Menthol-based deep eutectic solvent in dispersive liquid-liquid microextraction followed by solidification of floating organic droplet for the determination of three bisphenols with UPLC-MS/MS

Xiaomei Liu, Yuwei Bian, Jing Zhao, Yu Wang, Longshan Zhao*

School of Pharmacy, Shenyang Key Laboratory of Functional Drug Carrier Materials, Shenyang Pharmaceutical University, 103 Wenhua Road, Shenyang 110016, PR China

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ABSTRACT

An efficient dispersive liquid-liquid microextraction (DLLME) method based on the solidification of floating organic drop (SFO) has been developed for extraction of bisphenol S (BPS), bisphenol A (BPA) and bisphenol B (BPB) in canned fruit, in which green deep eutectic solvent (DES) was used as the extraction solvent. The analysis was determined by ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). All parameters affecting the extraction efficiency, including selection of DES, volume of DES, salt effect, extraction time, pH, and dispersion solvent type and volume, were investigated and optimized. The extraction efficiency of bisphenols was improved by a menthol-based DES. More importantly, the low melting point of DES makes the extracted bisphenols could be easily separated from sample solution with a syringe. This method showed good linearity (r > 0.9916) in the range of 10.0–200 ng g^{-1} with limits of detection (LODs) ranged from 1.5 to 3.0 ng g^{-1} and the limit of quantifications (LOQs) were ranged from 5.0 to 10.0 ng g^{-1}. The recoveries of three spiked levels were ranged from 79.5% to 101% with relative standard deviations (RSDs) were lower than 4.6%. This developed method was successfully applied in bisphenols extraction of different canned fruit samples and exhibited a simple and green extraction procedure. This environmentally friendly method offers an important reference for the separation of bisphenols in food.

1. Introduction

Materials used in packaging, such as bisphenols, are one of the main sources of food pollution. Bisphenol A [2,2-bis (4-hydroxyphenyl) propane, BPA] is a prototype of bisphenols used in the production of polycarbonate and epoxy resins, flame retardants, and other products. These products are widely used in the manufacture of many foodstuff containers, such as storage containers, baby bottles, lining, or coating for glass jars or food cans [1,2]. However, heat (sterilization or microwave heating) and direct contact with acid or essential compounds speed up decomposing of polycarbonate and resins and migration of bisphenol-type compounds [3,4]. Previous reports have demonstrated that BPA associated with a series of adverse effects on infant [5] and adults, such as diabetes [6], fertility problems [7], cardiovascular disease [8], obesity [9] and other endocrine-related diseases [10]. Therefore, the European Union (EU) has modified the regulation of

Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) and set BPA in the "Candidate List of substances of very high concern for Authorisation". Moreover, the United States Food and Drug Administration (USFDA) favors scrutinizing the safety of food packaging, the source of BPA [11]. The European Food Safety Authority (EFSA) [12], in agreement with the United States Environmental Protection Agency (USEPA) [13], set the tolerable daily intake (TDI) of BPA at 0.05 mg kg-body-weight^{-1} day^{-1}. The BPA permitted migration amount was set at 0.6 mg kg^{-1} by the EU commission (Commission Regulation EU 10/2011). As the increasing concerns of the safety of BPA, people began to consider other bisphenol alternatives. Bisphenol S [4, 4'-sulfonyldiphenol, BPS] and bisphenol B [2, 2-bis(4-hydroxyphenyl)butane, BPB], which are structurally similar to BPA and commonly used in the production of resins, are used as substitutes to BPA in the industrial production. However, several articles have reported that BPB and BPS show similar adverse effects to BPA [14,15].

* Corresponding author at: School of Pharmacy, Shenyang Pharmaceutical University, 103 Wenhua Road Shenhe District, 110016 Shenyang, Liaoning Province, PR China.
E-mail address: longshanzhao@163.com (L. Zhao).

Due to the safety concerning of bisphenols, an effective, fast and simple analytical method is necessary and urgently required [16,17]. The traditional extraction techniques for the determination of bisphenols from food and water samples include liquid–liquid extraction (LLE) [18–20] and solid-phase extraction (SPE) [21,22]. However, these methods have many disadvantages, such as lengthy extraction process and large consumption of toxic organic solvents. Recent trends in sample extraction include miniaturization of traditional techniques, getting normally simpler, faster, more green and efficient techniques [23], such as dispersive liquid–liquid microextraction (DLLME) [24].

