Dispersive Solid-Phase Extraction Based on Magnetic Dummy Molecularly Imprinted Microspheres for Selective Screening of Phthalates in Plastic Bottled Beverages

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ABSTRACT: A new magnetic dummy molecularly imprinted dispersive solid-phase extraction (MAG-MIM-dSPE) coupled with gas chromatography-FID was developed for selective determination of phthalates in plastic bottled beverages. The new magnetic dummy molecularly imprinted microspheres (MAG-MIM) using diisononyl phthalate as a template mimic were synthesized by coprecipitation coupled with aqueous suspension polymerization and were successfully applied as the adsorbents for MAG-MIM-dSPE to extract and isolate five phthalates from plastic bottled beverages. Validation experiments showed that the MAG-MIM-dSPE method had good linearity at 0.0040–0.40 μg/mL (0.9991–0.9998), good precision (3.1–6.9%), and high recovery (89.5–101.3%), and limits of detection were obtained in a range of 0.53–1.2 μg/L. The presented MAG-MIM-dSPE method combines the quick separation of magnetic particles, special selectivity of MIM, and high extraction efficiency of dSPE, which could potentially be applied to selective screening of phthalates in beverage products.

KEYWORDS: dispersive solid-phase extraction, molecularly imprinted microspheres, magnetic separation, phthalates, beverages

INTRODUCTION

Diesters of 1,2-benzenedicarboxylic acid (phthalic acid), commonly referred to as phthalate esters (PAEs), are synthetic, man-made chemicals of increasing public importance because of their potential toxicity.1,2 PAEs have been used as plasticizers for nearly 50 years; they are essential to keep polymers flexible and pliable.3 Therefore, this group of chemicals has a wide spectrum of industrial applications, and these chemicals appear, ultimately, in a wide range of consumer products, as well as in food processing and in medical applications.4–7 Phthalate plasticizers are not chemically bound to PVC; they can leach, migrate, or evaporate into foodstuffs and beverages from packaging materials, so human exposure to phthalate esters is widespread.2 Leaked PAEs in plastic-packed foods can cause adverse effects on human health, such as on the liver and kidney, and are toxic to the developing male reproductive system.5 Thus, measurement of PAEs in foodstuffs and beverages is necessary to accurately assess exposure.

In the past decades, modern analytical instrumentation has provided an edge to fast and cost-effective analytical methods. However, these new analytical techniques have commonly suffered from some limitations such as the sample matrix effect and compromised selectivity in the analysis of complicated samples.8 An effective sample cleanup helps to improve separation and detection, while a poor pretreatment procedure might invalidate the whole assay. Furthermore, cleaned samples extend the service life of analytical instruments and reduce analytical cost.9 Solid-phase extraction (SPE)10–12 solid-phase microextraction (SPME)13–16 headspace solid-phase microextraction (HS-SPME)17, dispersive liquid–liquid microextraction (DLLME),18,19 and hollow-fiber liquid-phase microextraction (LPME)20 prior to liquid chromatography (LC),10,18 gas chromatography coupled with FID (GC-FID),21 or mass spectrometry (GC-MS)11,14,19 detection have been developed for screening PAEs in different matrices. Although each method above has its advantage, they often suffer from poor selectivity and extraction efficiency for complex samples.22

Dispersive solid-phase extraction (dSPE) is a new sample pretreatment technique which offers unique advantages such as applicability to a wide variety of analytes, little use of glassware/plasticware, high cost-effectiveness, and easy automation.73–25 Generally, the adsorbents of dSPE are directly dispersed in sample solution containing target analytes. After extraction, the adsorbents with retained analytes are separated by centrifugation or other ways. The dSPE procedure enables adsorbents to interact with analytes fully, and avoid channeling or blocking of the cartridges or disks, which occurs in traditional SPE. In addition, the common adsorbents, including primary secondary amine, C18 (octadecylsilane), and graphitized carbon black, lack special selectivity.26

