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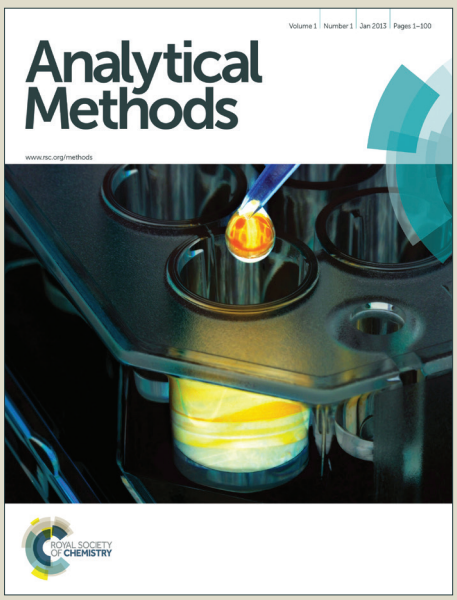

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ARTICLE

Centrifugal microextraction tube - cloud point extraction coupled with gas chromatography for simultaneous determination of six phthalate esters in mineral water

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A homemade centrifugal microextraction tube (CMET) was developed and applied to cloud point extraction coupled with microwave assisted back extraction and gas chromatographic separation of six phthalate esters (PAEs) from mineral water. All phthalate esters were entrapped in the micelles of the non-ionic surfactant Triton X-114 and removed from the bulk phase by centrifugation. The obtained surfactant-rich phase was treated with water-immiscible solvents, and the target analytes were back extracted by short-term microwave application and determined by GC-FID directly. The whole process was finished in the CMET. The proposed method demonstrated good performance concerning linearity (R^2 = 0.9977-0.9998), precision (2.3-5.7%), the limit of detection and quantitation (LOD, 11.5-19.3 μg L^{-1}; LOQ, 37.0-63.3 μg L^{-1}), spiked recoveries (89.1%-96.3%) and enrichment factor (71-85). The proposed method was successfully applied to the determination of trace amount of phthalate esters in mineral water. DBP and BBP were found in actual mineral water samples.

Introduction

As plasticizer, Phthalate esters (PAEs) are widely used in plastics packaging materials because they improve the softness and flexibility of plastics. These plasticizers are low molecule organic compound and non-covalent bonding in plastic, so they can migrate from the plastic into the food. Certain phthalates together with their metabolites and degradation products have been found in the liver, kidney and testicles of humans and these compounds have adverse effects on human health.[1-4] Therefore, the problem of plasticizer in food products has been paid close attention by the governments and the consumers. The specific migration limits (SML) of dibutyl phthalate (DBP, 0.3 mg kg^{-1}), benzyl butyl ester (BBP, 30 mg kg^{-1}), di(2-ethylhexyl)phthalate (DEHP, 1.5 mg kg^{-1}), Diisodecylphthalate (DIDP, 9.0 mg kg^{-1}) and Diisononyl phthalate (DINP, 9.0 mg kg^{-1}) mg kg^{-1} in food were specified by the EU and Chinese Ministry of Health.[5,6]

The most widely used methods for analyzing phthalate esters are chromatographic techniques such as HPLC,[3,7] GC,[8] HPLC/MS[1] and GC/MS,[9] but the sensitivity and selectivity of the direct determination was restricted at a very low levels of concentration in food and environmental samples with complex matrix. Consequently, a sample pretreatment prior to chromatographic analysis, such as liquid-liquid extraction[10,11] and solid-phase extraction (SPE),[4,7,12] is usually necessary. Unfortunately, all of these methods are time-consuming and require large amounts of organic solvents, and the materials of SPE are expensive and not reusable. As a result, the green liquid-liquid extraction method - cloud point extraction (CPE) has been developed for preconcentration of organic compounds, metal ions and biomolecules in the last decades.[13-15] Cloud point phase separation is the procedure during which aqueous solutions of several surfactants undergo phase separation under specific conditions such as temperature and addition of salts or acids. The result is the formation of two distinct phases: a surfactant-rich phase and an aqueous phase with concentration of surfactant close to the critical micellar concentration (CMC). Compared with the traditional organic liquid-liquid extraction, CPE has some advantages, such as simple procedure, inexpensive, highly efficient, environmentally lower toxicity and a very small amount of relatively nonflammable and nonvolatile surfactants.[13-16]

