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Combination of Solid-Phase Micro-Extraction and Direct Analysis in Real Time-Fourier Transform Ion Cyclotron Resonance Mass Spectrometry for Sensitive and Rapid Analysis of 15 Phthalate Plasticizers in Beverages

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A method for rapid identification and quantification of phthalate plasticizers in beverages was developed. A number of 15 phthalate plasticizers which covered all the phthalates concerned in the US Consumer Product Safety Improvement Act (CPSIA), European Union legislations and Chinese national standards (GB) were analyzed. By a combined solid-phase micro-extraction (SPME) and direct analysis in real time mass spectrometry (DART-MS) approach, phthalates at sub-ng•mL^{-1} levels can be qualitatively and quantitatively analyzed in a short time. The use of ultrahigh-resolving power and the accurate mass measurement capacity naturally provided by Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR-MS) minimizes the matrix interferences and thus enables the evaluation of phthalates in a complex matrix without extensive sample handlings or preparations. The limits of quantification (LOQs) were estimated to be at 0.3—5.0 ng•mL^{-1}, lower than the Maximum Residue Limit (MRL) regulated by the European Union legislations (2007/19/EC) in foods, beverages, food packaging and toys (0.3—30 ng•mL^{-1}). This rapid and easy-to-use SPME-DART-FT-ICR-MS method provided a relatively high-throughput and powerful analytical approach for quick testing and screening phthalates in beverages and water samples to ensure food safety.

Keywords solid-phase micro-extraction, direct analysis in real time, Fourier transform ion cyclotron resonance mass spectrometry, phthalates

Introduction

Phthalates are synthetic organic compounds used as plasticizers in a broad spectrum of industrial and commercial applications.[1] They are widely used as additives in the manufacturing of polyvinyl chloride (PVC) plastics to improve their flexibility and durability. Consequently, they are ubiquitous environmental contaminants due to volatilization and leaching from, for instance, food packaging and medical devices.[2] Plasticizers are suspicious to have mutagenic, carcinogenic and endocrine disrupting properties.[3,4] Because of these potential health impacts on humans, the European Commission proposed a ban on the use of phthalate esters for making baby toys.[5] The phthalate esters are not allowed to be used in food additives in China either, so the detected presence of phthalates in drinks, *e.g.* milky tea in Taiwan in May, 2011, has caused a severe food safety crisis in China. To develop an accurate, fast and reliable method for the determination of phthalates in food and food products is of particular importance for the assurance of food safety.

The most commonly used methods for the determination of phthalates are liquid chromatography mass spectrometry (LC-MS) and gas chromatography mass spectrometry (GC-MS).[6] U.S. Food and Drug Administration (FDA) drafted a testing method for phthalate plasticizers in foods, in this method, 6 phthalates were determined by LC-MS/MS with sample extraction preparation.[7] The method of gel-permeation chromatograph (GPC) separation followed by GC-MS was chosen as the Chinese National Standard (GB) method for

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the determination of phthalates in food.[8] LODs of this method were 1.5 mg•kg^{-1} for fat-containing samples and 0.05 mg•kg^{-1} for fat-free samples. Beside these official methods, researchers also focus on finding new analysis approaches. Fernandez *et al.*[9] developed a head space (HS) SPME GC/MS method for phthalate analysis, and then Marcé[10] and Sensenstein.[11] adopted this method for the determination of phthalate esters in water and cow milk samples, respectively. This method was also recommended by European Commission Joint Research Centre for the determination of DEHP in sports drinks.[12] With this method, however, only 6 phthalates or less can be analyzed at one time, and the time to accomplish the analysis is lengthy.

These existing methods have not been good enough for most of the real sample analysis, and the time associated with sample preparation has been very costly. The continuous increasing of phthalate species that have been added to the list for detection urgently called for a new approach of testing. So we are trying to develop a new method which can provide rapid and easy-to-use phthalates testing without tedious sample treatment. Direct analysis in real time (DART) is one of the newly developed ambient ionization techniques.[13,14] It ionizes samples directly in their native condition and transfers ions into the mass analyzer without any separation steps, which takes up most of the consumed time for the analysis of raw materials.[15] By simplifying or even eliminating the sample pre-treatment, DART-MS can obtain a spectrum in just several seconds. Over the past years, DART has been successfully applied to a wide range of fields including the quality control of food and drugs.[16] Recently, our group has established an analytical method for the rapid identification of synthetic compounds in natural repellent products by DART-TOF-MS (time of flight mass spectrometry).[17] Studies also proved phthalates ionized well in DART,[18-21] inspiring us for further explorations of phthalates detection by DART-MS.

