mucous membrane, have attracted public attention. Many countries and organizations have issued the standards for the types and contents of FAs allowed for use. In Japan, the use of nitro-musks has been banned since the 1980s. The European Union has stipulated the limits for dozens of FAs that may exist in children's toys and cosmetics (4, 5). In China, the current standard for daily essence product is *GB/T 22731–2017 Daily Essence Limit* (6). Among 11 common household goods, the maximal limits of 99 FAs and the prohibition of 82 FAs were stipulated, including toys, baby wipes, baby creams, etc.

Up to now, the determination of FAs focused mainly on liquid samples with simple matrixes such as perfumes, skin care products, cosmetics, and toy samples (7–10). However, common solid household goods such as wet tissue, wet toilet paper, makeup remover wipes, sanitary napkins, and baby diapers are rarely reported. Therefore, it is urgent to establish an accurate and sensitive method for the determination of FAs in household goods with paper matrices.

GC-MS is often used to detect volatile organic compounds (VOCs). It combines the powerful separation ability of GC and the excellent qualitative and quantitative ability of MS, and it can achieve sensitive and specific analysis of VOCs. Until now, the reported pretreatment methods for extraction of FAs include dilution, liquid-liquid extraction (LLE), headspace (HS), solid phase microextraction (SPME), and so on. The dilution method is easy to operate, but only suitable for liquid samples with simple matrix (11). The traditional LLE method is quick and simple; however, it has low sensitivity and requires large amounts of organic reagents (12). Although HS is widely applied in fragrance analysis (9, 13), the static headspace (SHS) method has relatively low sensitivity, whereas the dynamic headspace (DHS) method requires special instruments. SPME is environmentally friendly and can integrate sampling, extraction, concentration, and injection (14); however, it suffers from much difficulty to process samples in a batch quickly. In recent years, different types of liquid-liquid microextraction (LLME) methods have been used in the pretreatment of samples with various matrixes. Dispersive liquid-liquid microextraction (DLLME), as one of the improved LLE techniques, has the advantages of simple operation, less organic reagent consumption, and environmental friendliness and has been extensively used in the extraction of analytes from liquid samples such as water and beverage (15). However, DLLME is rarely used for the pretreatment of solid samples.

To the best of our knowledge, there is no standard detection method for FAs in complex paper matrix samples. In addition, the applicability of the DLLME method for solid sample pretreatment needs to be further explored and verified. Therefore, nineteen FAs including limonene, linalool, furfuryl alcohol, citral, benzyl acetate, citronellol, geraniol, diethyl maleate, benzyl alcohol, hydroxy citronellal, cinnamaldehyde, eugenol, amyl cinnamaldehyde, isoeugenol, and amylcinnamyl alcohol were chosen according to the FAs lists of the European Union, China, and International Fragrance Association (4, 6, 16). The aim of this work is to establish a simple, rapid, sensitive, and economical method of solid-liquid extraction (SLE) -DLLME-GC-MS for the 19 FAs in common paper household goods. The samples such as tissues, makeup remover wipes, and wet toilet paper are made of paper, whereas infant diapers and sanitary napkins are synthesized from paper and other ingredients such as resin. It can offer the reference for the establishment and improvement of the detection standards of FAs.

Experimental

Chemicals and Reagents

Limonene (98.0%), linalool (98.0%), furfuryl alcohol (97.1%), citral (98.0%), benzyl acetate (98.0%), citronellol (96.8%), geraniol (96.8%), diethyl maleate (96.8%), benzyl alcohol (99.8%), hydroxy citronellal (98.8%), cinnamaldehyde (98.0%), eugenol (97.0%), amyl cinnamaldehyde (92.1%), isoeugenol (95.5%), amylcinnamyl alcohol (88.9%), and the internal standard 1-fluoronaphthalene (99.0%) were purchased from Dr. Ehrenstorfer (Augsburg, Germany). Phenethyl alcohol (97.0%) was acquired from Chemservice (USA). Cinnamyl alcohol (98.0%) and 7-methylcoumarin (98.0%) were obtained from Aoke Biotechnology (Beijing, China). Carvacrol (99.4%) was obtained from ANPEL Laboratory Technologies (Shanghai, China). The internal standard of benzyl alcohol–D7 (98.0%) was provided by Macklin Biochemical (Shanghai, China).

Acetonitrile (99.8%) was purchased from Zhiyuan Chemical Co., Ltd. (Tianjin, China). Ethyl acetate (99.9%), *n*-hexane (99.5%), methanol (99.9%), and toluene (99.5%) were purchased from Kermel Chemical (Tianjin, China). Tetrachloromethane, acetone (99.8%), dichloromethane (99.5%), and chloroform (99.5%) were purchased from Knowles Chemicals (Chengdu, China). All the reagents mentioned above are HPLC grade. Sodium chloride (99.9%, GR grade) was purchased from DE Salt (Jiangsu, China). The ultrapure water (18.2 megohm-cm) used was prepared with a Millipore Milli-Q System (Bedford, MA).

