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Research Article

Survey of Octylphenol, Nonylphenol, and Bisphenol A in Infant Milk Powders by Solid-Phase Extraction Combined GC/MS Method

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A detection method for 3 kinds of phenolic compounds of endocrine disruptors (4-nonylphenol, 4-octylphenol, and bisphenol A) in infant milk powders by solid-phase extraction combined GC-MS was established. This method can effectively remove interference materials from infant milk powder products. The limit of detection and the limit of quantitation of the 3 kinds of compounds were 0.8 μg/kg and 2.5 μg/kg, respectively, with the relative standard deviations of 4.3–12.1%. The recovery rates of 4-nonylphenol, 4-octylphenol, and bisphenol A were of 68.5–89.2%, 64.8–87.0%, and 97.8–110.0%, respectively. Concentrations of the bisphenol A were from 0.8 to 14 μg/kg in 35 samples of the total 60 samples. And the other two compounds of 4-nonylphenol and 4-octylphenol were not found in all the 60 samples tested. The established method is simple, rapid, accurate, and highly sensitive, and the pollution of endocrine disruptors in some infant milk powders products was detectable in trace amounts.

1. Introduction

The endocrine disruptors (endocrine disrupting chemicals, EDCs) show potential adverse effects on the function of the hormonal system of humans and animals by reacting with natural hormone receptors [1]. The epidemiological studies showed that the reproduction system, immune system, nervous system, and abnormal behavior as well as the rise in the incidence of several cancers of humans and animals were associated with environmental endocrine disruptors. According to the structure characteristics of endocrine disruptors, EDCs are divided into many polychlorinated biphenyls, phthalates, phenols, heavy metals, organic tin compounds, etc. Phenol endocrine disruptors, including nonylphenol (4-nonylphenol, 4-NP), octylphenol (4-octylphenol, 4-OP), and bisphenol A (bisphenol A, BPA), are widely used as surface active agents, plasticizer, and so on in the production and synthesis of food packaging materials. The *n*-alkyl isomers are more important to our health than other isomeric compounds; for example, 4-t-alkyls are also widely used as plasticizers in industry.

For example, BPA is widely used in plastics, adhesives, flame retardants, and dental composite fillings, which has been investigated in numerous studies showing that its toxic effects are initiated by binding to the estrogen receptor [2]. A study indicated that in mice, BPA altered mammary gland development and caused urethral malformations as well as meiotic aneuploidy [3]. In contrast to other compounds lacking hormonal effects, BPA had been found to be biologically active at doses below the range typically used in toxicological studies [4], several samples of canned fish [5], river water [6, 7], sewage effluents [8], and sewage sludge [9] and had been surveyed for BPA concentration. Similarily to BPA, 4-NP and 4-OP also show high lipophilic ability, and

they are easily concentrated in animal foods with high concentrations of lipid and protein. The present of the three compounds had been detected in some fishery products [10], meat [11], milk [12, 13], and cereal products [14]. And there are many kinds of infant milk powders on the market that are usually packaged by plastic bottles, and the infant milk powders are vulnerable to be polluted by the packaging materials which contain the compounds such as BPA, 4-NP, and 4-OP. Several methods including liquid chromatographic/tandem mass spectrometric (LC-MS) [15], gas chromatography mass spectrometry (GC/MS) [16], liquid chromatography mass spectrometry (LC/MS) [17], and so on were used for trace phenol compounds analysis. The phthalates of dibutyl phthalate, benzyl butyl phthalate, di-"isononyl" phthalate, and di-"isodecyl" phthalate in milk and milk products including infant formulas were extracted by a mixture of tert-butyl methyl ether and hexane from liquid samples, and di-"isononyl" phthalate, di-"isodecyl" phthalate were cleaned up on deactivated silica and the phthalates were detected in positive ion mode after separation on a reversed-phase C_5 analytical column [15]. BPA in 63 of 105 samples, including fresh turkey, canned green beans, and canned infant formula, were detected by GC/MS (GC 6890 Hewlett-Packard and MS 5973 Hewlett-Packard); the levels ranged from 0.23 to 65.0 ng/g and BPA levels were higher for foods of pH 5 compared to more acidic and alkaline foods [16]. Li et al. [17] developed a novel method for the simultaneous determination of five phthalate esters in water by single-drop microextraction (SDME) coupled with gas chromatography.