As the phthalates in liquid samples often present at sub-ng•mL^{-1} levels, an enrichment step by SPME prior to the DART-MS analysis for improving sensitivity has been developed. The SPME technique was introduced in the early1990's.[22] The target analytes were extracted from a sample matrix to a fiber either by directly immersing the fiber into a liquid sample (direct SPME), or in a headspace (HS-SPME).[11] HS-SPME usually coupled with GC-MS to analyze compounds contained in complex matrix.[23,24] And we applied the direct-SPME approach to simplify the pre-concentration step, that is, shortened analysis time and got a higher through-put without any further treatment procedures. Silva proved the efficient absorption of phthalates in water in 2004.[25] The open air nature of the DART ionization source benefited the placement of the SPME fiber directly in front of the DART inlet and with the use of linear rail, automated sampling and signal acquisition could be achieved. The combination of SPME and DART ionization was applied for the determination of triazine herbicides in water by Liu's group recently and also achieved good results.[26,27]

FT-ICR-MS offers ultra-high resolving power and measures masses of interest at extremely high accuracy constantly even if the concentrations of the analytes are at 0.1 — 1.0 ppm levels.[28] In our past studies FT-ICR-MS was used in combination with MALDI (matrix-assisted laser desorption) ion source, and has been proved to be a powerful tool for high resolving quantitative analysis of different analytes without complex sample preparation.[29-33] The importance of MALDI-FT-ICR-MS in the analysis of low molecular weight compounds was also reviewed in 2011.[34] The use of FT-ICR-MS for detection of phthalates directly sampled by SPME and ionized by DART provides a good match for the analysis of compounds present in a complex mixture at low concentration levels without a need of tedious chromatographic separations. Hence, we report a simple, rapid, and reliable SPME-DART-FT-ICR-MS method to determine 15 phthalates in beverages. By making use of the deuterated internal standards, d_4-phthalates synthesized by our group, all of the 15 phthalates are quantitatively analyzed in one run with a much shortened analysis time.

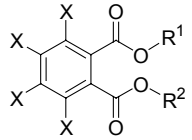
Experimental

Chemicals and reagents

HPLC-grade water was purchased from Thermo Fischer Scientific. 15 phthalate plasticizers are as shown in Figure 1 and Table 1, the mixed reference standards (100 μg•L^{-1}) in acetone was provided by Shanghai Institute of Measurement and Testing Technology. The mixed tetra-deuterated internal standards (100 μg•L^{-1}) (d_4-DEP, d_4-DIBP, d_4-DBP, d_4-DMEP, d_4-BMPP, d_4-DEEP, d_4-DPP, d_4-DHXP, d_4-BBP, d_4-DBEP, d_4-DCHP, d_4-DEHP, d_4-DPhP, d_4-DNOP, d_4-DNP) in *n*-hexane were synthesized in our labs (for more details, see Supporting Information). All chemicals and reagents were used without further purification. Three kinds of beverages: drinking water, tea drinks and drinks containing milk were purchased in a local supermarket in Shanghai, China.

SPME-DART-FT-ICR-MS analysis

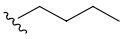
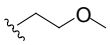
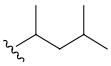
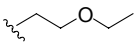
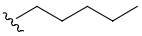
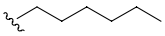
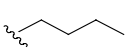
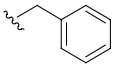
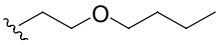
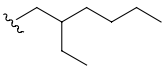
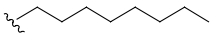
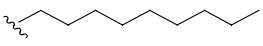
SPME sampling 50 mL of liquid sample was added into a 100 mL beaker. A magnetic stirring bar and



X=H for d_0-phthalates and X=D for d_4-phthalates

Figure 1 The chemical structures of phthalate plasticizers, where R^1 and R^2 might be the same or different alkyl groups.