CPE has been exploited in the past few years for the extraction and preconcentration of organic compounds prior to HPLC,[16] GC,[17] flow injection analysis,[18] capillary electrophoresis,[19] GC/MS[20] and HPLC/MS.[21] But the existence of surfactant also caused the background interference in the ultraviolet region for HPLC, FIA, and CE when UV detection is employed. Due to the complicated preconcentration, time-consuming steps and high-cost instruments in the analysis

process of HPLC/MS and GC/MS, these problems restricted the wide application of these methods. Capillary GC column was easily blocked by surfactant. To solve this problem, injection of the surfactant phase into the gas chromatograph is made possible after extensive cleanup with two columns (silica and Florisil) in order that the surfactant could be completely removed.[15] Recently, some studies reported a simple and fast method that those analytes were back-extracted from the surfactant-rich phase into a water-immiscible solvent, by applying microwaves or ultrasonic, and directly analyzed with GC-FID without the need for any supplemental cleanup.[15,22]

In this work, we attempted to apply the cloud point extraction coupled with microwave assisted back extraction for the determination of phthalate esters in mineral water. However, in the process of detection, the residual aqueous solution in the surfactant phase and surfactant mixed into the isooctane would cause interference, which affected the accuracy of detection. In order to solve these problems, a homemade, simple, low cost and efficient centrifugal microextraction tube (CMET) was used for cloud point extraction and back-extraction process, which improved enrichment factor and clean-up effect of PAEs from mineral water.

Experimental

Materials and chemicals

All chemicals were of analytical grade. Six phthalates, dimethyl phthalate (DMP), diethyl phthalate (DEP), phthalic acid benzyl butyl ester (BBP), diallyl phthalate (DAP), dibutyl phthalate (DBP) dioctyl phthalate (DOP) tetradecane (internal standard) and Triton X-114, were purchased from Aladdin reagent Co., Ltd. (Shanghai, China). HPLC-grade Hexane, isooctane, chloroform and dichloromethane were obtained from Tianjin Kemiou Chemical Reagent Co., Ltd (Tianjin, China). All the other chemicals were of the analytical grade. Doubly deionized water (DDW) was used throughout.

Standard stock solutions containing phthalate esters compounds were prepared at a concentration of 100 mg L^{-1} in methanol and stored at -18 °C in a refrigerator. Then, the stock solution was further diluted with doubly distilled water to prepare working solutions (35-1000 μg L^{-1}). The methanol content, which usually hampers clouding, was less than 1%.[15]

Gas chromatographic conditions

For qualitative and quantitative analysis of the selected analytes, a gas chromatograph GC-14C (Shimadzu, Japan) with a flame ionization detector (FID) was used, equipped with a 30 m × 0.25 mm fused silica capillary column, coated with 0.50 μm film (KB-5, Kromat Corporation, USA). The carrier gas was nitrogen. The GC conditions were as follows: The temperature of injector was maintained at 260 °C while the detector was set at 300 °C. The column temperature was raised from 120 to 285 °C at a rate of 15°C/min where it remained for 3 min. The determination was carried at a split (1:20) mode.

Cloud Point Extraction from Aqueous Samples

The mineral water samples were obtained from a local supermarket. 9 mL of mineral water samples spiked with different concentrations (100, 200 and 500 μg L^{-1}) were placed in the centrifugal microextraction tube (Fig. 1). A 300-μL of Triton X-114 stock solution, 1 mL of 1 M phosphate buffer pH 7.0, and 0.5 mL of saturated NaCl solution were added, and the centrifugal microextraction tubes were left to stand in a thermostat bath at 50 °C for 40 min. Separation of the surfactant rich phase from the bulk aqueous was achieved by centrifugation at 4000 rpm for 10 min. In order to separate the phases completely the solution was cooled in an ice bath for 5 min to increase the viscosity of the surfactant-rich phase, and the bulk aqueous phase was slowly removed with a pipette. Finally a small volume of the surfactant-rich phase remained at the bottom of the centrifuge tube.