Molecularly imprinted polymers (MIPs), first constructed by Wulff and Mosbach,27,28 have shown potential applications as a stationary phase in chromatography and as adsorbent materials for SPE,29–31 chromatographic separation,32 chemical sensors33,34 catalysis35 and many other fields. Commonly, MIPs are synthesized by copolymerization of functional monomers and cross-linkers in the presence of template molecules. Binding sites with molecular recognition properties are formed...
after removal of template molecules from polymers, leaving behind cavities for subsequent rebinding, which can selectively rebind target molecules from a mixture of closely related compounds. Compared with biological macromolecules such as antibodies, receptors, and enzymes, MIPs are much more stable and can be used under more demanding conditions. However, most MIPs suffer from problems of poor recognition in water and template leakage at the present stage.

Furthermore, magnetic particles can be collected and separated from the liquid phase under an external magnetic field, which avoids tedious filtration or centrifugation procedures and allow particles to be easily retrieved at low cost. If some magnetic components are encapsulated into MIPs, the resulting composite magnetic MIPs would not only have susceptible magnetic characteristics but also have high selectivity for the target molecule. Composite magnetic MIPs have been prepared, as reported in the literature, and they all exhibited higher recognition selectivity and certain magnetic responses to external magnetic fields.

The aim of this work was to develop a new MAG-MIM-dSPE-GC method using composite magnetic dummy molecularly imprinted microspheres (MAG-MIM) as the adsorbents for dSPE in the selective extraction and determination of five phthalates from plastic bottled beverages. The new MAG-MIM adsorbents, which were synthesized by coprecipitation coupled with aqueous suspension polymerization using diisononyl phthalate as the dummy template, improve the poor selectivity of MIPs in a water environment and eliminate the effect of template leakage of MIPs upon quantitative analysis. The MAG-MIM-dSPE-GC method combines the quick separation of magnetic particles, special selectivity of MIM, and high extraction efficiency of dSPE and potentially could be applied to selective screening of phthalates in beverages.

**EXPERIMENTAL PROCEDURES**

**Chemicals and Reagents.** Butyl benzyl phthalate (BBP), diethyl phthalate (DEP), dibutyl phthalate (DBP), dioctyl phthalate (DIDP), diisononyl phthalate (DINP), and dioctyl phthalate (DNOP) were obtained from Crystal Pure Industrial Co., Ltd. (Shanghai, China). Methanol (HPLC grade) was from Xingke Biochem. Co., Ltd. Chloroform, dichloromethane, polyvinylpyrrolidone (PVP), and ammonia were purchased from Huaxin Chemical Reagent Co., Ltd. (Baoding, China). Acetone, ethyl acetate, methanol, ethanol, and acetic acid were obtained from Huadong Chemical Reagent Co. (Tianjin, China). Iron(II) chloride tetrahydrate (FeCl₂·4H₂O), iron(III) chloride hexahydrate (FeCl₃·6H₂O), oleic acid, 2,2-azobis(isobutyronitrile) (AIBN), methacrylic acid (MAA), and acetonitrile were obtained from Kernel Chemical Reagents Center (Tianjin, China). Ethylene glycol dimethacrylate (EGDMA) was obtained from Sigma-Aldrich (St. Louis, MO). A Nd–Fe–B magnet (80 × 60 × 17 mm) was purchased from a local market in Baoding, China. All the reagents used in this work were of analytical grade (purity ≥99%). Double deionized water was filtered through a 0.45 μm filter membrane before use.