Two kinds of baby wipes (category A), nine kinds of wet tissues (category B), three kinds of wet toilet paper (category C), three kinds of makeup remover wipe (category D), one kind of baby diaper (category E), and two kinds of sanitary napkin (category F) were purchased from local markets in Chengdu, Sichuan Province. The samples were stored at 4°C. The flake samples were analyzed immediately after unsealed.

Preparation of Standards

Individual stock solutions of 1000 μg/mL were prepared in methanol and then stored at −18°C. A mixed standard solution of nineteen FAs was prepared in chloroform and then stored at 4°C. Next, the working standard solutions were freshly prepared by diluting the mixed standard solution and mixed internal standard solution to the required concentrations with chloroform. The concentration of internal standards of 1-fluoronaphthalene and benzyl methanol-D7 were 0.20 μg/mL and 8.00 μg/mL, respectively. At the same time, a mixed standard solution of 2.00 μg/mL was prepared for the optimization experiment of conditions.

GC-MS

All experiments were performed with an Agilent GC (Agilent 7890A) equipped with an HP-INNOWax capillary column (30 m × 0.25 mm × 0.25 μm) and connected to a MS system

(Agilent 7000B). An Agilent G4513A automatic injector was used for injection of sample solution.

The samples were injected with an injection port temperature of 250°C and in split mode with a split ratio of 5:1. Helium gas (purity 99.999%) was used as carrier gas at a constant flow rate of 1.0 mL/min, and the injection volume was 1.0 μL. The GC oven temperature was programmed from 60°C (held for 3 min) to 105°C at 15°C/min (held for 2 min), to 150°C at 20°C/min, and to 250°C at 10°C/min followed by the post run at 250°C for 3 min. The total running time of the temperature program was 19.25 min.

The temperatures of the transfer line, quadrupole, and ion source were 250°C, 150°C, and 230°C, respectively. The analytes were ionized by electron impact. A solvent delay of 5.60 min was employed to increase the service life of the filament. The analytes were identified by comparing the mass spectra and retention times with those of the standards, and the quantification was operated in a selected ion monitoring (SIM) mode.

Sample Pretreatment

(a) *SLE*.—The samples were cut into small pieces of 5 mm × 5 mm and mixed thoroughly, and 0.10 g of the sample was accurately weighed into a polypropylene centrifugal tube. Then 40 μL of the mixed internal standard solution was added. After standing for a few minutes, 2.00 mL of methanol was added, followed by agitating on an oscillator for 30 min extraction.

(b) *DLLME*.—1.00 mL of the solvent supernatant was transferred into a 5.0 mL glass centrifuge tube, and 2.50 mL of ultrapure water and 0.5% (0.018 g) of NaCl were added into the solution and mixed for 1 min by vortex. Then 100 μL of chloroform was added, immediately followed by vortex for 1 min. Subsequently, the mixture was centrifuged at 4000 rpm for 3 min. Finally, the chloroform phase was taken from the bottom of the tube and transferred into the vials for GC-MS analysis. The procedure of SLE-DLLME-GC-MS is shown in Figure 1.

Results and Discussion

Optimization of GC-MS Condition

The polarity of the separation column has a great influence on the determination of target compounds. The 19 analytes possess quite different boiling points and polarity. In this study, low-polar capillary column HP-5 and high-polar capillary column HP-INNOWax were compared through the peak shape, separation resolution, and sensitivity. The analysis time with HP-5 column was shorter than that with HP-INNOWax. However, when the HP-5 column was used, the peaks of furfuryl alcohol, benzyl alcohol, and phenyl ethanol were seriously tailed. In addition, the retention times of citronellol, *cis*-citral, and geraniol with the same quantitative ion of m/z = 69 was very close even when the temperature programming was adjusted, which compromised the quantitation accuracy of these three compounds. On the contrary, when the HP-INNOWax column was used, all the analytes exhibited sharp and symmetrical peak shapes (Figure 2). Although several analytes showed similar retention time, the accuracy of qualitative and quantitative analysis would not be affected due to the different characteristic ions. Therefore, we chose HP-INNOWax column for subsequent analysis.

In addition, the proper GC oven temperature program and split ratio were beneficial to the separation of the compounds with different boiling points and made the peak shapes symmetrical. When the oven temperature was raised from 60°C to 250°C at a rate of 10°C/min, the peak of each compound could be separated well. However, the retention times (Δt) between limonene and adjacent linalool varied up to 5 min, thereby prolonging total analysis time. Thus, a faster heating rate was tried before linalool flowed out. The optimal GC oven temperature was programmed from 60°C (held for 3 min) to 105°C at 15°C/min, and then to 150°C at 20°C/min, and finally to 250°C at 10°C/min (held for 1 min). The total analysis time was 19.25 min. The split ratio would affect the shape and height of the target peaks, too. When the split ratio was 4:1, the peak areas were higher, while the peak widths of trans-citral, benzyl acetate, 1-fluoronaphthalene, citronellol, and diethyl maleate during the