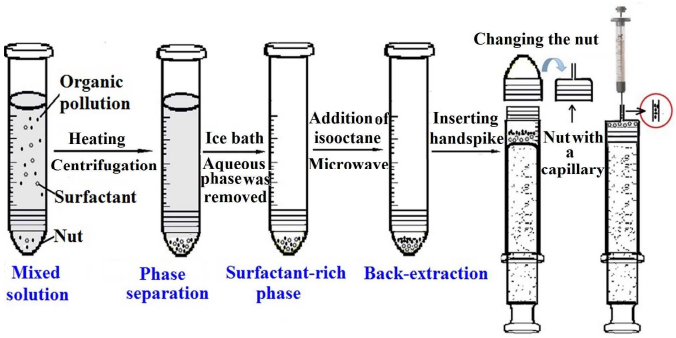

Fig. 1 Steps involved in cloud point extraction (CPE) using a centrifugal microextraction tube (CMET) prior to GC analysis.

A 100 μL aliquot of isooctane containing 0.1 mg L^{-1} of the internal standard (tetradecane) was added to the surfactant-rich phase, and the preconcentrated analytes were extracted with microwave (600 W) assisted extraction for 10 min. After that, a syringe putter was put into the centrifugal microextraction tube, and the nut was replaced by a nut with a capillary. The tube was inverted for five minutes. At last, two distinct layers were formed: the surfactant rich phase containing some water remnants (lower) and the isooctane phase (upper). The analytes were extracted from surfactant rich phase to isooctane phase. A 1 μL sample of this supernatant isooctane phase was sampled from the capillary and injected into the chromatograph.

Results and discussion

The performance of a homemade centrifugal microextraction tube and optimization of GC analytical conditions

A series of different GC programmed temperature was investigated for simultaneous separation of six phthalate esters. As a consequence, six analytes could be completely separated under the optimized conditions, and standard solution chromatograms were shown in Fig. 2a. In order to simultaneous determination of trace PAEs in mineral water, a sample pretreatment method of cloud point extraction with microwave assisted back extraction was applied according to the procedure

as reported by Zygoura et al.,[22] and the result was shown in Fig. 2b. The baseline drifted in the chromatogram was found from Fig 2b, which is attributed to partially ternary mixtures of water, surfactant and organic solvent in the supernatant isooctane phase and the inclined tube sampling mode. In order to avoid this phenomenon and improve the enrichment factor, a homemade centrifugal microextraction tube was developed and used in CPE procedure. There was a capillary at the top of the CMET. The isooctane phase went into the capillary and the miscible ternary mixture was in the lower after placing for 5 min. 1 μL sample of this supernatant isooctane phase was sampled from the capillary and injected into the chromatograph. A trace amount of back-extraction solvent in the CMET is easy to be learned by a gas chromatography syringe, and the enrichment factor and clean-up effect compared with reference reported by Zygoura et al were improved (Fig. 2). The CMET using as a centrifugal microextraction process is simple and convenient and is promising as a general liquid-liquid microextraction.

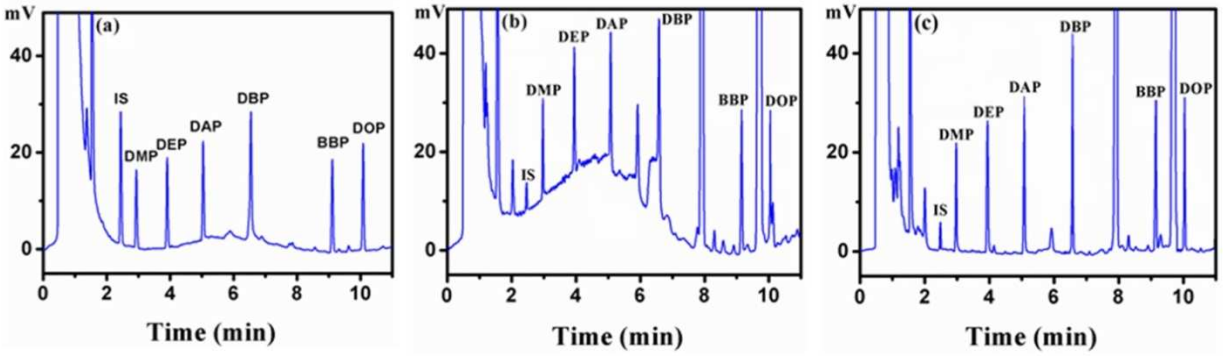

Fig. 2 Chromatograms of (a) the mixture standard solution (six PAEs, 5 mg L^{-1}; tetradecane, 5 mg L^{-1}), (b) the mixture standard solution (six PAEs, 0.1 mg L^{-1}; tetradecane, 0.1 mg L^{-1}) after CPE with centrifugal tube, and (c) the mixture standard solution (six PAEs, 0.1 mg L^{-1}; tetradecane, 0.1 mg L^{-1}) after CPE with centrifugal microextraction tube.