Detection of BPA and its precursor compounds in commercial milk by HPLC [10] needs special equipment of gel chromatography for pretreatment which can remove the macromolecular compounds such as triglycerides, but the small molecular compounds such as fatty acids, pigments, and phytosterol are not able to be removed, and some of the pretreatment methods need optimization for decreasing the interferences of other chemicals in the samples. The aim of this study was to establish a method for simultaneous analysis of BPA, 4-NP, and 4-OP in infant milk powders by the solid-phase extraction combined GC-MS method and to survey 60 infant milk powders samples in markets of Hangzhou, China.

2. Material and Methods

2.1. Apparatus and Reagents. 6890 GC-5973MS instrument (Agilent, USA) was used for analysis, along with the ultrasonic cleaning machine (Jiangsu Kunshan Ultrasonic Instruments Co., LTD.), solid-phase extraction apparatus (Waters), spiral vortex mixer, nitrogen blowing apparatus, and centrifuge, all from Shanghai Jing Ke Corporation.

n-Hexane, methylene chloride, acetonitrile, and acetone were chromatographic pure from Sinopharm Chemical Reagent Co., Ltd. Sodium bicarbonate and heptafluorobutyric anhydride (HFBA) were analytic pure from Aladdin Corporation, Shanghai, China. 4-OP, 4-NP, BPA, and D_{16}-bisphenol A (D_{16}-BPA) were purchased form Dr Ehrenstorfer GmbH (Germany), and silicone/N-propyl ethylenediamine (silica/PSA) glass hybrid solid phase extraction column was of 1.0 g/6 mL (Hangzhou Fu yu technology service co., LTD). Stock solutions of 4-OP, 4-NP, and BPA (1.0 mg/mL) were made by diluting 25 mg 4-OP, 4-NP, and BPA in 25 mL volumetric flask by chromatographic pure acetonitrile, and then the stock solutions were diluted by chromatographic pure acetonitrile to 0.5 mg/L and stored at 4°C till used.

The internal standard D_{16}-BPA was prepared by diluting 10 mg D_{16}-BPA with 10 mL chromatographic pure acetonitrile, and then the solution was further diluted to 2.0 mg/L and stored at 4°C till used. One percent of sodium bicarbonate solution was made by diluting 1.0 g sodium bicarbonate with pure water to 100 mL. Trichloroacetic acid (TCA, 1% solution) in water was made by diluting 1.0 g TCA with pure water to 100 mL. Sixty milk powders were purchased from a local supermarket in Hangzhou for analysis in 2015.

2.2. Sample Preparation

2.2.1. Samples Pretreatment. All samples were purchased from a local supermarket in Hangzhou, China. Those samples containing starches were mixed, and 2.0 g of the samples was added to a 50 mL centrifuge tube, then 20 μL 2.0 mg/L internal standard solutions was added, and after addition of 0.05 g amylase and 10 mL 45–50°C purified water, the tubes were covered and reacted in 45 ± 1°C for 30 min. The tubes were then cooled to room temperature. Two grams of the samples without starch were added to 50 mL centrifuged tube, and then 20 μL 2.0 mg/L internal standard solutions was added and mixed for further use.

2.2.2. Extraction. The pretreated samples were mixed with 15 mL of 1% TCA and 2 mL of acetonitrile, and then 10 mL of ethyl acetate was added. After vortex blending for 1 min and centrifugation at 10000 rpm for 10 min, the upper ethyl acetate layer was collected into a new 10 mL tube, which contains a few anhydrous sodium sulfate for removal of the water, and then the upper ethyl acetate layer was transferred to a new tube and dried by N_2. The dried sample was dissolved by 2 mL acetonitrile and centrifuged at 10000 rpm for 5 min, and then 2 mL of the acetonitrile phase was collected for purification.