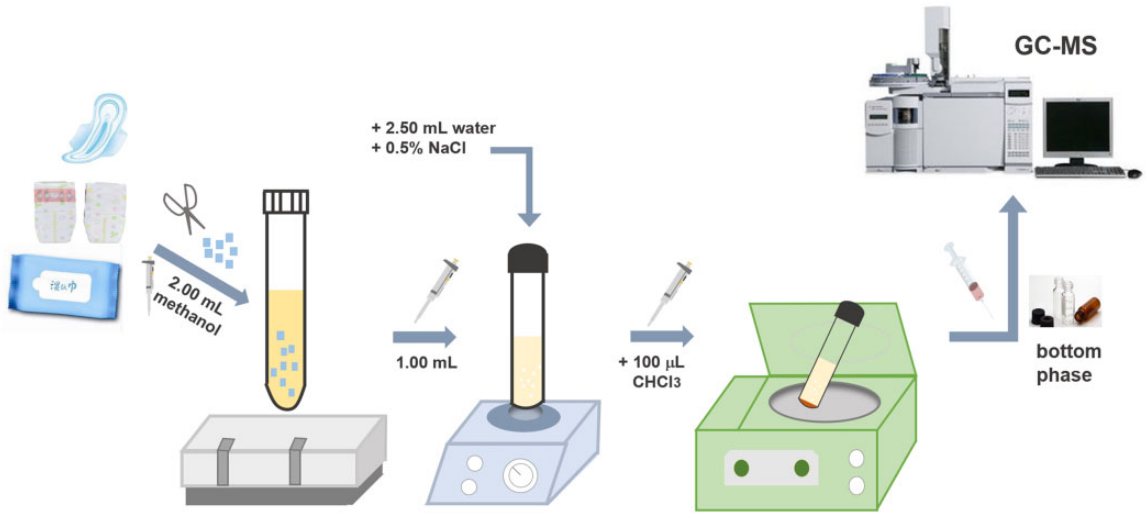

Figure 1. The diagram of SLE-DLLME-GC-MS procedure.

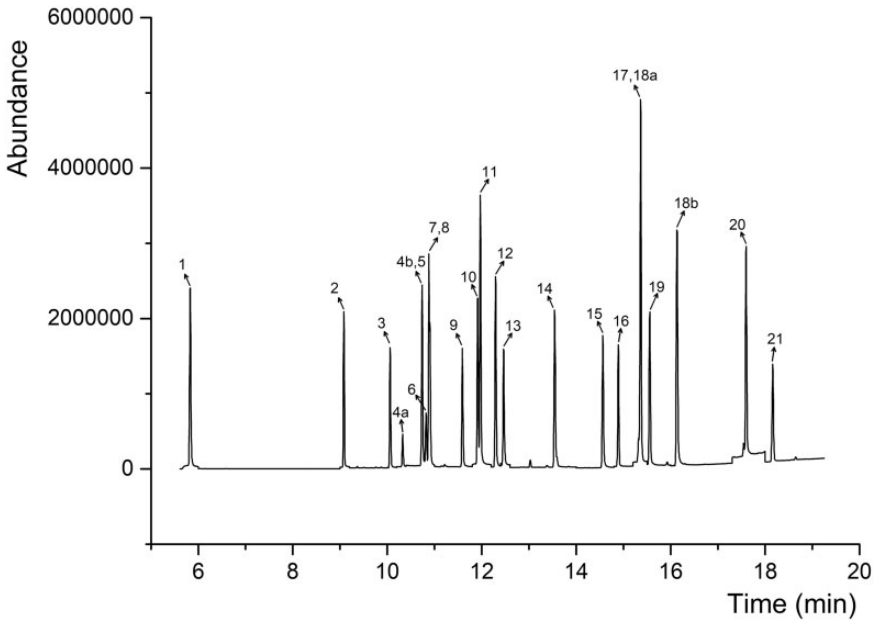

Figure 2. TIC of 19 FAs and two internal standards separated by HP-INNOWax column. (1) Limonene, (2) Linalool, (3) Furfuryl alcohol, (4a) *Cis*-citral, (4b) *Trans*-citral, (5) Benzyl acetate, (6) 1-Fluoronaphthalene, (7) Citronellol, (8) Diethyl maleate, (9) Geraniol, (10) Benzyl alcohol-D7, (11) Benzyl alcohol, (12) Phenethyl alcohol, (13) Hydroxy citronellal, (14) Cinnamaldehyde, (15) Eugenol, (16) Carvacrol, (17) Amyl cinnamaldehyde, (18a) *Cis*-isoeugenol, (18b) *Trans*-isoeugenol, (19) Cinnamyl alcohol, (20) Isoeugenol, (21) 7-Methylcoumarin.

period of 10.40 min to 11.00 min were increased. Due to the problem of co-elution and decrease of separation resolutions, it was difficult to achieve accurate qualitative analysis. When the split ratio was 5:1, it could meet the requirements of LODs and ensure the separation resolution at the same time, so 5:1 was selected as the final split ratio.