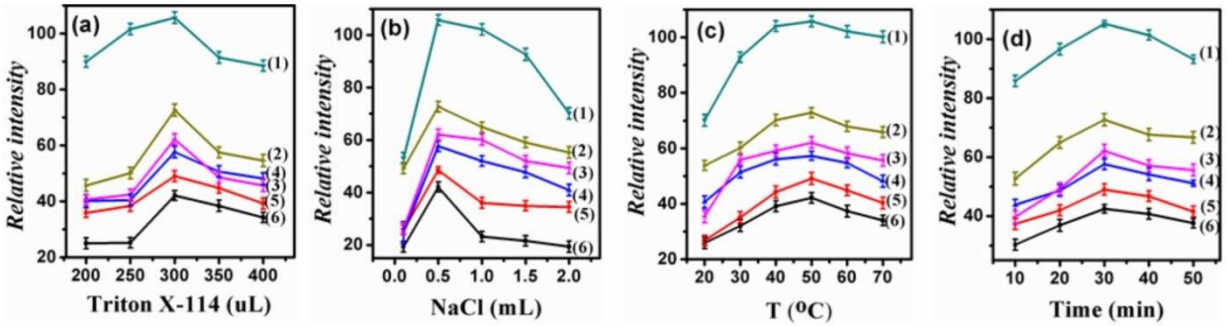

Fig. 3 Effect of the experimental conditions on the cloud point extraction of 0.1 mg L^{-1} (1) DBP, (2) DOP, (3) BBP, (4) DAP, (5) DEP and (6) DMP. The experimental conditions: (a) Triton X-114 concentration, (b) ionic strength, (c) equilibration temperature and (d) equilibration time. Other conditions as described in the text.

It was found from Fig. 2c that there were two major peaks after CPE, these peaks correspond to octylphenol and octylphenyl ether fragments, which were typical of Triton X-114.[15] As can be seen from the chromatogram, the rest of the chromatogram was relatively clear, presenting a smooth baseline, and there was no differentiation in the obtained retention times. So these peaks appear free from any interference by the presence of the surfactant.

Optimization of CPE

In order to optimize the CPE efficiency, the CPE procedure (step 2.3) was applied to 0.1 mg L^{-1} standard solution containing six PAEs. Several parameters influencing the CPE efficiency were investigated, including pH, surfactant concentration, ionic strength, extraction temperature and time, back-extraction solvent, the parameters of microwave and ultrasonication.

Effect of pH on CPE. The extraction efficiency is almost impervious to the prevailing pH conditions for a pH range of 2-11 as was expected due to the nature of the target analytes. To ensure uniform conditions, the pH was adjusted to 7 with a phosphate buffer and 1 mL of this solution was added to standard solution or sample solutions.

Effect of surfactant concentration. The nonionic Triton X-114 and Triton X-100 surfactant are commonly used in the CPE. Triton X-114 was chosen for the CPE, which has a low cloud point temperature compared with Triton X-100 and can facilitate the phase separation by centrifugation because of its high density.

The optimization of the amount of surfactant is an important parameter in the present work because its amount should be

sufficient for the quantitative extraction of the target analytes, but not excessive in order not to interfere with the back-extraction process.[15] As can be seen from Fig. 3a, a volume of 200-400 μL of the 100 g L^{-1} stock solution, corresponding to 20-40 mg of surfactant in 9 mL of sample, produced optimum results when 300 μL of isooctane was used for back-extraction. Larger amounts of surfactant led to an incomplete separation of the surfactant and the isooctane layer (formation of slurry).A surfactant volume of 300 μL (30 mg, 3 g L^{-1}) was finally selected with a view of further optimizing the volume of the organic solvent used for back-extraction.