Table 1 The abbreviation, chemical names and structures of the phthalate plasticizers

No.	Plasticizer	Name	X	R^1	R^2
1	DEP	Diethyl phthalate	H		
2	DIBP	Diisobutyl phthalate	H		
3	DBP	Dibutyl phthalate	H		
4	DMEP	Bis(2-methoxyethyl) phthalate	H		
5	BMPP	Bis(4-methyl-2-pentyl) phthalate	H		
6	DEEP	Bis(2-ethoxyethyl) phthalate	H		
7	DPP	Diamyl phthalate	H		
8	DHXP	Di-*n*-hexyl phthalate	H		
9	BBP	Butyl benzyl phthalate	H		
10	DBEP	Bis(2-*n*-butoxyethyl) phthalate	H		
11	DCHP	Dicyclohexyl phthalate	H		
12	DEHP	Bis(2-ethylhexyl) phthalate	H		
13	DPhP	Diphenyl phthalate	H		
14	DNOP	Di-*n*-octyl phthalate	H		
15	DNP	Dinonyl phthalate	H		

[a] d_4-Phthalates X＝D (4 hydrogen atoms on the benzene ring were replaced by 4 deuterium respectively).

200 μL of the internal standard mixture (100 μg•L^{-1}) were added. That is 400 ng•mL^{-1} for the testing solution. The stirring speed was adjusted to make the solution well stirred. After 2 min, the SPME needle was punched into the liquid. The SPME holder was placed at a height that the whole SPME needle was immersed under the sample liquid surface but did not touch the bottom of the beaker for 0.5 h. After the sampling was finished, the fiber was immediately placed onto the 12-Dip-it glass tip linear rail for DART-MS detection.

The used SPME needles were washed by a mixed solvent of acetonitrile and methanol, after soaking for 5－10 min, they were taken out and stocked in the newly replaced mixed solvent. The cleaned SPME needles were only taken out and dried by the air blower right before the next use.

DART ion source DART® SVP ionization source (IonSense, Saugus, MA, USA) interfaced to a linear ion trap-Fourier transform ion cyclotron resonance mass spectrometer (LTQ- FT Ultra MS) (ThermoFisher Scientific, Bermen, Germany) was used for all data and spectral acquisition. The DART source settings were optimized to be as following: positive ion mode; nitrogen and helium gas tank outlet pressure: 0.5 MPa; the

DART gas temperature: 350 ℃; the grid electrode voltage 350 V. The high purity helium (99.998%) was used as the ionizing gas. A small vacuum pump (WELCH, Ilmvac, Shanghai, China) was used to create a vacuum in the evacuated VAPUR® flange (IonSense, Saugus, MA, USA) located between the DART ion source and the mass spectrometer. The DART source was oriented such that the outlet of the source was in line with the ceramic tube leading into the VAPUR® flange before the inlet of the mass spectrometer. A 12-Dip-it glass tip linear rail that ran between the DART ion source and the ceramic tube was used to carry the samples into the source ionization region at a constant speed of 0.5 mm•s^{-1}. The distance between the DART ion source outlet and ceramic tube leading into the VAPUR® flange was maintained at 15.0 mm.

FT-ICR mass spectrometry The mass spectrometer settings were: capillary voltage: 200 V; tube lens voltage: 100 V; capillary temperature: 200 ℃. The ion optics settings were as follows: multipole 00 offset voltage, –4 V; multipole 0 offset voltage, –4.5 V; multipole 1 offset voltage, –15.5 V; lens 0 voltage, –4.5 V; lens 1 voltage, –40.0 V; gate lens voltage, –48.0 V; front lens voltage, –5.5 V. The mass range typically acquired was *m/z* 50－500. Peak integration and data output were accomplished through the instrument embedded Xcalibur® software.