Citral has *cis* and *trans* isomers with different boiling points of 120°C and 229°C, respectively, so they have different retention behaviors in the same separation column. According to the boiling point and ratio of characteristic ion abundance, it can be inferred that the retention time of *cis*-citral was shorter than that of *trans*-citral, thus *cis*- and *trans*-citral can be identified. In quantitative analysis, they were regarded as one analyte. The peak areas of *cis*-*trans* isomers of iso-eugenol were combined for eugenol quantitation, too. Under optimal GC-MS conditions, the retention times and characteristic ions of 19 analytes and two internal standards are shown in Table 1. The total ion chromatogram (TIC) of the target FAs is shown in Figure 2.

Optimization of Sample Pretreatment

Sample pretreatment is one of the key steps affecting the analysis results. Proper pretreatment method can remove the impurities in the matrix that may interfere with the analysis. What is more, the pretreatment process can concentrate the analytes, and thus improve the sensitivity and selectivity of the method. In this study, the SLE-DLLME method was selected for the sample pretreatment. The solvent, extractant, salt concentration, auxiliary extraction method, and extraction time can affect the extraction efficiency of SLE-DLLME. Therefore, in this study, the mixed standard solution of 4.00 mg/kg (i.e., the final concentration for injection was 2.00 μg/mL) was added into the blank sample (tissue sample with target FAs undetected in preliminary experiment), which was used to determine the optimal experiment conditions by comparing the peak area of each analyte.

In the SLE process, the solvent choice is the key to improve the extraction efficiency. The suitable solvent has strong dissolution ability to the analytes and can efficiently extract analytes from the solid sample matrix. In addition, it will affect the subsequent extraction efficiency of DLLME. In the process of DLLME, the solvent and the extractant form the binary phase with the assistance of water. The difference of solubility in the two phases promotes the analytes from the upper solvent-water phase to the lower extractant phase for further purification and concentration. The suitable extractant usually has the characteristics of higher density than water, low water-solubility, high affinity to analytes, and good chromatographic performance. However, the ionic strength of the solvent can affect the partition coefficient of analytes in the solvent and extractant, thus affecting the extraction efficiency. In the pre-experiment, the single factor optimization could not evaluate the interaction between the factors, which failed to select the optimal combination of solvent, extractant and salt concentration. Therefore, the optimal combination was explored by 3^3 enumeration methods.

According to the references 11 and 17–19, acetonitrile, acetone, methanol, and *n*-hexane embrace good solubility for the target analytes, and they were tried as the solvent to extract the analytes from solid samples, separately. The pre-experiment showed that the peak areas of most analytes were very low when *n*-hexane was used. This may be due to the strong polarity of most FAs and the low polarity of *n*-hexane. According to the principle of similar solubility, it was difficult to transfer the analytes from the sample matrix to *n*-hexane, and the subsequent DLLME had poor stratification effect. Therefore, *n*-hexane was not adopted in the subsequent optimization experiment. Commonly used extractants in SLE include carbon disulfide, dichloromethane, chloroform, and tetrachloromethane. However, when dichloromethane was used as the extractant, the solvent effect made limonene chromatographic bimodal. The distance between the two peaks decreased with the

Table 1. Retention times and characteristic ions of the analytes and internal standards

No.	FAs	Chemical Abstracts Service Number (CAS)	Retention time, min	Identification ions, *m/z*
1	Limonene	5989–27-5	5.82	67, 68[a], 93
2	Linalool	78–70-6	9.09	71, 93[a], 55
3	Furfuryl alcohol	98–00-0	10.07	81, 97, 98[a]
4	Citral	5392–40-5	10.32; 10.76	69[a], 41, 94; 69[a], 84, 109
5	Benzyl acetate	140–11-4	10.74	91, 108[a], 150
6	1-Fluoronaphthalene	321–38-0	10.82	146[a]
7	Citronellol	106–22-9	10.89	55, 69[a], 81
8	Diethyl maleate	141–05-9	10.91	99[a], 126, 127
9	Geraniol	106–24-1	11.60	41, 68, 69[a]
10	Benzyl alcohol-D7	71258–23-6	11.82	85, 113, 115[a]
11	Benzyl alcohol	100–51-6	11.99	79, 107, 108[a]
12	Phenethyl alcohol	60–12-8	12.31	91[a], 92, 122
13	Hydroxy citronellal	107–75-5	12.47	43, 59[a], 71
14	Cinnamaldehyde	104–55-2	13.54	103, 131[a], 132
15	Eugenol	97–53-0	14.57	131, 149, 164[a]
16	Carvacrol	499–75-2	14.91	91, 135[a], 150
17	Amyl cinnamaldehyde	122–40-7	15.36	91, 117, 129[a]
18	Isoeugenol	97–54-1	15.37; 16.14	103, 149, 164[a]; 133, 149, 164[a]
19	Cinnamyl alcohol	104–54-1	15.57	91, 92[a], 134
20	Amylcinnamyl alcohol	101–85-9	17.60	91[a], 115, 133
21	7-Methylcoumarin	2445–83-2	18.15	131, 132, 160[a]

[a] Represents the ion used for quantification.