DLLME consists of a three-component solvent system: sample solution, extraction solvent and dispersant solvent. In DLLME, most of the extraction solvents such as carbon tetrachloride, chloroform, chlorobenzene are toxic. In order to reduce the toxicity in the DLLME procedure, deep eutectic solvents (DESs) which have similar physicochemical characteristics to ionic liquids (ILs), including low melting point, low volatility, low flammability, chemical stability and high dissolution ability, can be a good substitute for toxic organic solvents. Besides, DESs are more inexpensive and biodegradable than ILs, and have become a superior environment-friendly replacement [25,26]. DESs are commonly formed of hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD) [27]. DESs can be synthesized easily without the requirement of complex conditions and expensive instruments, and they are made from inexpensive compounds with low toxicity. These merits make the application of DESs expended. Recently, reports on the application of DESs in DLLME have also expanded, such as determination of caffeine in beverages [28], analysis of two auxins in water and fruit juice samples using the hydrophobic DES [29], determination of sulfonamides from fruit juices by using a hydrophobic DES [30]. After extraction, the mixture solution must be centrifuged in order to separate the extraction solvent and sample solution. However, the microliter amount of extraction solvent make the collection procedure of DLLME difficult. To overcome the drawback of the collection procedure, a new approach which was introduced by Leong and Huang namely solidification of floating organic drop (SFO) was proposed [31]. In DLLME-SFO, the organic phase could solidify in ice bath or refrigerator for accessible collection because the extraction solvent with low-density and appropriate freezing point floats above the aqueous phase and solidifies in low temperature. After melting, the organic phase is conducted to analytical determination. Therefore, we introduce DESs as extraction solvent in the DLLME-SFO procedure. The uses of DESs in DLLME-SFO are receiving considerable attention, such as the extraction of benzoylureas [32], the determination of non-steroidal anti-inflammatory drugs in bovine milk [33]. Recently, El-Deen et al. [34] have introduced DES as a dispersive solvent in the DLLME-SFO procedure for extraction of steroids.

In this study, the objective was to develop a time-saving, less-toxic, sensitive and accurate method for extraction and determination of three bisphenols (BPA, BPS, and BPB) from canned fruit samples. The solidification of DES technology was applied to the determination of bisphenols in canned fruits for the first time. The DES-DLLME-SFO procedure combines merits of both DES and SFO techniques, which was novel, simple, green and easy for simultaneous extraction of three bisphenols. The relative parameters were optimized by one-factor-at-a-time approach to explore the optimal condition of extraction efficiency. Compared with other methods for bisphenols extraction, DES-DLLME-SFO shows better property in terms of operation and environmental protection. The main advantage of this method is that the DES purification procedure reduce the interference of co-extraction components in canned fruit samples. These characteristics emphasize the fact that this method is sensitive, simple, efficient and environmentally friendly. After validation, the established method could be applied for the determination of bisphenols from different canned fruit samples.

2. Experiment

2.1. Chemicals

HPLC-grade methanol and other reagents were purchased from Concord Chemical Co., Ltd. (Tianjin, China). Hydrochloric acid and acetone were supplied by Kaixin Chemical Industry Co., Ltd. (Tianjin, China). MS-grade acetonitrile (ACN) were purchased from Fisher Scientific (Fairlawn, NJ, USA). 1-decanol, decanoic acid, and undecanol were obtained from Aiwang Chemical Technology Co., Ltd. (Shanghai, China). Tetrabutylammonium bromide (TBABr) was bought from Damao Chemical Reagent Factory (Tianjin, China). Menthol was purchased from Bide Pharmaceutical Technology Co., Ltd. (Shanghai, China). BPS (purity > 98%), BPA (purity > 98%) and BPB (purity > 98%) were obtained from Dester Biological Technology Co., Ltd. (Chengdu, China).

Individual stock solutions of BPS (1 mg mL^{-1}), BPA (1 mg mL^{-1}) and BPB (1 mg mL^{-1}) were prepared in ACN and then stored in 10 mL brown volumetric flask at 4 °C. A series of the working solutions were prepared by stepwise dilution of these stock solutions with ACN.

2.2. Apparatus

The analysis of target bisphenols was performed by an ACQUITY Ultra Performance LC system (Waters, Milford, MA, USA) coupled with electrospray ionization (ESI) interface. The separation and determination of bisphenols were carried out on the ACQUITY^{TM} UPLC^{TM} BEH C18 column (2.1 mm × 100 mm, i.d., 1.7 μm), which was purchased from Waters (Milford, MA, USA). The flow rate was set at 0.2 mL min^{-1}, and the injection volume was 10 μL. The qualitative and quantitative analysis of each BP was operated in multiple reaction monitoring (MRM). The mass spectrometer parameters were: capillary voltage of 3.0 kV. The source temperature was 120 °C. The working conditions for the ESI-MS operated in a negative-ion mode. Nitrogen was used as the desolvation gas at flow rate of 500 L h^{-1} with the temperature at 400 °C. The argon gas was used for collision-induced dissociation.

The gradient elution was performed by water (A) and ACN (B). The gradient profile was as follows: (1) 0–4 min, 70% A, (2) 4–12 min, 70% A-20%A, (3) 12–13 min, 20% A, (4) 13–13.1 min, 20% A-70%A, (5) 13.1–15 min, 70% A. The column temperature was 30 °C and the MS parameters of the bisphenols were shown in Table S1. Typical chromatograms of BPS, BPA and BPB can be seen in Fig. 1

2.3. Sample collection

Different types of canned fruits were randomly obtained from a local supermarket in Shenyang. Sealed samples stored at room temperature before analysis. Before the analysis, each canned fruit sample was thoroughly homogenized by a blender with stainless steel cutters, then the homogenized canned fruits were freeze-dried for 36 h. Next, all the dried samples were homogenized again and preserved at 4 °C before analysis.