Results and Discussion

Calibration curves and linear range determination

As listed in Table 1, a total of 15 phthalates contained in Chinese National Standard were studied, of which 5 phthalates (DNOP, DEHP, BBP, DBP and DINP) were listed in European Union Directions 2007/19/EC. The protonated molecule $[M+H]^+$ for each phthalates were detected by FT-ICR-MS, and their corresponding accurate masses, as listed in Table 2, matched with each theoretical mass calculations. These ions were used for subsequent quantitative analysis.

The extracted ion chromatograms (XICs) were integrated and computed by the Xcalibur™ software for all 15 phthalates and their deuterated internal standards (IS). The peak area ratios (PAR) of analytes to IS were calculated according to Equation 1 and plotted. The extracted mass range is settled as ($[M+H]\pm\delta$) where δ is the delta masses to the measured ones of the phthalate plasticizers. A relatively narrow mass window for each plasticizer (*m/z* $[M+H]\pm\delta$, δ 0.0005) was selected for XIC plotting to minimize background interferences. The calibration curves were then generated for each set of standards, at concentrations between 20 to 1500 ng•mL^{-1}, and the internal standard was always at the concentration of 400 ng•mL^{-1}. For each concentration levels, three replicates were measured.

$$\mathrm{PAR}=\frac{A_0}{A_d} \quad (1)$$

where A_0 is the peak area of plasticizers and A_d is the peak area of d_4-plasticizers in XIC, respectively. A representative XIC was showed below in Figure 2.

Table 2 The accurate mass measurement results of the phthalate plasticizers

No.	Plasticizer		Mass detected (*m/z*)	Accurate masses of $[M+H]^+$ (*m/z*)	Relative error/ppm
1	DEP	d_0	223.0965	223.0965	0
		d_4	227.1216	227.1216	0
2	DIBP	d_0	279.1589	279.1591	–0.7
		d_4	283.1840	283.1842	–0.7
3	DBP	d_0	279.1589	279.1591	–0.7
		d_4	283.1840	283.1842	–0.7
4	DMEP	d_0	283.1173	283.1176	–1.1
		d_4	287.1425	287.1427	–0.7
5	BMPP	d_0	335.2214	335.2217	–0.9
		d_4	339.2465	339.2468	–0.9
6	DEE	d_0	311.1486	311.1489	–1.0
		d_4	315.1738	315.1740	–0.6
7	DPP	d_0	307.1902	307.1904	–0.7
		d_4	311.2152	311.2155	–1.0
8	DHXP	d_0	335.2214	335.2217	–0.9
		d_4	339.2464	339.2468	–1.2
9	BBP	d_0	313.1432	313.1434	–0.6
		d_4	317.1682	317.1685	–1.0
10	DBEP	d_0	367.2112	367.2115	–0.8
		d_4	371.2363	371.2366	–0.8
11	DCHP	d_0	331.1901	331.1904	–0.9
		d_4	335.2152	335.2155	–0.9
12	DEHP	d_0	391.2839	391.2843	–1.0
		d_4	395.3090	395.3094	–1.0
13	DPhP	d_0	319.0962	319.0965	–0.9
		d_4	323.1212	323.1216	–1.2
14	DNOP	d_0	391.2839	391.2843	–1.0
		d_4	395.3092	395.3094	–0.5
15	DNP	d_0	419.3152	419.3156	–0.9
		d_4	423.3403	423.3407	–0.9

A representative set of data is presented with a respectable determination coefficient (R^2 varies between 0.9840 and 0.9996), as listed in Table 3. Similar experiments were conducted at different times of a day and in different days to determine the reproducibility and the consistency of calibration curves. The accurate masses of their molecular ions were also listed.

The limits of detection (LODs) (signal-to-noise, S/N at 3) and the limits of quantification (LOQs) (S/N at 10) were summarized in Table 4, mostly at 0.1－1.0 ng•mL^{-1} (ppb) for LODs and 0.3－5 ppb for LOQs.