Table 2. The variables and levels investigated in the 3^3enumeration method

	Level		
Variable	1	2	3
Solvent	A1 = methanol	A2 = acetonitrile	A3 = acetone
Extractant	B1 = carbon disulfide	B2 = chloroform	B3 = tetrachloromethane
NaCl concentration	C1 = 0% (0 g)	C2 = 0.5% (0.018 g)	C3 = 2.0% (0.070 g)

increase of the split ratio. Nevertheless, adjusting the split ratio still cannot make a stable unimodal peak shape. Therefore, dichloromethane was excluded in subsequent experiments.

Finally, three kinds of solvents (methanol, acetonitrile, and acetone), three kinds of extractants (carbon disulfide, chloroform, and tetrachloromethane), and three levels of salt concentration (0%, 0.5%, and 2.0%, w/v) were taken for the 3^3 enumeration optimization. The variables and levels are shown in Table 2. In the optimization experiments, the solvent volume in the SLE process was 2.00 mL, and agitating extraction for 10 min was used for the auxiliary extraction. The volume of solvent (supernatant in the extraction process) and extractant in DLLME system were 1.00 mL and 100 μL, respectively.

Different solvent and extractant combinations exhibited significantly different extraction efficiencies, while salt concentration only affected the extraction results in a limited range. Since the optimization results of most analytes were similar to that of limonene, we took limonene as the representative to illustrate the results. The peak areas of acetonitrile-carbon disulfide combination (A2B1) and methanol-chloroform combination (A1B2) could reach more than 120 000, which were significantly higher than other combinations (Figure 3). However, for furfuryl alcohol, its peak area extracted by acetonitrile-carbon disulfide combination (A2B1) was less than 5000, and the extraction efficiency was extremely low (Figure 4). It was inferred that furfuryl alcohol had high polarity, and it was difficult to transfer from the high-polar acetonitrile phase to the nonpolar carbon disulfide phase. The analysis results of furfuryl alcohol showed that the peak area extracted by acetone-chloroform combination (A3B2) was the highest, and those by methanol-chloroform combination (A1B2) and acetonitrile-chloroform combination (A2B2) were lower. However, for limonene, the peak area extracted by acetone-chloroform combination (A3B2) was only two-thirds of that by methanol-chloroform combination (A1B2). For most of the analytes, the methanol-chloroform combination (A1B2) was the dominant combination, and the toxicities of methanol and chloroform were relatively low. After comprehensive consideration, methanol and chloroform combination were selected as solvent and extractant. After further investigation of three salt concentration levels with this combination (A1B2), it was found that the peak area of analytes decreased with the increase of the salt concentration in the system. The reason might be that the electrostatic interaction between the salt ions and the analytes was dominant in the system, which inhibited the continued migration of the analytes to chloroform phase. In addition, the increase of salt concentration can promote the delamination, and the increase of extractant volume was also related to the final concentration of the analytes. However, when sodium chloride was not added, although the peak area was the highest, the volume of chloroform layer