2.4. Preparation of hydrophobic DESs

In this experiment, TBABr and menthol were chosen as the HBA with 1-decanol, undecanol, and decanoic acid were composed as the HBD. HBA and HBD were mixed in a 100 mL erlenmeyer flask and the mixtures were stirred constantly with heated at 80 °C for 2 h until transparent clear liquids were obtained. The molar ratios of using HBA and HBD were shown in Table 1. After cooling, the DES was stored in 50 mL centrifuge tube at room temperature.
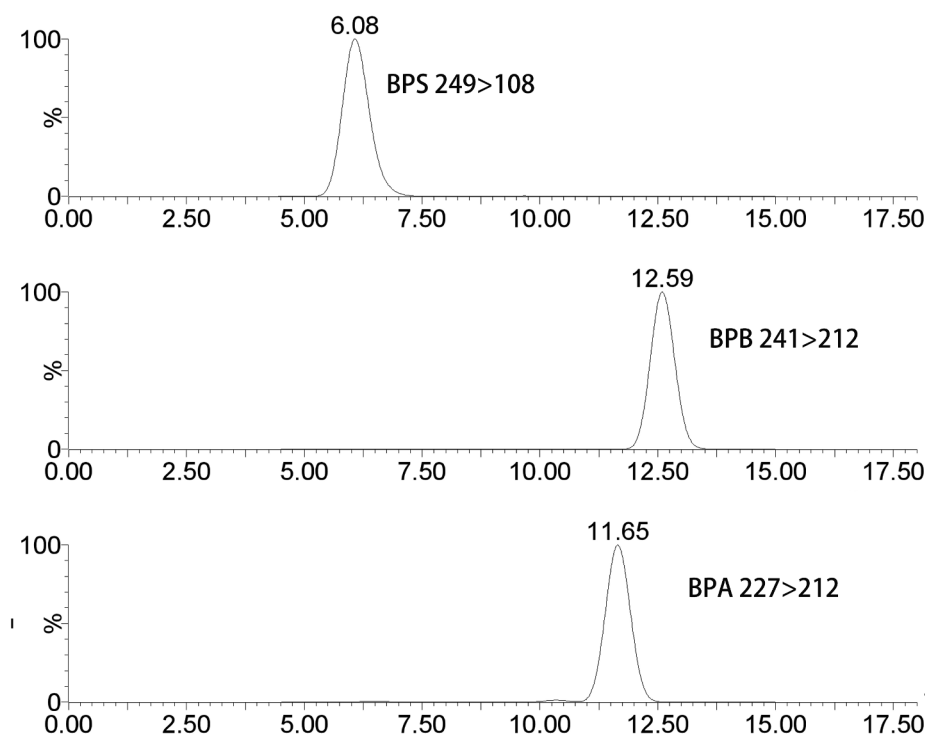
Fig. 1. Chromatogram of three bisphenols analysed by UPLC-MS/MS at 50 ng mL^{-1}.

Table 1
Components of the synthesized DESs.

Abbreviation	HBA	HBD	Mole ratio
DES1	TBABr	1-decanol	1:2
DES2	TBABr	Undecanol	1:2
DES3	Menthol	Undecanol	1:2
DES4	Menthol	Decanoic acid	1:2
DES5	Menthol	1-decanol	1:2
DES6	TBABr	Decanoic acid	1:2

2.5. DLLME-SFO procedure

0.5 g sample powder and 10 mL ACN were added in a centrifuge tube. The resulting solution was placed into an ultrasonic bath for 50 min. Then, the mixed solution was centrifuged at 4200 rpm for 10 min. 5 mL supernatant was transferred into a 10 mL centrifuge tube and evaporated with a gentle stream of nitrogen at 40 °C. The evaporated sample was added 1.0 g NaCl and diluted to 10 mL with ultrapure water. The mixture was adjusted to pH 4 with 1 mol L^{-1} HCl. 400 μL of ACN (dispersion solvent) and 300 μL DES (extraction solvent) were spiked, and then the mixed solution was vigorously shaken for 2 min to accelerate the dispersion of the DES droplets into the solution. In the next step, the mixture was centrifuged at 5000 rpm for 5 min. Consequently, the extraction solvent separated from the aqueous solution. The tubes were transferred into a refrigerator at −20 °C or an ice bath for the organic upper layer solidified. Then, the aqueous phase was rapidly removed by a syringe while solidified organic drop was collected and melted at room temperature. Once melted, the organic phase was diluted to 2 mL with ACN. Finally, the diluted sample solution was filtered through a 0.45 μm organic membrane filter and then subjected to UPLC-MS/MS analysis.

2.6. Calculation

2.6.1. Matrix effect

The study of matrix effect (ME) is very important, because complex matrix components can affect the ionization of target compounds, leading signal enhancement or suppression [35]. In this study, four kinds of canned fruit which added a certain of mixed standard solution were pre-treated. The same concentration of mixed standard solution were also analysis. Meanwhile, four kinds of canned fruit samples were analyzed. Record these response values. The ME was calculated from Eq (1)

$$ME\,(\%) = \left(\frac{A_{post-extraction-spike} - A_{unspiked}}{A_{standard}} - 1 \right) \times 100\% \tag{1}$$

where $A_{unspiked}$ is the area of each BP in blank canned food, $A_{post-extraction-spiked}$ is the area of each BP in post-extraction spiked samples, and $A_{standard}$ is the area of the standard solution.

3. Result and discussion

To achieve the best efficiency of extraction, the relevant parameters affecting the extraction conditions for DES-DLLME-SFO procedure including dispersion solvent, extraction solvent, the volume of dispersion solvent and extraction solvent, vortex time, NaCl amounts, and solution pH were investigated. In our study, the sample of canned fruit 1 was not detected with any analytes, which was set as the blank sample.