2.2.3. Purification. The silicone/N-propyl ethylenediamine (silica/PSA) glass hybrid solid-phase extraction column (1.0 g/6 mL) was selected for purification of the samples. Silica is highly pure silica (SiO_2) with strong polar adsorbent ability; it can react with the tested components by the hydrogen bonds or dipole interaction. N-propyl ethylenediamine solid-phase adsorbent has strong ion exchange capacity, and it can be used to remove organic acid, pigment, metal ions, and so on in the separation process. The silica/PSA column was firstly treated by addition of a few anhydrous sodium sulfate, and then the column was activated by 5 mL methylene chloride and 5 mL of acetonitrile. After that, the 2 mL collected acetonitrile layer was added to the solid-phase extraction column. After elution

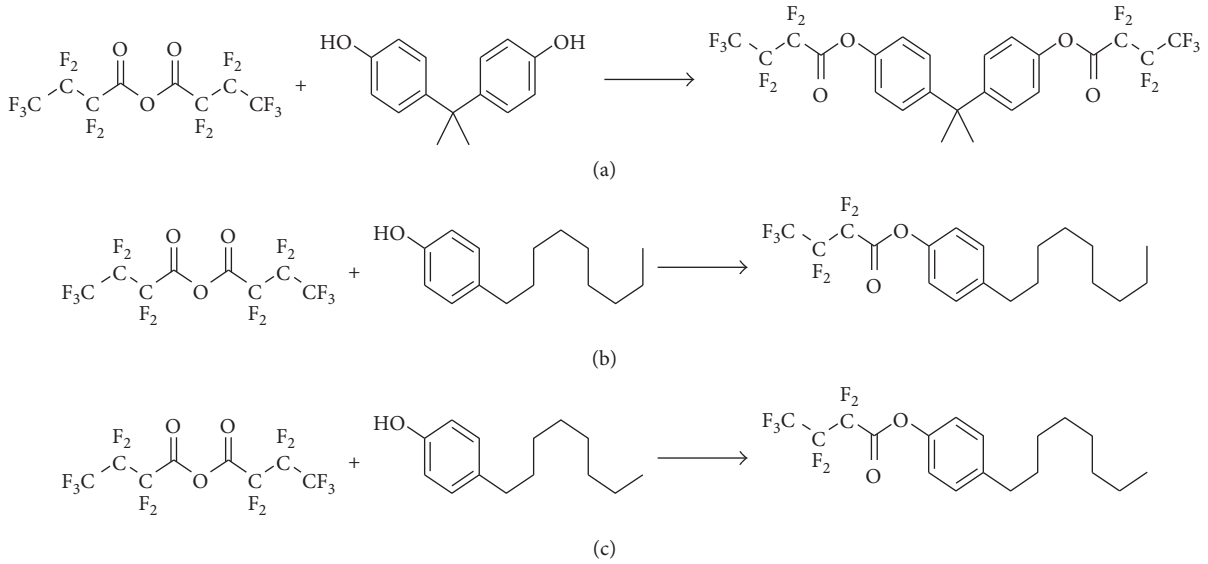

Figure 1: Reactions of HFBA with BPA (a), 4-NP (b), and 4-OP (c).

of the samples, the column was eluted by 5 mL acetonitrile for a second time. Then the two effluents were collected, combined, and dried by N_2. The residues were collected for further derivatization.

2.2.4. Derivatization. The residue was dissolved by 200 μL acetone, and then 60 μL Heptafluorobutyric anhydride was added; after vortex blending for 1 min, the solution was heated at 75°C for 30 min, when it cooled to room temperature, 2 mL 1% sodium bicarbonate was added and mixed. Then 0.5 mL of *n*-hexane was added and vortex blended, after that 0.5 mL *n*-hexane and ethyl acetate in ratio of 4 : 1 (v/v) was added and vortex blended for 1 min; the upper *n*-hexane and ethyl acetate layer was used for GC-MS analysis. Then 5 μL, 25 μL, 50 μL, 100 μL, and 250 μL 0.5 mg/L 4-OP, 4-NP, and BPA solutions with 50 μL 2.0 mg/L inner solution were treated as the standard solution. The reaction mechanism and formulas are listed in Figure 1. After derivatization, the treatments were analyzed by GC-MS for standard curve analysis between 5 and 250 μg/L.

2.2.5. Blank Experiment. The blank experiment was the same as previous steps. Briefly, the silica glass/PSA hybrid solid-phase extraction column was activated by 5 mL methylene chloride and 5 mL of acetonitrile, and then 3 mL of acetonitrile with 50 μL 2.0 mg/L internal standard solution was added, and the elution was collected. Then another 5 mL acetonitrile to the solid-phase column was added and the eluent was collected, and then the collections were combined and dried at 50°C by N_2. The residues were derivatized as the same and analyzed by GC-MS. The infant milk powder system blank experiments were processed as given in Sections 2.2.1–2.2.4.