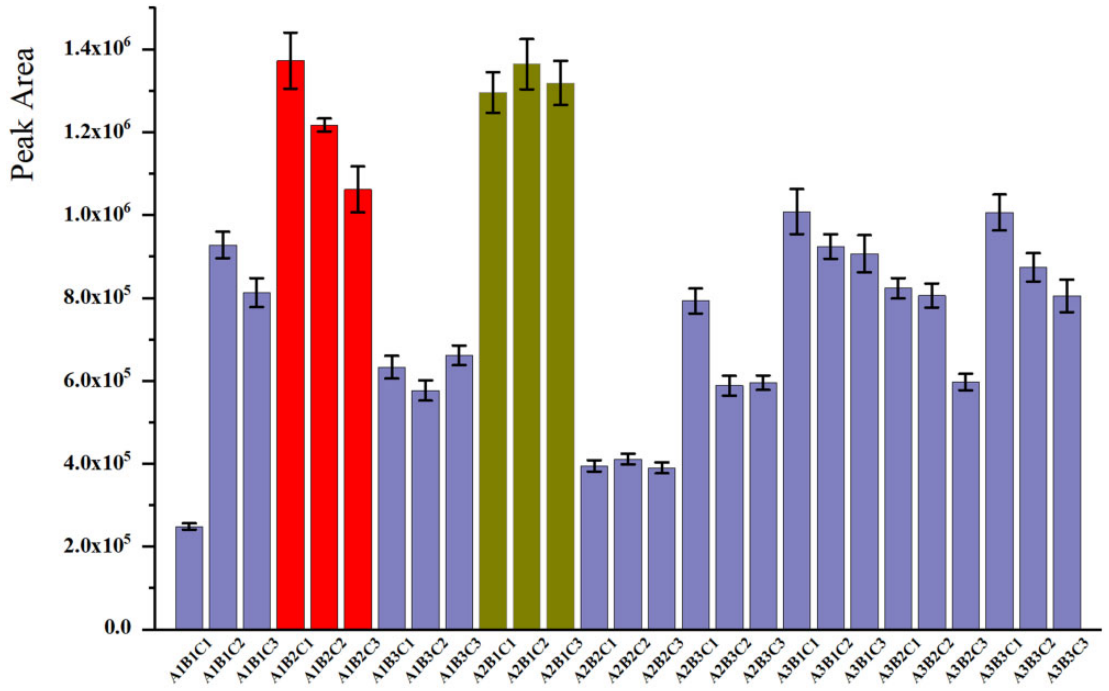

Figure 3. The effect of SLE solvent-extractant-salt concentration system on the peak area of limonene. (A) SLE solvent, (B) Extractant, (C) Salt concentration.

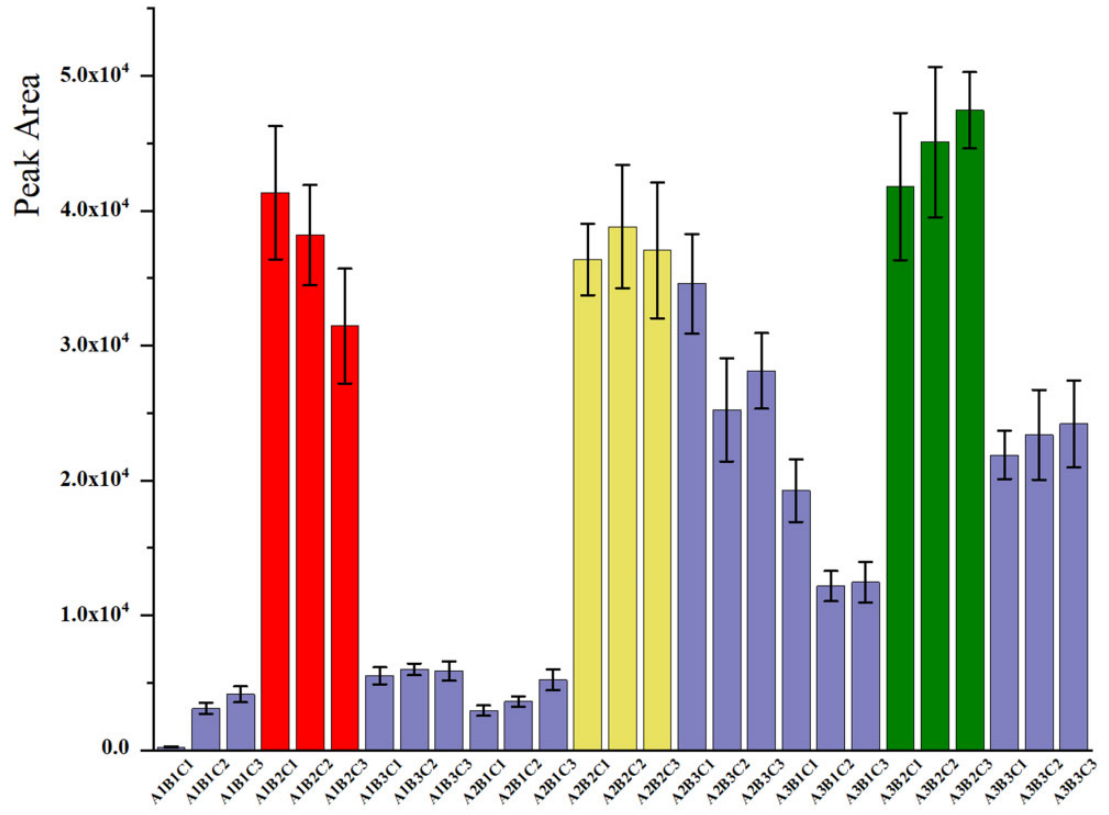

Figure 4. The effect of SLE solvent-extractant-salt concentration system on the peak area of furfuryl alcohol. (A) SLE solvent, (B) Extractant, (C) Salt concentration.

extracted was only about 40 μL. Since chloroform is volatile, it is difficult to ensure the stability and accuracy of the determination results during batch sampling. Therefore, the methanol-chloroform-0.5% sodium chloride combination (A1B2C2) was finally selected as the optimal combination of solvent-extractant-salt concentration for the subsequent experiments.

Mechanical effect and thermal effect caused by ultrasound, vortex, and agitating could increase the contact area between

the sample and the solvent, and further promoted the transfer of the analytes into the solution. These methods increased the contact area between the sample and the solvent and further promoted the transfer of the analytes to the solution. In this study, the effects of three auxiliary methods, including ultrasonic, vortex, and agitating on an oscillator, on extraction efficiency were investigated with the extraction time of 10 min. The results are shown in Supplemental Figure S1. For ultrasound-assisted extraction, the peak areas of most analytes were lower than those of the other two methods. In addition, the chromatogram of ultrasound extraction had a high baseline, and an interference peak appeared near furfuryl alcohol. This may be due to the strong mechanical and thermal effects of ultrasonic, leading to the impurities entering the extraction solution, and the impurities could not be removed in the subsequent treatment process, which would cause interference. For most of the analytes, the extraction efficiencies with vortex and agitating were similar, but the peak areas of benzyl alcohol and hydroxy citronellal with agitating were about 50% higher than those with vortex. Therefore, we selected agitating as the auxiliary extraction method.