3.1. Performance of DES as extraction solvent

3.1.1. Selection of DES

Six hydrophobic DESs were investigated for the extraction of bisphenols from canned fruit samples. The selection of DES in DLLME-
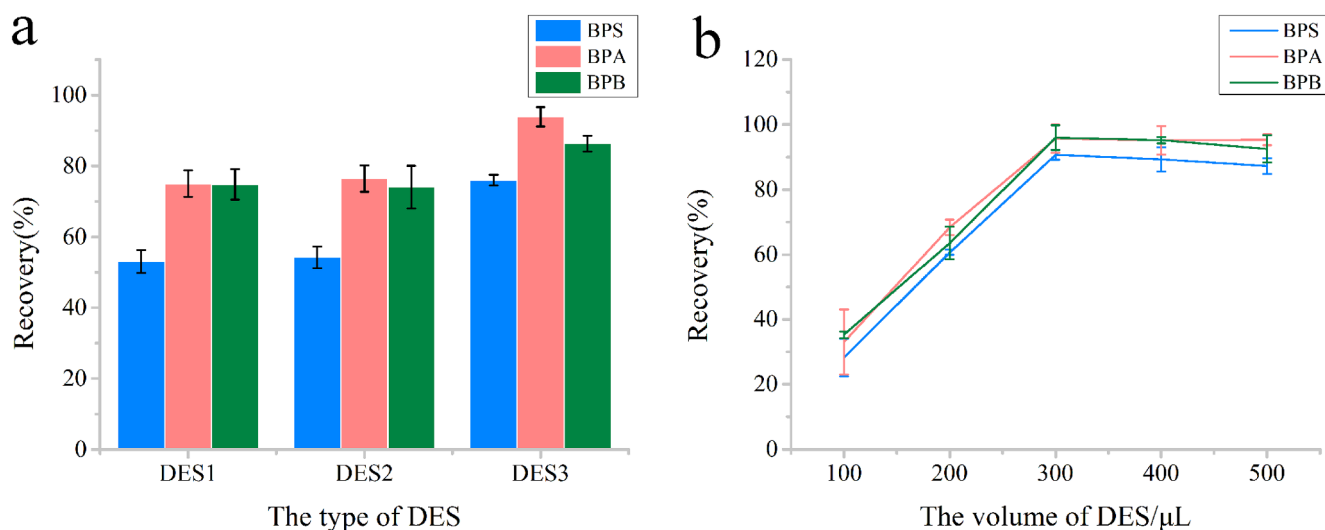
Fig. 2. Effect of different extraction solvent (a) (Conditions: DES volume = 400 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = acetonitrile; volume of dispersion solvent = 400 μL); Effect of different volume of DES (b) (Conditions: type of DES = DES3; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = acetonitrile; volume of dispersion solvent = 400 μL).

SFO depends on its electrostatic interactions with target analytes. The structure of DES greatly influences extraction efficiency. Moreover, the extraction solvent peaks should be well separated from those of the analytes in the case of chromatography. Accordingly, six DESs with the same mole ratio (1:2) were prepared and tested as extraction solvents (Table 1). Among them, DES4 and DES6 were quickly discarded because the occurrence of co-extraction interference peaks took place when they were used. DES5 was also discarded because its low freezing point resulted in a slow speed to solidify the extraction solvents. Finally, DES1, DES2, and DES3 were selected to compared their extraction efficiency. The results (Fig. 2a) indicated that the recoveries using DES3 as the extraction solvent were better than those of other DESs. Hence, DES3 was used as the extraction solvent for further studies.

3.1.2. Characterization of DES

The formation of hydrogen bonding is the leading force for the formation of DES. In this study, the characterization of DES was confirmed by FT-IR in Fig. S1. The stretching vibration peaks of menthol mainly showed at 3263; 2959, 2929; 1368 cm^{-1}, which were due to hydroxyl, methyl and isopropyl groups, respectively [26]. In FT-IR of undecanol, the peaks located at 3335, 2926, and 1058 cm^{-1} ascribed to the stretching vibrations of the O–H, C–H, and C-O groups, respectively. These characteristic absorption of menthol and undecanol were presented in the DES3 spectrum. In DES3 spectrum, the stretching vibration of 1370 cm^{-1} was ascribed to the vibration of isopropyl groups in menthol. As shown in Fig. S1, the peak near 1026 cm^{-1} of DES3 can be ascribed to –CH- vibration in menthol. The O–H vibration of menthol was observed at 3263 cm^{-1}, which shifted to 3346 cm^{-1} in DES3. These characteristic peaks should due to the formation of intermolecular hydrogen bond between menthol and undecanol, which indicated the successful synthesis of DES3.

3.1.3. Mechanism of extraction by DES3

These high extraction efficiencies to extract bisphenols from sample solutions are related to the DES hydrophobicity. BPA possesses a very low water solubility (0.12 g L^{-1} at 25 °C). The water solubility of BPB and BPS are 1.0 g L^{-1} and 1.1 g L^{-1} (at 20 °C), respectively. In addition, compare with TBABr (600 g L^{-1} at 20 °C), menthol has a lower water solubility (0.46 g L^{-1}) [27]. Based on the above considerations, bisphenols were easily interacted with the hydrophobic DES3 because of their low solubility. Both menthol (44 °C) and undecanol (19 °C) have a melting point near to room temperature to employ in DLLME-SFO.