**Instrumentation and Conditions.** Chromatographic analysis was performed on a Shimadzu GC-2014 system equipped with a split/splitless injector and an FID detector (Shimadzu, Japan). High-purity nitrogen (99.999%) was used as carrier gas. A GH-300 high-purity hydrogen generator and a GA-2000A air pump (Beijing ZXHL Co., Ltd., China) were used to supply hydrogen gas and auxiliary gas (supply oxygen) at the rate of 40 and 400 mL/min, respectively. The capillary column was KB-1 (100% dimethyl polysiloxane as stationary phase, 30 m × 0.25 mm × 0.25 μm, Kromat, Delran, NJ), and its flow rate was set at 1.7 mL/min with a split ratio of 10. An N-2000 workstation (Zheda Zineng, Hangzhou, China) was used as the data acquisition system. The temperature-programmed mode was as follows: the initial oven temperature was 150 °C for 2.0 min and then increased to 285 °C at the rate of 25 °C/min and held for 10 min. The temperatures of the injection port and FID detector were set at 290 °C and 300 °C, respectively. A Fourier transform infrared (FT-IR) spectrometer (Shimadzu, Japan) was employed to examine infrared spectra of obtained particles. Magnetic properties were measured with a LakeShore 7307 (Lakeshore Cryotronic) vibration magnetometer (VSM) at 300 K. The obtained particles were also characterized by thermogravimetric analysis (TGA, SDT TA851E). The morphology of MAG-MIM was characterized by field-emission scanning electron microscopy (FE-SEM), S-4200 (Hitachi, Ontario, Canada). The morphology of Fe₃O₄ magnetite was characterized by transmission electron microscopy (TEM; JEM-100SX, JEOL, Tokyo, Japan).

**Preparation of Fe₃O₄ Magnetite with a Hydrophobic Shell.** The Fe₃O₄ magnetites with a hydrophobic shell were prepared by the coprecipitation method as follows: FeCl₂·4H₂O (0.02 mol) and FeCl₃·6H₂O (0.03 mol) were dissolved into 100 mL of deaerated deionized water, 2.0 mL of oleic acid was added dropwise into the solution, and then the mixture was placed in an ultrasonic environment for 20 min under vigorous stirring. Fifteen milliliters of aqueous ammonia was added drop by drop when the temperature of the water bath was elevated to 60 °C. After 30 min, when the temperature was elevated to...
80 °C, another 2.0 mL of oleic acid was added. After 2.0 h, magnetic precipitates were isolated from the solvent by a permanent magnet and washed several times with highly purified deaerated water and ethanol to remove unreacted ferric chloride and oleic acid.

**Preparation of MAG-MIM.** The MAG-MIM were prepared as follows: Fe₃O₄ magnetite (4.0 mmol), diisononyl phthalate (DINP) (2.0 mmol), and MAA (8.0 mmol) were added into 20 mL of chloroform. After EGDMA (50 mmol) and AIBN (1.2 mmol) were added, the solution was sonicated for 5.0 min to fully dissolve them. Finally, the solution was added dropwise to PVP solution (27 mmol of PVP dissolved into 120 mL of water) by stirring at 600 rpm and heated at 60 °C for 24 h. After polymerization, the obtained MAG-MIM particles were separated, washed with methanol–acetic acid (9:1, v/v) and methanol, respectively, under ultrasound to remove template and unreacted reagents, and then dried under vacuum at 45 °C for 24 h. To verify the effectiveness of the cleaning process, the washing solvent (10 mL) was evaporated, and the sample mixture was reconstituted in acetone (0.5 mL) before injection into the gas chromatograph. The magnetic nonimprinted microspheres (MAG-MIM) were prepared and processed similarly as above, except that template was not added.

**MAG-MIM-dSPE Procedure.** Plastic bottled beverages were obtained from local supermarkets in Baoding, and the MAG-MIM-dSPE procedure was performed as shown in Figure 1. MAG-MIM (100 mg) were added into a 10 mL beverage sample and entirely dispersed by ultrasound at room temperature. After 10 min, phase separation was performed by magnetic separation with a applied magnetic field (Nd–Fe–B magnet) in the bottom of bottle, and then the MAG-MIM were eluted with 7.0 mL ethyl acetate–acetic acid (85:15, v/v) to desorb analytes from the adsorbents. Finally, the eluent was evaporated under a gentle nitrogen stream, and the sample was reconstituted with 0.5 mL of acetone for further GC analysis.