The extraction time is one of the factors affecting the efficiency of SLE, which is a dynamic equilibrium process. If the extraction time is too short, the analytes cannot be fully transferred to the extraction solvent; if the time is too long, the analytes may return to the sample matrix. The effects of agitating for 5 min, 10 min, 20 min, and 30 min on the extraction efficiency were compared. The results (Supplemental Figure S2) show that the effects of extraction time on all the analytes had the same tendency, and the peak areas of analytes were 5 min < 20 min < 10 min < 30 min. The reason might be that when the extraction time was 5 min, the extraction was not completed, and the poor extraction stability led to high RSDs. When the extraction time was 10 min, the extraction efficiency was improved with sufficient contact between methanol and the sample. However, due to the water absorption property of the paper matrix, the dynamic equilibrium between the sample matrix and methanol moved toward the opposite direction at 20 min, and the extraction efficiency of methanol decreased. With further extension of extraction time to 30 min, the paper sample became looser than the original dense state, which resulted in the full release of the analytes in methanol. Thus, the extraction effect of all the analytes was significantly improved, and the RSDs were reduced. Considering the effect and speed, 30 min was selected as the time of SLE.

Method Performance

The performance of the proposed SLE-DLLME-GC-MS method was evaluated in terms of linearity, LODs, and LOQs under optimal conditions mentioned above (Supplementary Table S1). The linear ranges for each analyte ranged from 0.01 to 128.0 mg/kg with the correlation coefficient (r) $\geq$ 0.9985. The LODs (S/N = 3) and LOQs (S/N = 10) of samples were calculated as 0.96–12 μg/kg and 3.2–40 μg/kg, respectively.

Solid samples usually have complex matrixes, which could affect the accuracy of quantitative analysis. Thus, the recovery tests were performed to validate the accuracy of the proposed method. In this study, blank tissue goods samples spiked with three concentration levels of the standard solutions were adopted for the recovery tests in triplicate. As illustrated in Supplementary Table S2, except furfuryl alcohol with low recoveries (53.8–64.6%), the low-level spiked recoveries for other analytes ranged from 70.6 to 121.0% with RSDs ranging from 2.2 to 13.6%. The recovery range spiked with medium concentration level were 85.6–128.2%, and RSDs were 2.2–7.9%. The recoveries spiked with high concentration level were 70.7–128.9%, and RSDs were 2.4–9.5%.

To the best of our knowledge, only two articles have reported the determination of FAs in paper household goods. Desmedt et al. (19) established a HS-GC-FID-MS method to detect FAs in absorbent hygiene products. However, their method had a narrow linearity range from 10 to 100 μg/g. Celeiro et al. (20) developed a pressurized liquid extraction (PLE) -GC-MS method to analyze the FAs in baby wipes, which required a specific pretreatment instrument. In addition, compared with the PLE-GC-MS method, the SLE-DLLME-GC-MS method proposed in this study had a wider linear range (5–64000 ng/mL vs. 2–2000 ng/mL) with the lower LODs (0.96–12.0 μg/kg vs. 1.1–31 μg/kg). Consequently, the proposed method was effective, sensitive, and simple.

Application to Real Samples

The established SLE-DLLME-GC-MS method was used to detect various samples of paper household goods, including two kinds of infant wet wipes, nine kinds of daily wet wipes, three kinds of wet toilet paper, three kinds of makeup removal wet wipes, one kind of infant diaper, and two kinds of sanitary napkins, all of which were purchased from local markets in Chengdu. Nine kinds of FAs were detected in these samples.

The detection rates and contents of 19 FAs in the samples are shown in Supplementary Table S3. Among them, benzyl alcohol was detected in 16 samples, with the highest detection rate (80%), and the contents ranged from 0.039 to 6.52 mg/kg. Benzyl alcohol was found in almost all the four types of wet wipes, including infant wipes, daily wipes, wet toilet paper (except C3), and makeup-removing wipes, which may be due to its wide use in wet wipes as a good fragrance sensitizer and deodorant. As a diluent and permeability enhancer with low toxicity and sensitivity, phenyl ethanol also had a high detection rate. It was detected in 12 samples, and the content range was <LOQ-3.89 mg/kg. FAs such as linalool, benzyl acetate, citronella, geraniol, and hydroxy citronella were detected commonly in the samples with fragrance of roses and cherry blossoms. The detection rates of linalool, benzyl acetate, citronellol, and geraniol ranged from 42.1 to 52.6%. Hydroxy citronellal was detected in only one sample with the content of 0.901 mg/kg. Limonene and citral are the main FAs for the preparation of lemon flavor. Limonene was detected in five samples, and citral in six samples. The content of limonene and citral was <LOQ-0.609 mg/kg and <LOQ-1.44 mg/kg, respectively. The other ten kinds of FAs were not detected in the 20 kinds of samples. The TIC/EIC chromatograms of B1, C3, and D3 samples are shown in Supplemental Figures S3 and S4 and Figure 5.