Here the power of FT-ICR-MS is very well used, as its ultra-high resolution does much to help obtaining the

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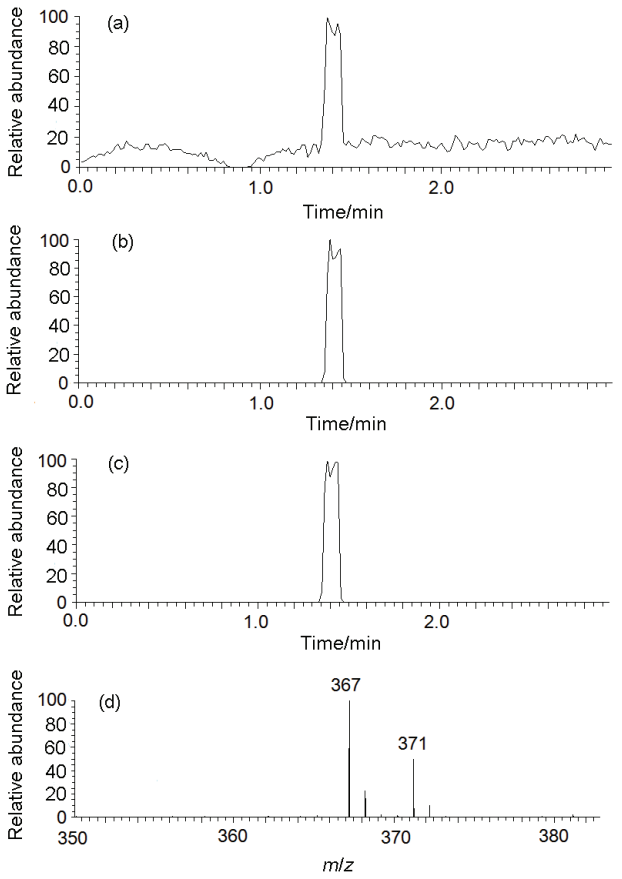

Figure 2 A representative chromatograph and mass spectrum of one out of 15 phthalates: DBEP by SPEM-DART-FT-ICR-MS, the concentrations of d_0-DBEP and d_4-DBEP were 500 and 400 ng•mL^{-1} respectively. (a) Total ion chromatogram (TIC); (b) The extracted ion chromatograms (XICs) of d_0-DBEP; (c) The extracted ion chromatograms (XICs) of d_4-DBEP; (d) Mass spectrum signals of d_0- and d_4-DBEP at 1.35−1.5 min.

Table 3 Quantitative data of SPME-DART-FT-ICR-MS analysis of phthalates in water

	Ions (m/z) for quantification[a]		Linearity ($y=ax+b$)		
	d_0	d_4	a	b	R^2
DEP	223.0961	227.1161	0.0039	–0.0429	0.9933
DIBP/DBP	279.1586	283.1786	0.0036	0.0031	0.9961
DMEP	283.1171	287.1371	0.0055	0.1880	0.9899
BMPP/DHXP	335.2209	339.2409	0.0033	1.5599	0.9964
DEEP	311.1482	315.1682	0.0041	–0.2103	0.9905
DPP	307.1897	311.2097	0.0093	–0.5322	0.9863
BBP	313.1429	317.1629	0.0066	–0.2436	0.9840
DBEP	367.2109	371.2309	0.0047	0.0317	0.9894
DCHP	331.1897	335.2097	0.0042	0.0588	0.9928
DEHP/DNOP	391.2795	395.3035	0.0028	–0.0134	0.9847
DNP	419.3055	423.3355	0.0063	–0.1860	0.9974
DPhP	320.1043	324.1243	0.0057	0.0202	0.9996

[a] There is an opening window of detection (exact ion mass range) M±δ, the value of δ was chosen to be 0.005.

Table 4 LODs and LOQs of 15 pthalates

	LOD/(ng•mL^{-1})	LOQ/(ng•mL^{-1})
DEP	1	5
DIBP/DBP	0.2	1
DMEP	0.2	0.5
BMPP/DHXP	0.2	0.5
DEEP	0.2	1
DPP	0.5	2
BBP	0.2	0.5
DBEP	0.1	0.2
DCHP	0.1	0.2
DEHP/DNOP	1	5
DNP	0.1	0.2
DPhP	0.5	2