**RESULTS AND DISCUSSION**

**Preparation of MAG-MIM.** The preparation of MAG-MIM particles involved the synthesis of hydrophobic superparamagnetic Fe₃O₄ particles, MIM functionalization of the magnetic particles, and removal of the template to generate the recognition sites. Hydrophobic superparamagnetic Fe₃O₄ particles were prepared by a modified coprecipitation method, and the TEM image of the hydrophobic Fe₃O₄ particles showed that their sizes were on nanoscale (Figure 2A). The surface of magnetite was hydrophobic with a coating of oleic acid, which avoided electrostatic agglomeration and ensured the uniform dispersion of magnetic nanoparticles in the polymerization solution and homogeneous embedding. Ultrasound treatment was employed for modification of Fe₃O₄ making the procedure simple, rapid, and easily controlled. This strategy was successful in the fabrication of magnetically susceptible polymer-supported imprinted microspheres. To improve binding capacity, selectivity, and compatibility of MAG-MIM in water, aqueous suspension polymerization was adopted. Moreover, diisononyl phthalate (DINP) was chosen as the template mimic, which eliminated the effect of template leaking during quantitative analysis and demonstrated special recognition ability for the five phthalates.

In the oil-in-water suspension polymerization, MAA was a common monomer, and EGDMA as a cross-linker maintained the stability of imprinting sites while making the polymer easier to be handled and processed. Generally, the molar ratios between template and monomer play an important role in the affinity and imprinting effect of MIM toward its template molecule. Therefore, the molar ratios between template and monomer of 1:2, 1:3, 1:4, and 1:6 were investigated, while a molar ratio of 4:25 between monomer and cross-linker was selected to ensure the formation of the defined recognition sites. When porogens had poor hydrogen bonding capacity, the interaction between template and functional monomer was mainly influenced by the dielectric constant of the solvent. The apricot porogen with a small dielectric constant favored the formation of a higher concentration of template–monomer complexes, which resulted in MIM with high affinity and selectivity. Therefore, taking hydrogen bonding capacity and dielectric constants of porogens into consideration, chloroform and toluene were investigated as porogens for the entire synthetic process. Figure 2B shows that the morphology of MAG-MIM was regular spherical when using chloroform as porogen and a molar ratio of 1:4:25 for template, monomer, and cross-linker. With further consideration to the mechanical strength and special affinity to phthalates, 20 mL of chloroform was chosen as porogenic solvent. Although water was considered to weaken, and even to eliminate, the noncovalent interaction (hydrogen bond, van der Waals force, etc.) between functional monomer and template, the MAG-MIM prepared by aqueous suspension polymerization using PVP as dispersing agent exhibited good recognition performance.

The GC-FID trace of washing solvent after five washes (Figure 8A) proved that methanol can dissolve and wash out DINP, allowing MAG-MIM to be cleaned. The preparation method for MAG-MIM applied in this work was aqueous suspension polymerization, and the solvent was water in which methanol can effectively disperse and wash out the DINP template. Moreover, some added acetic acid can destroy the hydrogen bond for imprinting and help methanol wash out the template. Actually, on the basis of the dummy template strategy adopted in this work, residual DINP template on MIM was not washed out and leaked during the extraction procedure but would still not affect the quantitative determination because the leaked template can be fully separated from the analytes during GC separation.

**Characterization of MAG-MIM.** The products of Fe₃O₄ and MAG-MIM were investigated by FT-IR spectroscopy (Figure 3A). A sharp and strong Fe–O stretching peak (≈584 cm⁻¹) was observed in the trace of Fe₃O₄, while this characteristic peak was not in the trace of MAG-MIM, indicating that Fe₃O₄ magnetite of MAG-MIM was coated with polymers. The band at 1732 cm⁻¹ was assigned to the absorption of COOH, and the band at 1233 cm⁻¹ was ascribed to stretching vibrations of C–O–C in MAG-MIM. The characteristic bands at 2900 cm⁻¹ and 1800 cm⁻¹ of diisononyl phthalate still markedly existed in the spectra of MAG-MIM without extraction of the template, but they greatly weakened after extraction. In addition, the GC-FID trace of washing solvent after five washes (Figure 8A) show that MAG-MIM had
been cleaned. All these observations indicated that MAG-MIM were prepared well.