Another possible reason for DES3 has a higher extraction efficiency is that excess branches of alcohol-based HBD (1-decanol and undecanol) results in steric hindrance between the bisphenols and bromide anion (TBABr) [36].

3.2. Optimization of the extraction procedure

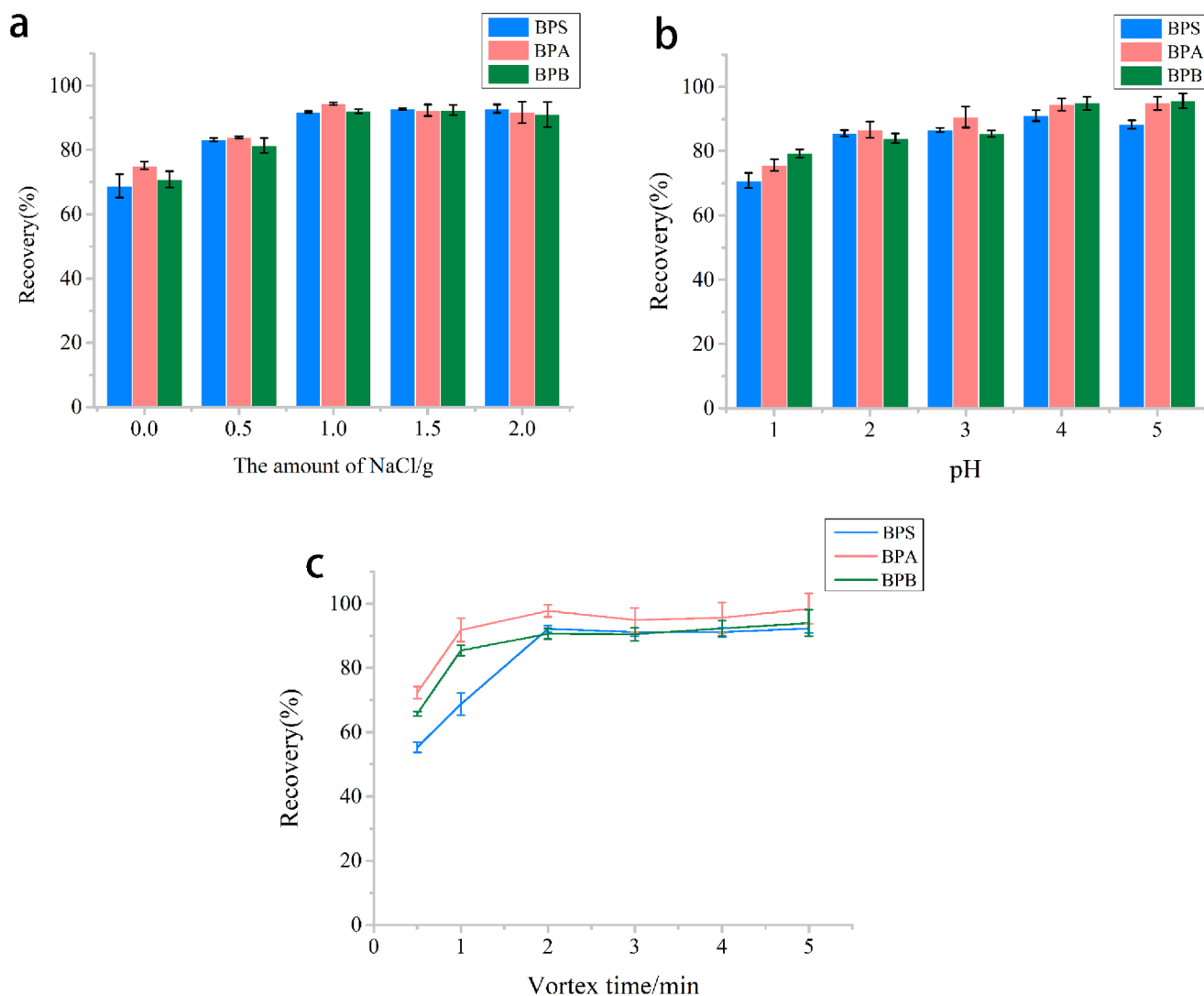#### 3.2.1. Effect of the volume of DES

The volume of the extraction solvent was an important parameter in DLLME-SFO procedure. Sufficient volume of extraction solvent ensures complete extraction of analytes with good recovery. In this experiment, the influence of DES3 volume on the recovery was investigated from 100 μL to 500 μL. The results were shown in Fig. 2b. The extraction recoveries of bisphenols increased when the volume of DES3 increased from 100 μL to 300 μL, and the maximum was obtained at 300 μL. When the volume of DES3 increased from 300 μL to 500 μL, there was no significant change in bisphenols recoveries. Therefore, 300 μL of DES3 was used in the following tests.