2.3. GC-MS Chromatographic Conditions. DB-5ms capillary chromatography columns of 30 m × 0.25 mm (inner diameter) x 0.25 μm (film thickness) were used. The injection port temperature was 260°C. The column temperature was initially set at 100°C for 3 min; then it was increased to 270°C at 10°C/min intervals and maintained for 2 min; again it was increased to 300°C at 10°C/min intervals and maintained for 2 min. The carrier gas was high purity helium (99.999%). The injection of 1 μL of sample was splitless at a flow rate of 1 mL/min and was ionized by electron ionization source at 70 eV and 230°C. The results were scanned from 35 to 650 *m/z*. The three kinds of phenolic compounds were qualitatively and quantitatively analyzed by the retention time and fragment ions, respectively. Briefly, the concentrations of the three kinds of phenolic compounds were calculated by the following equation:

$$X = \left(C_i - C_{0i}\right) * 0.5/\mathrm{m}, \tag{1}$$

where X is the concentration of the phenolic compound in the milk sample (μg/kg), m is the milk sample weight (g), C_i is the concentrations of the three kinds of phenolic compounds analyzed (μg/kg), C_{0i} is the concentrations of the three kinds of phenolic compounds analyzed in blank experiments (μg/kg), and 0.5L is the sample diluted volume.

2.4. Validation Experiments. The established analytical method was validated in terms of linearity, standard recovery, and accuracy. To demonstrate linearity, the regression coefficient was calculated using D_{16}-BPA for the three chemicals; the spiked calibrants were analyzed in duplicates during the measurement of the samples. The recovery of the three compounds was determined by spiking experiments of three different spiking levels. A full set of calibration standards and a blank standard were carried out with each analysis.

Table 1: Chromatographic parameters of standard phenol compounds.

Number	Compounds	Retention time	Qualifier ions	Quantifier ions
1	D_{16}-BPA	13.34	616	624
2	4-OP*	10.67	402, 316, 275	303
3	4-NP*	11.76	416, 275, 250	303
4	BPA*	13.42	620, 331, 315	605

*4-OP, 4-NP, and BPA were all quantified by D_{16}-BPA as the inner standards method.

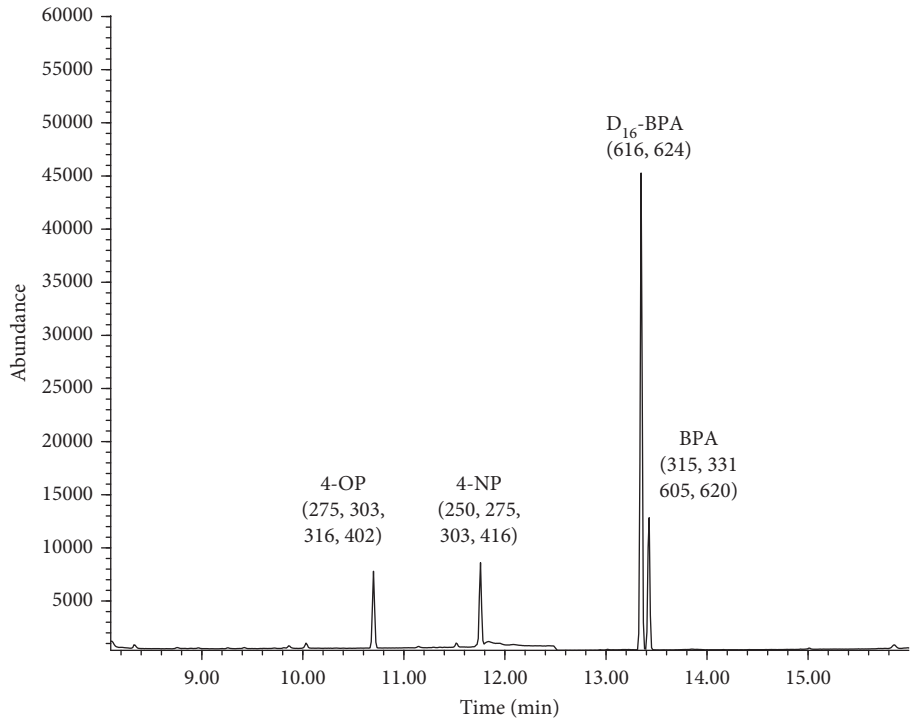

Figure 2: Total ion flow diagrams of 4-octylphenol, 4-nonylphenol, bisphenol A, and D_{16}-BPA.