Figure 3B shows the TGA curve of MAG-MIM and MAG-NIM compared with Fe3O4 magnetite and hydrophobic Fe3O4 magnetite. There was no dramatic weight loss below temperature of 240 °C, which means that all materials were stable under 240 °C. Significant weight loss occurred from 270 °C to 450 °C owing to the thermal degradation of MIM polymer (c) and NIM polymer (d). The outside layer of beads was a polymer mixture resulting from a different degree of polymerization. This caused the inflection (e.g., at about 10%) and different degradation rates in the TGA trace of MIM (c) and NIM (d). The remaining weight was attributed to the existence of Fe3O4 particles, and the quantity of loss of hydrophobic Fe3O4 magnetite (b) was more than Fe3O4 magnetite (a) without chemical modification, respectively.

The magnetic properties of the obtained materials were analyzed by VSM at room temperature, and the results are illustrated in Figure 3C. It is obvious that there was no hysteresis; both remanence and coercivity were zero, suggesting that the materials were superparamagnetic. The saturation magnetization ($M_s$) values of Fe3O4 magnetite, hydrophobic Fe3O4 magnetite, and MAG-MIM were about 51, 44, and 26 emu/g, respectively. The decrease of the $M_s$ value was due to the coating of a hydrophobic layer and an organic polymer shell layer. Although the $M_s$ value of MAG-MIM was reduced to 26 emu/g, they were susceptible to magnetic fields and could be easily separated from a suspension.

**Optimization of MAG-MIM-dSPE Procedures.** Various factors influencing the MAG-MIM-dSPE extraction effect were investigated, and the results are shown in Figures 4−6. Regarding the MAG-MIM particles that were dispersed in 10 mL of sample solution to rebind the five phthalates during the extraction procedure, the amount of adsorbent used should provide sufficient binding sites for the analytes and achieve good recoveries. Therefore, the minimum amount of MAG-MIM to achieve efficient recoveries was investigated, and Figure 4 shows that the recoveries for the five phthalates were more than 90.5% when 100 mg of MAG-MIM was added to samples, while the recoveries kept constant with a further increase to 175 mg. Therefore, 100 mg of MAG-MIM was selected as the optimal amount of dSPE adsorbent.

When 100 mg of MAG-MIM was dispersed in a sample solution, the analytes should contact the surface of sorbents and attain adsorption−desorption equilibrium in the appropriate time. As shown in Figure 5A, the influence of adsorption time was studied, and extraction equilibria were obtained in a short time. DBP and BBP achieved the largest extraction recoveries in 3 min, while DEP, DIOP, and DNOP needed 10 min to ensure full extraction because the structures of DBP and BBP matched the binding sites of MAG-MIM better than DEP, DIOP, and DNOP.
Therefore, the time of adsorption was determined for 10 min. Generally, an increase in ionic strength decreased the concentration of analytes in sample solution and enhanced the extraction efficiency of MAG-MIM. To evaluate the possibility of a salting out effect, extraction efficiency was studied with an increase in sodium chloride concentration over a range of 0−6% (w/v). As shown in Figure 5B, there was almost constant extraction recovery with an increase of salt concentration from 0% to 1% and then a slight decrease in recovery with a further increase to 6% in salt concentration, which indicated that the ionic strength of the samples hardly interfere with extraction efficiency. Similarly, when the influence of pH was investigated, as shown in Figure 5C, there was no obvious variation in extraction efficiency in a pH range from 3.0 to 9.0 probably because the phthalate structures

Figure 5. Effect of adsorption time (A), salt concentration (B), pH value (C), and desorption time (D) in MAG-MIM-dSPE.