3.2.2. Effect of NaCl addition

When ionic concentration increases in the aqueous phase, the solubility of the target compounds usually decreases. To investigate the influence of NaCl addition on the recovery of bisphenols, a series of experiments had investigated the influence of different amounts of NaCl in the range of 0–2.0 g. As shown in Fig. 3a, the efficiency of bisphenols for extraction increased when the NaCl addition was increased in the range of 0–1.0 g. The amount of salt can affect the analytes' diffusion between the sample solution and the extraction solvent decreasing the solubility of the analytes in the sample solution and, therefore, increasing extraction efficiency. The recoveries of bisphenols decreased slightly as the salt addition increased from 1.0 to 2.0 g. Too much addition of salt led to the viscosity of the solution increase and induced the partitioning and diffusion rate of the analytes to decrease. Therefore, 1.0 g NaCl was selected for all subsequent experiments.

3.2.3. Effect of vortex time

Vortex agitation has an essential role in transferring of the bisphenols from the aqueous phase to the DES phase by increasing the large surface area between bisphenols and extraction solvent. Increased vortex time promoted the diffusion of the bisphenols between DES3 and sample solution and improved the extraction efficiency. The effects of the vortex time were investigated in the range of 0.5–5.0 min with

Fig. 3. Effect of different amounts of NaCl (a) (Conditions: type of DES = DES3; DES volume = 300 μL; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = acetonitrile; volume of dispersion solvent = 400 μL); Effect of different pH (b) (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; vortex time = 2 min; dispersion solvent = acetonitrile; volume of dispersion solvent = 400 μL); Effect of different vortex time (c) (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; dispersion solvent = acetonitrile; volume of dispersion solvent = 400 μL).

other experimental conditions keeping constant. As shown in Fig. 3b, the recoveries of three bisphenols increased with the vortex time prolonged before 2 min, possibly because the DES had not completely dispersed in the solution within 2 min. After 2 min, the recoveries showed no significant improvement when the vortex time was prolonged to 5 min. Therefore, the best vortex time was 2 min.

### 3.2.4. Effect of sample solution pH

Another important parameter for bisphenols extraction is the pH of the extraction solvent since it determines the degree of ionization and speciation of the analytes, which cause the different distribution coefficient [26]. The highest extraction efficiency in DLLME-SFO is expected for analytes in their un-ionized form [37]. Under alkaline conditions, crystallization of DES3 has occurred, a series of experiments had investigated the effect of sample solution pH values in the range 1–5. π–π interaction, hydrogen bonding and hydrophobic interaction are usually important forces in the extraction by DESs as solvents. The pKa values of three target analytes (BPA, BPB and BPS) were in the range of 7–10 [38,39] (Table S2) for which these target analytes exist in neutral form in neutral and acidic solutions. Accordingly, three bisphenols could be extracted by DES3 via π–π interaction, hydrogen

bonding and hydrophobic interaction. As shown in Fig. 3c, it was found that the recoveries of bisphenols slightly increased in the range of pH 1–4 but had no significant improvement in the range of pH 4–5, which indicated that the ionization of the analytes in pH 4 was crucial to the extraction procedure. The best extraction recoveries were achieved at pH 4. Therefore, pH 4 was chosen as the optimum pH for further experiments.

3.2.5. Effect of dispersion solvent type and volume

The dispersion solvent should dissolve in both the DES and sample solution. Because dispersion solvent assists the formation of the fine droplets of extraction solvent in the aqueous phase, accordingly improving the extraction of analytes. Thereby, several dispersion solvents were selected as candidates, including ACN, methanol and acetone. According to the results in Fig. 4a, ACN achieved the best extraction efficiency for most analytes. Recoveries achieved with methanol and acetone were slightly lower than those obtained with ACN. Therefore, ACN was selected as the dispersion solvent.

The volume of dispersion solvent should be studied because the variation of the volume of ACN causes the formation and volume of floated phase consequently affecting extraction [40]. To minimize the
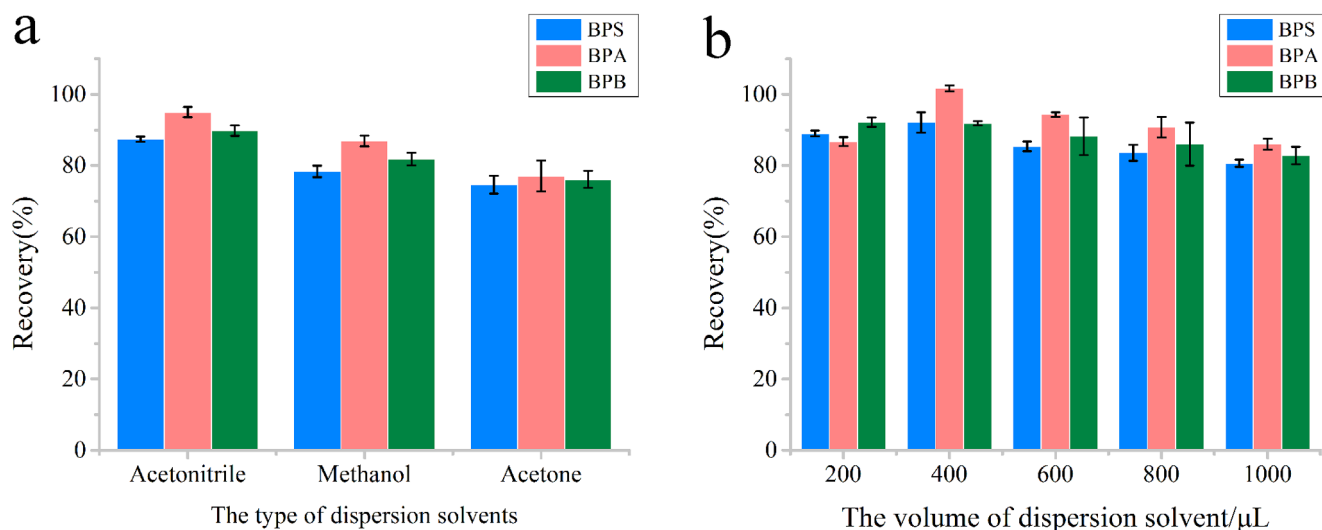
Fig. 4. Optimization of dispersion solvent (a) (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; volume of dispersion solvent = 400 μL); Optimization of volume of dispersion solvent (b) (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = acetonitrile).