3. Results and Discussion

3.1. Sample Extraction Optimization. Several pretreatment methods for 4-NP, 4-OP, and BPA analysis were used till now, but some of the purification methods did not meet good analytical standard for the impurities and interferences after derivatization and GC-MS analysis. The authors used acetonitrile to extract phthalic acid esters from infant milk powders [18] and met a good result with removal of most of the glycerides. As for acetonitrile, the impurities were less, most of the acidic acid, pigment, and phytosterol compounds were removed, and the recovery rate of the added standard met the analytical standard. So acetonitrile was selected for 4-NP, 4-OP, and BPA extraction in the further study.

3.2. Solid-Phase Extraction Purification. Two purification methods of gel chromatography and solid-phase extraction are mainly used in 4-NP, 4-OP, and BPA analysis in infant milk powders. The gel chromatography method is difficult to be widely utilized owing to the high price of instrument, high reagent dosage, and high technical requirements, while solid-phase extraction methods are more and more wildly used due to their simple operation procedures and more selectivity in the purification of some complex matrix samples. The silicone/N-propyl ethylenediamine (silica/PSA) glass hybrid solid-phase extraction column (1.0 g/6 mL) was selected for purification of the samples. Silica is the pure silica (SiO_2) with strong polar adsorbent ability; it can react with the tested components by the hydrogen bonds or dipole interaction. N-propyl ethylenediamine solid-phase adsorbent has strong ion exchange capacity, and it can be used to remove organic acid, pigment, metal ions, and so on. in the separation process. In this study, the positive silica glass/PSA

Table 2: LOQ and LOD of 4-OP, 4-NP, and BPA.

Component	LOQ (μg/kg)	LOD (μg/kg)
4-OP	2.5	0.8
4-NP	2.5	0.8
BPA	2.5	0.8

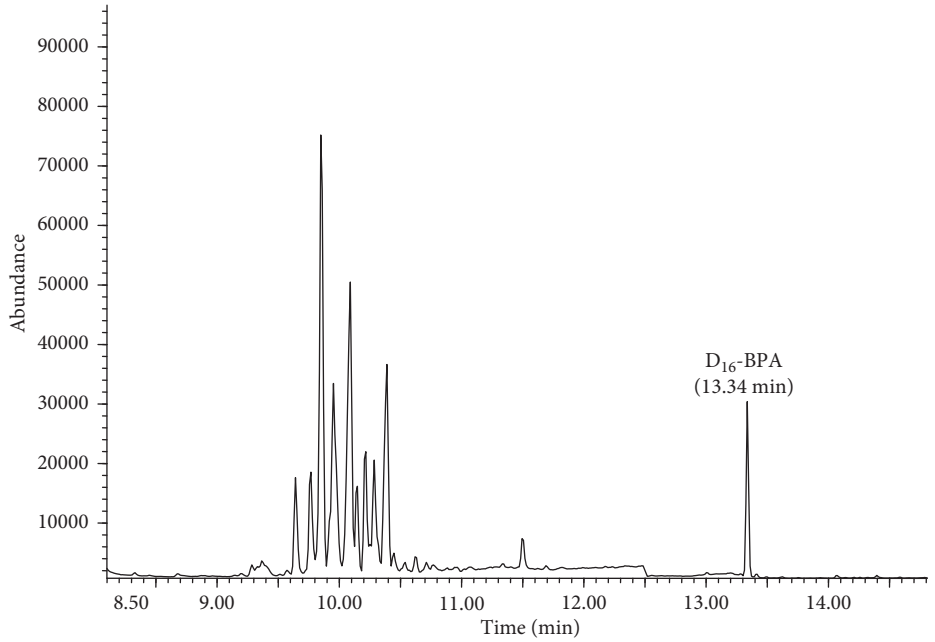

Figure 3: Total ion flow diagram of phenol compounds in blank infant milk powders.