accurate masses of the phthalates analyzed. And the relatively narrow mass window for each plasticizers (m/z [M+H]±δ, δ=0.0005) was selected for XIC plotting to minimize background interferences. Air background can be deducted directly in the data processing software Xcalibur® by Thermo Scientific to minimize its effect. No chromatography separation or multi reaction monitoring (MRM) mode were required, and it can be combined with a broad band spectrum of DART and without discrimination hence the analysis time was reduced and steps were simplified. The value of δ, which determined the mass window opened in the XICs was very well concerned, as it affected the peak area notably. During our data processing, we have tried to select different δ value for the measured phthalate plasticizers, and found that as the mass window opened wider the result was definitely affected, especially when the concentration of analyte dropped below 100 ng•mL^{-1}; the XICs were not extractable when δ value was larger than 0.001. The accurate masses of the phthalate plasticizers were listed in Table 2, from which we found that the accurate masses of the protonated molecule $[M+H]^+$ for d_0-BMPP/d_0-DHXP (m/z 335.2217) and d_4-DCHP (m/z 335.2155) are very close, the delta m/z is only 0.006. The δ value we chose to determine the extract ranges of the XICs should be able to tell d_0-BMPP/d_0-DHXP and d_4-DCHP apart, so it should be no larger than 0.003. And due to the relative error between the detected masses and the accurate ones, δ should be larger than 0.0004, so that all ions detected were covered. Five δ values 0.0005, 0.001, 0.0015, 0.002 and 0.003 were tested for all compounds in different concentrations; the differences were negligible as tested by statistical method t-test. Some of the results were listed below in Table 5. As the δ value increased from 0.0005 to 0.003, the peak area of phthalates varied far from significant, and the δ value of 0.0005 was chosen in order to get the most accurate results. The detail view of mass spectrum at m/z around 335.2 was showed in Figure 3,

from which we can find the well separation of d_0-BMPP/d_0-DHXP and d_4-DCHP, proving that the δ value of 0.0005 was appropriate.

Table 5 The peak areas of phthalates from XICs at different δ (exact ion mass range) value

	δ				
	0.0005	0.001	0.0015	0.002	0.003
d_0-DNP[a]	8.878×10^6	8.882×10^6	8.887×10^6	8.889×10^6	8.899×10^6
d_4-DPhP[b]	6.268×10^6	6.268×10^6	6.268×10^6	6.268×10^6	6.644×10^6

[a] The concentration of d_0-/d_4-mixed standard phthalates was 10 and 400 ng•mL^{-1}; [b] The concentration of d_0-/d_4-mixed standard phthalates was 3000 and 400 ng•mL^{-1}.

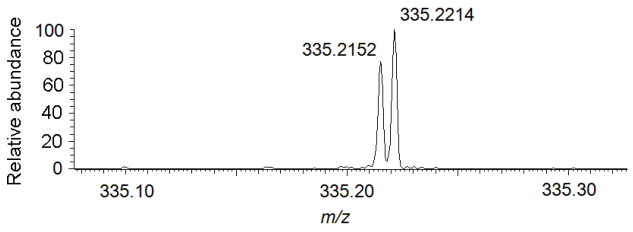

Figure 3 Detail view of mass spectrum at m/z around 335.2.

It should be noted that the 3 isomeric pairs of phthalates: DIBP/DBP (diisobutyl phthalate and dibutyl phthalate), BMPP/DHXP (bis(4-methyl-2-pentyl) phthalate and di-*n*-hexyl phthalate), DEHP/DNOP (bis(2-ethylhexyl) phthalate and di-*n*-octyl phthalate) are not distinguishable from each other as their molecular composition and hence the accurate masses are the same. However, these will not affect the detection results as this new SPME-DART method is a preliminary and rapid screening testing tactic, and only the unqualified samples need to be further analyzed by the regulation method, proving to be a time-saving and efficiently assisting technique.

Method validation

To evaluate the extraction recovery, a set of mixed standards were spiked into 50 mL of water sample for three replicates at three spiking concentrations, *i.e.*, each analyte was at the concentration of 20, 800 and 1500 ng•mL^{-1} approximately. The recovery of each spiked standard was calculated based on Equation 2, and the obtained values of method validation parameters were listed in Table 6.

$$\text{recovery}=\frac{A_1-A_0}{A_b}\times100\% \quad (2)$$

where A_0, A_1, and A_b each stands for the peak area of every individual standard in the non-spiked, spiked water, and blank samples respectively. Method precision was evaluated through the relative standard deviation (RSD) of recovery of those spiked replicates.