Effect of ionic strength. The addition of salt to the solution may influence the extraction process. In the case of most non-ionic surfactant, the presence of salts may facilitate phase separation since it increases the density of the aqueous phase. Available electrolytes can also change the cloud-point temperatures of nonionic surfactant. So the salt concentration has a significant influence. In this work, the saturated NaCl was added to the solution in the range of 0.1-2 mL. When the volume is higher than 0.5 mL, the surfactant-rich phase will be on the surface of the solution, which may make it more difficult to separate the extraction system into two phases and the accuracy and reproducibility were probably not satisfactory. As shown in Fig. 3b, the highest extraction efficiency can be obtained at a volume of 0.5 mL.

Effect of extraction temperature and time. When the cloud point extraction procedure was processed at equilibration temperature of the surfactant, the best extraction efficiency was achieved. If the temperature is lower than the cloud point, the phase separation is difficult to be formed. Theoretically, the cloud point temperature of Triton X-114 is 25 ^{o}C. Then, the temperature over the range of 20-70 ^{o}C was investigated. Fig. 3c showed an increase in the signal intensity from 20 ^{o}C to 50 ^{o}C, and then a decrease as the temperature went up. As a consequence, 50 ^{o}C was adopted as the optimum equilibration temperature.

Surfactant can exhibit different behaviors when the equilibration time varies. A time span of 10-50 min was studied. Fig. 3d showed the effects of equilibration time on the extraction efficiency and the maximum signal was presented at 30 min. At last, 30 min was chosen as the optimum equilibration time.

Effect of Back-extraction solvent. The target analytes were extracted from the surfactant-rich phase into organic solvent to avoid blocking the capillary column for the high viscosity of the surfactant. Thus, four water-immiscible and higher soluble solvents (hexane, isooctane, chloroform, dichloromethane) for phthalates were investigated to obtain a high extraction efficiency. After a series of research, hexane and chloroform had poor reproducibility due to the high volatility of them when microwave-assisted back-extraction was applied. For dichloromethane, it was difficult to take samples on account of dichloromethane occupying in the lower of the centrifugal microextraction tube. Finally, isooctane was selected as the extraction solvent.

The volume of isooctane was finally optimized with a view to recover the target analyte from the surfactant rich phase yielding a high preconcentration factor. The isooctane volume over the range of 50-300 μL was investigated. While 50 μL produced slurries due perhaps to the formation of partially miscible ternary mixtures among water, surfactant, and organic solvent. The optimum results were obtained when 100 μL of isooctane was used.

Effect of microwave and ultrasonication parameters on Back-extraction. The influence of microwave or ultrasonic method on the back-extraction was evaluated for the quantitative preconcentrated analytes from the surfactant-rich phase into the organic solvent. For microwave, the surfactant-rich phase along with isooctane (100 μL) was treated in a microwave oven for a period of time. The results showed that the relative intensity reached a plateau in the analytical response when microwave irradiation power and time was 600 W and 10 min, respectively (Fig. 4a and Fig. 4b). In order to achieve the highest possible analytical signal, 600 W and 10 min were applied in our experiments.

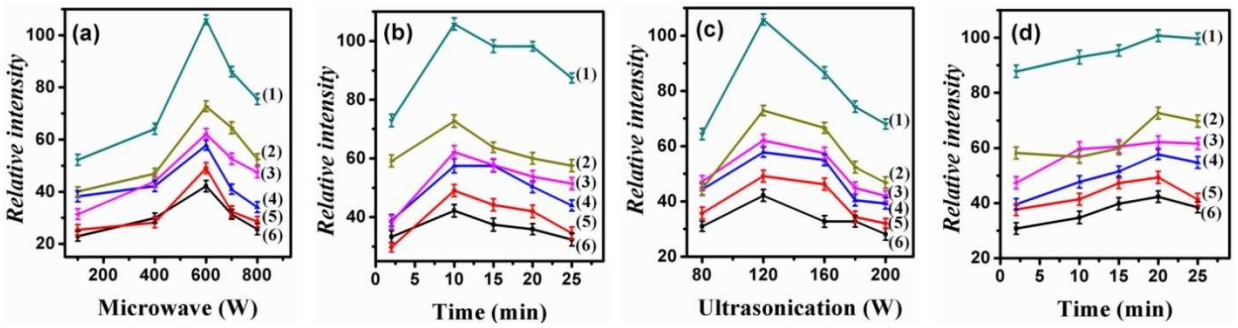

Fig. 4 Effect of the experimental conditions on the extraction efficiency of back-extraction for 0.1 mg L^{-1} of DBP (1), DOP (2), BBP (3), DAP (4), DEP (5) and DMP (6). The experimental conditions: (a) microwave powers, (b) microwave time, (c) ultrasonication powers and (d) ultrasonication time. Other conditions as described in the text.