use of organic solvents, the volume of dispersion solvent was evaluated in the range of 200–1000 μL. As the results were shown in Fig. 4b, when the volume of ACN was increased to 400 μL, the extraction efficiency of three analytes increased. Then, with the volume of ACN increased from 400 μL to 1000 μL, the recoveries of three bisphenols decreased slightly. This effect was explained that a large amount of ACN increased the solubility of bisphenols in the aqueous phase. Therefore, 400 μL of ACN was chosen as the optimum dispersion solvent volume.

3.3. Method validation

To investigate the performance of this method regarding the determination of bisphenols in canned fruit samples, the method was validated in terms of linearity, limit of detection (LOD), limit of quantification (LOQ), precision and enrichment factors (EFs). The matrix-matched calibration curves of three bisphenols were obtained under optimized conditions by spiking the standards to the sample solutions at different concentration levels (10–200 ng g^{-1}). As shown in Table 2, satisfactory linearity fell in the range of 10–200 ng g^{-1} for three bisphenols, with correlation coefficients (r) ranged from 0.9919 to 0.9961. LOD was calculated based on the concentration corresponding to signal-to-noise (S/N) of 3, and LOQ was calculated by S/N of 10. The value of LOD and LOQ was in the range of 1.5–3 ng g^{-1} and 5–10 ng g^{-1}.

Intra-day and inter-day precision were carried out at concentration of 50 ng g^{-1} for each analyte by three replicate experiment on the same day and on three different days, respectively. The relative standard deviations (RSDs) were in the range of 1.3–4.6% for intra-day precision and of 2.3–4.4% for inter-day precision. As shown in Table 2, the results

illustrated that the optimized method could properly quantify BPS, BPA and BPB in the canned fruit.

3.4. Matrix effect

Matrix effects are commonly related to methods and recognized as an enhancement or suppression of the response of target analytes [41]. Because the presence of co-elution undesirable components in samples alter the ionization efficiency [39]. Therefore, the matrix effect was investigated by comparing the response of the spiked sample solution and the standard solution. Calculated by Eq. (1), ME% value of canned fruit was 85.3–87.7% (Table 2). The results illustrated that the signal suppression for three compounds was low. Therefore, in this study, matrix-matched calibration curves were used to ensure the accuracy of this method.

3.5. Analysis of real samples recovery studies

To investigate the practicability of the developed DES-DLLME-SFO method, four kinds of canned fruit samples were subjected to DES-DLLME-SFO followed by UPLC-MS/MS detection, and the results were shown in Table 3 (n = 3). The results showed that BPS concentration was lower than the LOD in four kinds of canned fruit samples (Fig. S2). BPA and BPB were detected in canned fruit 2 and canned fruit 4, respectively, but the concentration levels lower than the LOQ of the method. These results are similar to the reports of Cunha et al. (BPA < 10.2 ng g^{-1}; BPB < 3.4 ng g^{-1}) [24]. The recovery was calculated with the following formula: recovery (%) = (detected amount-original amount)/spiked amount × 100. Four kinds of canned

Table 2
Analytical characteristics of three target analytes by the proposed method (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = ACN; volume of dispersion solvent = 400 μL).

Analyte	Linear range (ng g^{-1})	r^2	LOD (ng g^{-1})	LOQ (ng g^{-1})	RSD (%)		EF	ME ± RSD (%) (n = 3)			
					Intra-day	Inter-day		Can-1	Can-2	Can-3	Can-4
BPS	10–200	0.9961	1.5	5	1.3	2.4	4.6	86.2 ± 1.14	86.6 ± 1.37	86.3 ± 4.13	87.7 ± 1.84
BPA	10–200	0.9942	3	10	1.5	3.2	4.4	86.7 ± 3.79	85.3 ± 1.46	86.0 ± 4.33	86.0 ± 2.50
BPB	10–200	0.9919	3	10	4.6	4.4	4.9	87.1 ± 3.10	87.7 ± 3.08	87.1 ± 3.10	86.5 ± 2.04

Table 3

Analytical results for bisphenols in canned fruit samples via propsed procedure (Conditions: type of DES = DES3; DES volume = 300 μL; amount of NaCl = 1.0 g; pH of the solution = 4.0; vortex time = 2 min; dispersion solvent = ACN; volume of dispersion solvent = 400 μL).