Figure 6. Effect of organic matter in (A) beverages and (B) desorption solvent in MAG-MIM-dSPE.

Figure 7. Comparison of MAG-MIM-dSPE, MAG-NIM-dSPE, and simple ethyl acetate extraction.
were stable and the MAG-MIM-dSPE extraction procedure was not easily affected by an acid or alkaline environment. Considering that the beverage samples were neutral or slightly acidic, pH was not adjusted for further experiments. The effect of organic matter in the sample matrix was also investigated. The beverage samples used in this work were vitamin drinks, and most of the compounds in the sample matrices were water-soluble vitamins (such as vitamins B6, B12, and C and niacinamide). These vitamins were hardly absorbed by MAG-MIM in the aqueous matrix, so there was very little effect on the recovery of PAEs (Figure 6A).

After phase separation by an applied magnetic field in the bottom of bottle, the MAG-MIM adsorbent was eluted to desorb the analytes. The phthalates were extracted well by most organic solvents. The solvent molecules were adsorbed easily on the surface of the adsorbent polymer to replace the analyte molecules. A small amount of acetic acid was added to contribute to the destruction of the hydrogen bonds between analytes and binding sites on the adsorbents. Therefore, different kinds and volumes of organic solvents coupled with 15% acetic acid were investigated. Figure 6B shows that 7.0 mL of ethyl acetate–acetic acid (85:15, v/v) was used as the desorption solvent to strip the adsorbed analytes from MAG-MIM.

The time of desorption also investigated as shown in Figure 6D. The new adsorption–desorption equilibria were obtained in a short time. The polarity of DEP can be inferred from its structure, so the extraction equilibrium in strong hydrophobic solvent would take a longer time than that of other analytes. Considering time efficiency, 5 min was selected as the optimum desorption time.

Moreover, the MAG-MIM-dSPE method was compared with MAG-NIM-dSPE in parallel using simple ethyl acetate extraction according to their optimization steps. Recoveries with MAG-MIM-dSPE for phthalates were more than those with MAG-NIM-dSPE or liquid–liquid extraction (LLE), as shown in Figure 7, obtained for spiked beverages (0.040 μg/mL). The chromatograms of MAG-MIM-dSPE, MAG-NIM-dSPE, and LLE are shown in Figure 8A, and the effect of nonselective uptake (interferences) from LLE was worse than that of MAG-NIM-dSPE. The lack of selectivity aggravated the serious inaccuracies in determination. There were many impurity peaks that interfered with the determination of the phthalates as shown in the chromatograms of MAG-NIM-dSPE and LLE. MAG-MIM-dSPE-GC background from the beverage matrix was more or less identical to that of MAG-NIM-dSPE-GC. For example, a peak (≈6 min) was observed in the chromatogram of LLE and MAG-NIM-dSPE-GC, while it did not appear in the chromatogram of MAG-MIM-dSPE-GC. The reason for this may be the effective utilization of functional groups on polyacrylate during the templating process of MAG-MIM, resulting in relatively reduced nonselective binding for the beverage constituents. All aforementioned details indicate that the templating of MIM was successful. In summary, the utility of MAG-MIM-dSPE is reliable for selective screening of phthalates in beverages.

Validation of the MAG-MIM-dSPE-GC Method. To validate the analytical methodology of the MAG-MIM-dSPE-GC method, several parameters such as linearity, recovery, and detection limit were considered. The features of the MAG-MIM-dSPE-GC method are shown in Table 1. The recoveries of phthalates obtained by comparing the MAG-MIM-dSPE-GC method with LLE are shown in Table 2. The chromatograms of the spiked beverage sample and real sample are shown in Figure 8.