In the case of ultrasonication, the surfactant-rich phase along with isooctane (100 μL) was treated in an ultrasonic apparatus for a period of time. As can be seen from Fig. 4c and Fig. 4d**,** the relative intensity reached a plateau when 120 W and 25 min were selected. Through the above results, microwave time was shorter than ultrasonic time. On the other hand, the temperature

of the microwave oven can be controlled to avoid the volatilization of isooctane in my experiment. Therefore, a microwave method was used in back-extraction.

Analytical performance of the method

The analytical characteristics data for simultaneous determination of six phthalate esters in mineral water using centrifugal microextraction tube - cloud point extraction coupled with gas chromatography are shown in Table 1. The linearities of the six kinds of phthalate esters were in the range of 35-1000 μg L^{-1}, and the correlation coefficients are greater than 0.9977.

Table 1 The linear regression equations, correlation coefficient (r), linear range and enrichment factors (EF) of six PAEs.

	analyte	linear regression equations	correlation coefficient	linear range (μg L^{-1})	EF[b]
Standard solution	DMP	$E^a = 1.05\times10^{-4}$ C - 0.003	0.9998	35-1000	
	DEP	$E^a = 1.14\times10^{-4}$ C + 0.004	0.9997		
	DAP	$E^a = 1.25\times10^{-4}$ C - 0.003	0.9997		
	DBP	$E^a = 1.20\times10^{-4}$ C + 0.51	0.9978		
	BBP	$E^a = 1.20\times10^{-4}$ C + 0.04	0.9989		
	DOP	$E^a = 1.30\times10^{-4}$ C + 0.14	0.9986		
Enrichment of CPE	DMP	$E^a = 7.46\times10^{-3}$ C - 0.15	0.9988		71
	DEP	$E^a = 8.55\times10^{-3}$ C + 0.18	0.9998		75
	DAP	$E^a = 9.13\times10^{-3}$ C - 0.14	0.9977		73
	DBP	$E^a = 1.02\times10^{-2}$ C + 28.79	0.9978		85
	BBP	$E^a = 9.84\times10^{-3}$ C + 2.38	0.9997		82
	DOP	$E^a = 1.04\times10^{-2}$ C + 6.53	0.9978		80

[a] Relative peak area (analyte/internal standard). [b] Defined the ratio of the sensitivity after CPE to that obtained by direct injection of 1 μL of standard solution.

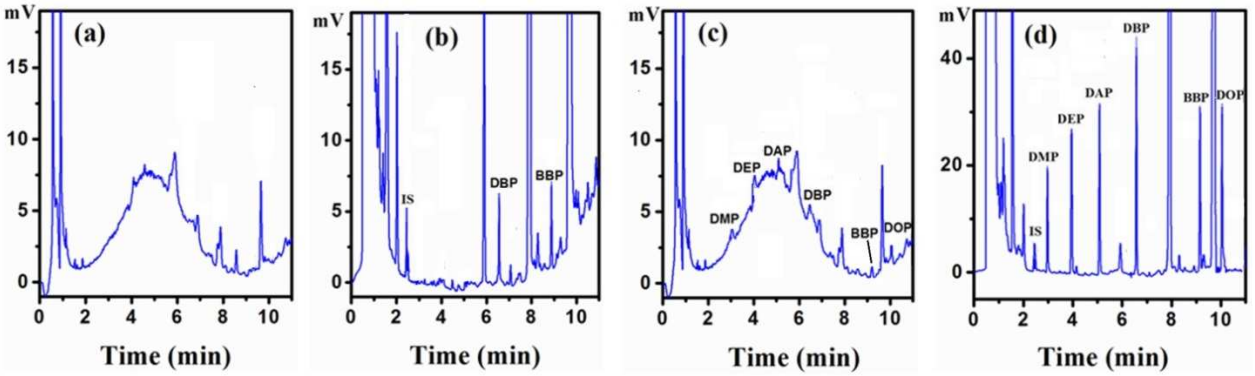

Fig. 5 Chromatograms obtained from the extraction of six PAEs from the mineral water. (a) blank mineral water (non-spiked); (b) mineral water after CPE; (c) spiked mineral water (spiked with 0.1 mg L^{-1}); (d) spiked mineral water (spiked with 0.1 mg L^{-1}) after CPE.