The recoveries are at a range from 61.7% to 142.2% at low spiked concentrations, and are gradually getting to 100% as the spiked concentrations increase. The method shows relatively acceptable precision at all three spiked concentration levels (RSD＜23%). Compared to those reported in other SPME related studies, these deviations are relatively high,[18-23] but as a quick and primary testing method, it is acceptable. And more studies are needed to improve the method reproducibility.

Plasticizer contamination in beverages

Plasticizers content of 3 kinds of beverages were evaluated based on the developed SPME-DART-FT-ICR-MS method. As listed in Table 7, beverages number 1 to 3 each stands for the testing sample of drinking water, tea drinks and drinks containing milk. DMEP and BMPP/DHXP were detected in all three samples. Most other phthalates were not found in any of the beverages. And of those being detected, their concentrations were

Table 6 Method validation parameters

	50 ng•mL^{-1}		800 ng•mL^{-1}		1500 ng•mL^{-1}	
	Recovery/%	RSD/%	Recovery/%	RSD/%	Recovery/%	RSD/%
DEP	101.1	3.0	110.3	13.9	97.1	5.6
DIBP/DBP	110.9	11.9	106.4	6.7	96.8	7.7
DMEP	61.7	3.0	112.4	7.5	95.9	14.9
BMPP/DHXP	131.6	15.8	95.0	15.5	101.5	13.8
DEEP	130.2	17.9	87.5	13.1	102.8	10.7
DPP	142.2	18.6	86.5	22.9	104.3	7.3
BBP	126.1	16.8	84.5	2.9	104.5	8.3
DBEP	77.3	19.2	114.6	5.6	97.1	15.6
DCHP	92.8	12.1	108.6	21.7	99.1	14.6
DEHP/DNOP	73.6	9.7	116.8	23.0	96.9	12.2
DNP	135.3	6.3	101.0	15.4	77.0	4.9
DPhP	84.0	0.6	97.3	7.0	99.8	19.2

Table 7 Plasticizer contamination in soft drinks (ng•mL^{-1})[a]

Phthalate	1	2	3
DEP	nd	nd	nd
DIBP/DBP	nd	nd	nd
DMEP	bq	59.1	bq
BMPP/DHXP	bq	bq	189.6
DEEP	nd	53.9	nd
DPP	nd	nd	nd
BBP	nd	nd	nd
DBEP	bq	nd	nd
DCHP	nd	bq	nd
DEHP/DNOP	nd	bq	nd
DNP	30.7	nd	33
DPhP	nd	32.8	nd

[a] nd stands for "below LOD", while bq stands for "below LOQ", indicating a concentration higher than LOD, but lower than LOQ.

far below the allowance of Chinese National Standard and of European Union Council Directive. As far as these samples are concerned, they qualify as safety drinks accordingly.

Conclusions

A combination of SPME and DART-FT-ICR-MS for rapid and sensitive analysis of phthalate esters in beverages has been developed. SPME minimizes the pre-concentration steps as it is an efficient extraction and enrichment method that no further clean-up steps are necessary. DART gives a direct and fast desorption and ionization of analytes without the need of commonly used tedious chromatographic separations. And the ultra-high resolution and accurate mass measurements of FT-ICR-MS enable direct analysis of a signal of interest from a complex mixture. The limits of detection (LODs) of 15 evaluated phthalates were estimated to be at 0.1—1.0 ng•mL^{-1} levels, up to 3 orders of magnitude lower than the limitation of European Union Directions 2007/19/EC relating to plastic materials in contact with food stuffs. This method has been applied to the screening and identification of phthalates in 3 kinds of beverages. The use of FT-ICR-MS for detection of phthalates directly sampled by SPME and ionized by DART provides a good combination for the analysis of compounds present in a complex mixture at low concentration levels. To our knowledge, this is the first report showing the application of SPME and a direct combining with DART-FT-ICR-MS in the detection of phthalates.

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