Table 1. Features of the MAG-MIM-dSPE-GC Method

<table>
<thead>
<tr>
<th>compounds</th>
<th>regression equation</th>
<th>r²</th>
<th>LOD (μg/L)</th>
<th>LOQ (μg/L)</th>
<th>RSD</th>
</tr>
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<tbody>
<tr>
<td>DEP</td>
<td>Y = 4.57 × 10^3X + 215.3</td>
<td>0.9995</td>
<td>1.2</td>
<td>4.0</td>
<td>4.3</td>
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<tr>
<td>DBP</td>
<td>Y = 4.76 × 10^3X + 1.10 × 10^4</td>
<td>0.9997</td>
<td>0.60</td>
<td>2.0</td>
<td>3.1</td>
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<tr>
<td>BBP</td>
<td>Y = 7.01 × 10^3X + 389.4</td>
<td>0.9991</td>
<td>0.53</td>
<td>1.8</td>
<td>6.9</td>
</tr>
<tr>
<td>DIOP</td>
<td>Y = 6.95 × 10^3X + 3.56 × 10^4</td>
<td>0.9991</td>
<td>0.56</td>
<td>1.9</td>
<td>5.3</td>
</tr>
<tr>
<td>DNOP</td>
<td>Y = 6.40 × 10^3X + 883.3</td>
<td>0.9998</td>
<td>0.74</td>
<td>2.5</td>
<td>4.9</td>
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Table 2. Recoveries in the MAG-MIM-dSPE-GC Method for Spiked Beverage (n = 3)

<table>
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<tr>
<th>spiked level of analytes</th>
<th>recovery (%)</th>
<th>RSD (%)</th>
<th>recovery (%)</th>
<th>RSD (%)</th>
<th>recovery (%)</th>
<th>RSD (%)</th>
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<tbody>
<tr>
<td>DEP</td>
<td>100.5</td>
<td>6.7</td>
<td>96.1</td>
<td>4.6</td>
<td>95.8</td>
<td>3.3</td>
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<tr>
<td>DBP</td>
<td>101.3</td>
<td>4.6</td>
<td>95.0</td>
<td>3.6</td>
<td>97.9</td>
<td>2.5</td>
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<tr>
<td>BBP</td>
<td>89.5</td>
<td>5.2</td>
<td>93.4</td>
<td>2.7</td>
<td>100.2</td>
<td>2.1</td>
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<tr>
<td>DIOP</td>
<td>92.9</td>
<td>5.9</td>
<td>96.4</td>
<td>3.5</td>
<td>99.2</td>
<td>3.6</td>
</tr>
<tr>
<td>DNOP</td>
<td>97.9</td>
<td>4.9</td>
<td>94.4</td>
<td>3.8</td>
<td>98.2</td>
<td>2.4</td>
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Figure 8. Chromatograms of (A) spiked beverage sample and (B) real sample.
reproducibility, limit of detection (LOD), and limit of quantification (LOQ) were evaluated. All parallel experiments were repeated three times, and the results are tabulated in Table 1. The linearity of the MAG-MIM-dSPE-GC method was tested using the areas of chromatographic peaks measured at nine increasing spiked levels in a range of 0.0040–0.43 μg/mL. Good linearity was obtained throughout the concentration range for all analytes with the correlation coefficient (r²) ≥ 0.9991. Analyses of reproducibility of intraday and interday were carried out for spiked beverage samples (0.08 μg/mL), and RSD values of intraday and interday were less than 6.9% and 7.2%, respectively. The LOD values calculated on the basis of S/N = 10, the LOQ values of analytes were less than 6.9%, and RSD values of intraday and interday were less than 6.9% and 7.2%, respectively. The LOD values calculated on the basis of S/N = 3 were in a range of 0.53–1.2 μg/L for all analytes. On the basis of S/N = 10, the LOQ values of analytes were from 1.8 to 4.0 μg/L. Spiked recoveries were determined to validate the method on the basis of the obtained linearity (taking the form of Y = ax + b). Recoveries were calculated as:

$$R = \frac{P - b}{a \times C_s} \times 100\%$$

In the equation, R stands for the recovery value, P is the peak area, C_s is the actual concentration, and a and b are two coefficients of the obtained linear equation. The average recoveries for the five phthalates in spiked samples were in a range of 89.5–101.3% (Table 2), which demonstrated that the proposed MAG-MIM-dSPE-GC technique was reliable. The parameters of the present MAG-MIM-dSPE-GC method (such as recovery, LOD, RSD, and estimated time) were justified briefly in comparison with other procedures reported in the literature, indicating that the method is reliable and practical (Table 3).