Desmedt et al. (19) detected FAs in 10 kinds of water-absorbent sanitary products, including sanitary napkins, tampons, and sanitary underpants. The results showed that limonene, linalool, citronellol, geraniol, and hydroxy citronellal were detected. Linalool was detected in one sample exceeding 10 mg/kg, while the contents of other analytes in this sample and all analytes in other samples were less than 10 mg/kg. Celeiro et al. (20) also found that limonene, benzyl alcohol, and linalool were the most frequently FAs found in baby wipes. In the 20 samples tested in our study, only one sample contained more than 10 mg/kg of linalool, and most of the FAs were less than 10 mg/kg. The kinds and contents of FAs detected in our study were similar to those of Desmedt. In their study (19),

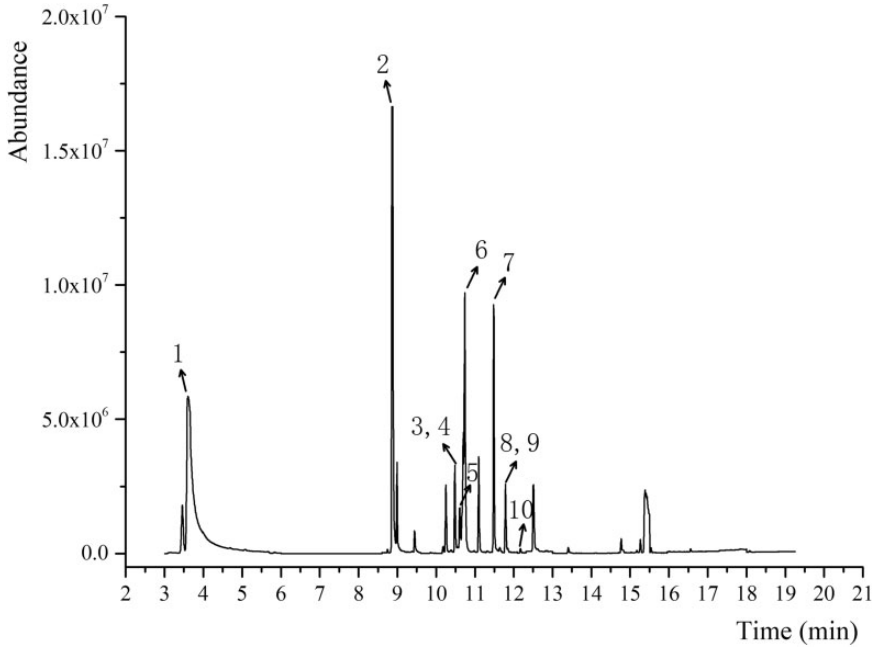

Figure 5. Chromatograms of D3 sample analyzed by SLE-DLLME-GC-MS. (1) Limonene, (2) Linalool, (3) Trans-citral, (4) Benzyl acetate, (5) 1-Fluoronaphthalene, (6) Citronellol, (7) Geraniol, (8) Benzyl alcohol-D7, (9) Benzyl alcohol, (10) Phenethyl alcohol.

benzyl alcohol was not detected in water-free paper products including sanitary napkins, tampons, and sanitary underpants, which was also consistent with the results of the two sanitary napkins in our study.

The FAs in the tested samples did not exceed the daily fragrance limits of category 5 (face, hand, body wipes, or fresh paper towels), category 7 (personal cleaning products, infant cleaning products), category 9 (sanitary napkins), and category 10 (infant diapers) in GB/T 22731–2017 of China. Furthermore, the contents of these FAs detected in real samples were compared with the standards for FAs in cosmetics of (EC) 1223/2009 (as a reference), and all the samples meet the requirement of the EU standards.

Conclusions

In this study, a method of SLE-DLLME-GC-MS was developed for trace analysis of 19 FAs in paper household goods. The main experimental parameters affecting the sample pretreatment procedure were optimized to obtain high extraction efficiency, and the internal standard method was adopted to assure reliable quantification. Furthermore, SLE-DLLME endows this method with satisfactory LODs. Consequently, the proposed method embraced the advantages of simple operation, high sensitivity, and short time consumption. It was applied for the determination of 19 FAs in 20 real paper household goods samples, and nine FAs were detected. The proposed method provides theoretical and experimental basis for the establishment of relevant detection standards for FAs in household goods in the future.

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Conflict of Interest

The authors declare that we have no financial interests or personal relationships that could inappropriately influence the work reported in this paper.

Supplemental Information

Supplemental information is available on the *J. AOAC Int.* website.

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