Analyte	Content (ng g^{-1})				Spiked (ng·g^{-1})	Recovery ± RSD (%) (n = 3)			
	Can-1	Can-2	Can-3	Can-4		Can-1	Can-2	Can-3	Can-4
BPS	–	–	–	–	20	86.1 ± 1.03	84.0 ± 4.34	81.8 ± 1.79	90.6 ± 4.09
					50	86.0 ± 2.90	89.2 ± 4.32	84.9 ± 4.76	88.6 ± 4.45
					150	88.7 ± 2.79	91.9 ± 4.29	91.1 ± 1.58	90.4 ± 3.23
BPA	–	< LOQ	–	–	20	83.9 ± 3.85	90.3 ± 3.57	86.0 ± 2.17	88.2 ± 4.22
					50	85.3 ± 3.05	91.3 ± 3.98	85.3 ± 3.05	101 ± 4.56
					150	88.7 ± 4.81	89.3 ± 3.57	86.0 ± 4.33	94.6 ± 3.55
BPB	–	–	–	< LOQ	20	86.5 ± 4.68	83.8 ± 3.65	98.9 ± 3.09	79.5 ± 3.33
					50	90.7 ± 4.55	86.5 ± 3.65	83.0 ± 4.66	80.1 ± 4.11
					150	98.5 ± 4.72	95.8 ± 2.11	99.8 ± 4.66	99.5 ± 4.41

-: Not detected.

Table 4

Comparison of the analytical features of the reported methods with this developed method for analysis of bisphenols.

Method	Analyte (BPs)	Matrix	Extraction Time	Recovery (%)	LOD	Ref
SBSE	BF,BPA,BPF,BPZ	Canned beverages and canned vegetables	3 h	86.0–122	2.5 ng L^{-1}	[42]
SPE	BPA	Milk	–	83.0–106	1.7 ng g^{-1}	[22]
QuEChERS-IL-DLLME	BPA	Canned foods	27 min	90.0–102	0.1 μg L^{-1}	[43]
LLE	BPA, BPF	Canned food and beverages	> 65 min	60.0–90.0%	1.0–4.0 ng g^{-1}	[44]
LLE + d-SPE	7 kinds of Bisphenols	Baby food products	> 47 min	91.0%-110%	0.1–1.0 ng g^{-1}	[2]
DES-DLLME-SFOD	BPS, BPA, BPB	Canned fruit	102 min	79.5–101%	1.5–3 ng g^{-1}	this work

fruit samples were spiked with three concentration levels (16, 40 and 120 ng g^{-1}) of bisphenols mixed standard solution (Table 3). Afterwards, the DLLME-SFO procedure of three concentration was carried out in triplicate, and then each sample was analyzed by UPLC-MS/MS. The average recoveries were in the range of 79.49–100.7% with RSD of the peak areas of each concentration replicated experiments in the range of 2.5–4.9%. The results indicated that the content of bisphenols in these canned fruit samples was not to concern, the LOQ value was far less than the limitation of EU (600 ng g^{-1}). Meanwhile, the results of Table 3 revealed the developed method was reliable in real canned fruit samples, so that matrix constituents of the samples including hydrophobic substances had no significant effects on the extraction of BPS, BPA, and BPB.

3.6. Comparison with other methods

The characteristics of the developed method based on DES-DLLME-SFO were compared with other extraction methods for the analysis of bisphenols in different samples. The co-extracted components in the sample may interfere with the ionization ability of the analyte, resulting in an increase or decrease in the response of the analyte, thereby affecting the accuracy of the measurement result. Compared with ACN extraction procedure, the DES-DLLME-SFO procedure was more sensitive and selective (Fig. S3). In our study, the purpose of DES-DLLME-SFO procedure is to further purify the canned fruit samples, thereby reducing the interference of co-extraction components in the samples. Moreover, compared with other extraction methods, the extraction time, recovery, and LOD were listed in Table 4. SPE [22] procedure was a detailed extraction process, which was time-consuming and multistep. We can see that in the DLLME-SFO process of this study, 300 μL DES3 were used. The method of LLE combined with d-SPE procedure [2] consumed lots of organic extraction solvent, and also required to dryness the extraction solvents after d-SPE. In comparison with other methods, this study was green and environmentally friendly. Meanwhile, this method has relatively good recoveries, which illustrates the suitability of this method to the analysis of real canned fruit samples. Therefore, this developed method showed the merits of low organic solvent consumption and simple operation. This study could become an alternative choice for the extraction of bisphenols in the complex food matrix.

4. Conclusion

A simple, green and efficient method based on DES-DLLME-SFO procedure coupled with UPLC-MS/MS was developed to determine BPS, BPA, and BPB in canned fruit. In this study, menthol and undecanol with a ratio of 1:2 were formed a low-toxic DES extraction solvent instead of traditional high-toxic solvents in DLLME. The process of DLLME-SFO provided a method to purify and extract bisphenols in canned food without complicated procedures. The developed method showed short extraction time, reliable recovery, simplicity in operation, and high extraction efficiency. Therefore, this method was an attractive candidate method for the determination of trace levels bisphenols in food matrices.

CRediT authorship contribution statement

Xiaomei Liu: Writing - original draft, Visualization, Investigation. **Yuwei Bian:** Conceptualization, Methodology, Validation, Data curation. **Jing Zhao:** Project administration, Methodology, Software. **Yu Wang:** Validation, Visualization. **Longshan Zhao:** Supervision, Conceptualization, Writing - review & editing.

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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.microc.2020.105438.

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