Table 2 Average recoveries (*R*), relative standard deviations (RSDs, *n* = 3), limit of detection (LOD) and limit of quantitation (LOQ) of six PAEs obtained after CPE of the spiked mineral water (*n* = 5).

Analyte	Found (μg L^{-1})	Spiked level (μg L^{-1})	Detected (μg L^{-1})	Recoveries (%)	RSDs (%)	LOD[a] (μg L^{-1})	LOQ[b] (μg L^{-1})
DMP	N	100	96.2	95.2	5.7	19.3	63.3
		200	183.8	92.9	3.7		
		500	449	89.8	4.3		
DEP	N	100	96.0	95.0	4.5	16.8	56
		200	184.6	92.3	4.1		
		500	451	90.2	3.6		
DAP	N	100	95.9	95.9	4.7	13.8	49
		200	186.4	93.2	4.2		
		500	450.5	90.1	2.4		
DBP	14	100	110.3	96.3	3.7	11.5	37
		200	200.2	93.1	3.2		
		500	469.5	91.1	2.3		
BBP	20	100	115.8	96.1	5.1	15.8	52.6
		200	205.2	92.6	4.2		
		500	466.5	89.3	3.5		
DOP	N	100	95.6	95.0	4.5	15.3	50.9
		200	184.6	92.3	3.9		
		500	445.5	89.1	3.2		

[a] LOD calculated as 3 times the signal-to-noise ratio. [b] LOQ calculated as 10 times the signal-to-noise ratio.

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To evaluate the enrichment ability of the CPE, the enrichment factor (EF) is defined by the expression EF = C_s /C_{in} , where C_s is the concentration of analyte in the surfactant-rich phase, after phase separation, and C_{in} is the concentration of the analyte in the initial solution. As a result, the high enrichment factors were obtained by the proposed method, which were 71 for DMP, 75 for DEP, 73 for DAP, 85 for DBP, 82 for BBP and 80 for DOP, respectively.

Analysis of real and spiked samples

To verify the applicability of the proposed method to real samples under the selected conditions, a mineral water sample had been separated and detected by CMET-GC-FID. The results were shown in Table 2. Both DBP and BBP were detected out, which respectively were 14 and 20 μg L^{-1} in the selected mineral water samples. The mean recoveries of DMP, DEP, DAP, DBP, BBP and DOP in mineral water evaluated by three spiking samples with different concentrations (100, 200 and 500 (g L^{-1}) were 89.8-95.2%, 90.2-95.0%, 90.1-95.9%, 91.1-96.3%, 89.3-96.1% and 89.1-95.0%, respectively, with relative standard deviations (RSD) of 2.3-5.7%. The limits of detection (LOD, S/N = 3) and the limits of quantitation (LOQ, S/N = 10) of the proposed method were 19.3 and 63.3 μg L-1 for DMP, 16.8 and 56 μg L^{-1} for DEP, 13.8 and 49.0 μg L^{-1} for DAP, 11.5 and 37.0 μg L^{-1} for DBP, 15.8 and 52.6 μg L^{-1} for BBP, 15.3 and 50.9 μg L^{-1} for DOP, respectively. In addition, there is a good purification effect (Fig. 5). The results were shown that the method is effective for the determination of phthalate esters at a low level. Compared with other reported methods,[10,12] the repeatability and recovery of the method are satisfactory, and the limits of detection could meet the requirement of specific migration limits determination.

Conclusions

The application of a homemade centrifugal microextraction tube to cloud point extraction coupled with microwave assisted back-extraction was proved as an efficient preconcentration step. The proposed method is reliable and the detection of PAEs can be permitted at levels as low as 11.5-19.3 μg L^{-1}. This method of centrifugal microextraction is simple, convenient and efficient, and the centrifugal microextraction tube is promising for liquid-liquid microextraction.

Acknowledgements

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Notes and references

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