**Real Sample Analysis.** To demonstrate the suitability and application of the MAG-MIM-dSPE-GC method for actual samples, five brands of vitamin beverage products collected from local markets in Baoding were pretreated and analyzed under optimal MAG-MIM-dSPE-GC conditions. Figure 8B shows that trace levels of DBP and DIOP at concentrations of 5.7 μg/L and 4.0 μg/L were observed in one of the beverage products, and water-soluble vitamins (such as vitamins B6, B12, and C and niacinamide) (which are the main components in beverage matrices) did not interfere with the screening of the phthalates.

### Funding
The project was sponsored by National Natural Science Foundation of China (31301464, 21175031) and the Natural Science Foundation of Hebei Province (B2012201052).

### Notes
The authors declare no competing financial interest.

### REFERENCES


### Table 3. Comparison of Different Analytical Methods for Screening of Phthalates

<table>
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<tr>
<th>sample matrix</th>
<th>treatment method</th>
<th>detection method</th>
<th>recovery (%)</th>
<th>LOD</th>
<th>estimated time (min)</th>
<th>RSD (%)</th>
<th>ref no.</th>
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<td>soybean milk</td>
<td>SPE</td>
<td>GC-MS</td>
<td>75.8–107.5</td>
<td>13–22 μg/L</td>
<td>&gt;100</td>
<td>1.8–10.08</td>
<td>10</td>
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<tr>
<td>water</td>
<td>SPEM</td>
<td>GC-ECID</td>
<td>109–116</td>
<td>1–4 ng/L</td>
<td>&gt;70</td>
<td>4–10</td>
<td>16</td>
</tr>
<tr>
<td>vegetable oil</td>
<td>HS-SPEM</td>
<td>GC-ECID/MSD</td>
<td>“—”</td>
<td>0.06–0.3 mg/kg</td>
<td>60–70</td>
<td>14–23</td>
<td>17</td>
</tr>
<tr>
<td>water</td>
<td>DLLME</td>
<td>GC-MS</td>
<td>68.1–88.9</td>
<td>2–8 ng/L</td>
<td>&lt;45</td>
<td>4.6–6.8</td>
<td>19</td>
</tr>
<tr>
<td>water</td>
<td>LPEM</td>
<td>GC-FID</td>
<td>84–102</td>
<td>0.43–4 μg/L</td>
<td>&lt;30</td>
<td>5.2–6.4</td>
<td>21</td>
</tr>
<tr>
<td>beverage, water, and perfume</td>
<td>MPSPE&lt;sup&gt;b&lt;/sup&gt;</td>
<td>GC-MS</td>
<td>64.6–125.6</td>
<td>4.9–38 ng/L</td>
<td>&lt;30</td>
<td>2–16.5</td>
<td>47</td>
</tr>
<tr>
<td>urine</td>
<td>MPSPE&lt;sup&gt;b&lt;/sup&gt;</td>
<td>GC-MS</td>
<td>92.6–98.8</td>
<td>0.025–0.05 ng/mL</td>
<td>200</td>
<td>5.28–11.45</td>
<td>48</td>
</tr>
<tr>
<td>beverage</td>
<td>dSPE&lt;sup&gt;+&lt;/sup&gt;</td>
<td>GC-FID</td>
<td>89.5–101.3</td>
<td>0.53–1.2 μg/L</td>
<td>40</td>
<td>2–6.7</td>
<td>present</td>
</tr>
</tbody>
</table>

<sup>Refer to Table 3</sup>

*Not given in the literature. Magneto-solid-phase extraction, the same as dSPE.*

### AUTHOR INFORMATION

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