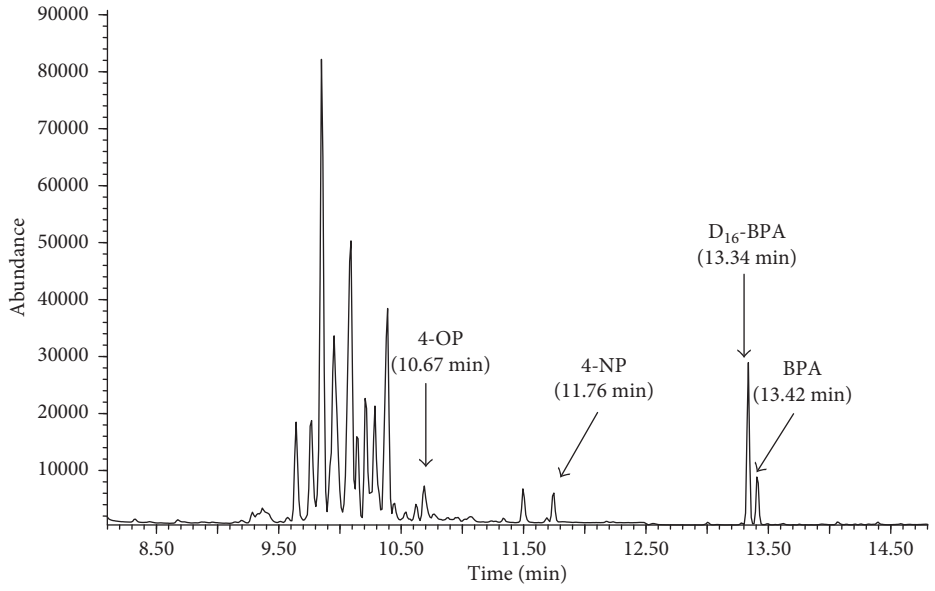

Figure 4: Total ion flow diagram of phenol compounds in infant milk powders with addition of the internal standard (6 μg/kg).

hybrid solid phase extraction column was firstly treated by addition of some anhydrous sodium sulfate to remove water, and then the column was activated by 5 mL methylene chloride and 5 mL of acetonitrile. The activation is based on the opening of the group chain, which will promote the matrix efficiency. Feng et al. [19] and Niu et al. [20] found that there were a certain amount of 4-NP, 4-OP, and BPA in some commercial solid-phase extraction packed material, sieve plate, and tube wall, which introduced higher blank values and was not suitable for analysis. Silica glass/PSA solid-phase extraction column could remove the impurities such as trace phenols in the packing material and sieve plate after elution by methylene chloride and acetonitrile. By this method, the blank values of 4-NP, 4-OP, and BPA in this experiment were all less than the limit of detection (LOD), which showed that it was feasible in terms of control blank value in this study. The silica/PSA glass column could remove pigments and chemical compounds such as phytosterols through adsorption, while 4-NP, 4-OP, and BPA could not be adsorbed and were eluted with acetonitrile. This study

showed a good result by purification of 4-NP, 4-OP, and BPA with acetonitrile and the silica/PSA glass solid-phase column.

3.3. Samples Derivatization. The chemicals of 4-NP, 4-OP, and BPA should be derivatized before being analyzed by GC-MS. The derivatization methods for phenolic compounds analysis include silicon alkylation method and acetoxylation method. The results showed that silicon alkylation reagent can react with many impurities, which led to diverse ion flow diagram of phenolic compounds, so that it is not easy to analyze the fragment ions. The derivatization results between phenolic compounds and acetoxylation chemicals led to high molecular weight of ion fragments which are not susceptible to interference by impurities and were quantitatively accurated. So, the heptafluorobutyric anhydride was used as a derivatization agent in this study.

3.4. Instrument Analysis. The qualitative and quantitative ions and total ions of 4-NP, 4-OP, BPA, and inner standard derivatives of GC-MS are shown in Table 1 and Figure 2, respectively. The LOD and limit of quantitation (LOQ) of all the compounds are shown in Table 2. It is indicated that with D_{16}-BPA as the internal standard, the minimum detectable concentration is 0.8 μg/kg, and the LOQ is 2.5 μg/kg.

3.5. Blank Test. The phenolic compounds were widely presented in the environment due to their pollution, so it was critical to control the blank value for determination of these phenolic compounds. In order to minimize the interference of the background, the glass containers instead of plastic containers were selected. After being heated at 300°C or eluted by *n*-hexane, the glass containers could remove the phenolic compounds. The glass solid-phase extraction column, methylene chloride, and acetonitrile were utilized in this experiment to remove phenolic compounds in the sieve plate and the packing material. The results showed that the contents of 4-OP, 4-NP, and BPA were all less than the LOD concentration of 0.8 μg/kg.

3.6. Precision, Detection Limit, and Recovery Rate. In accordance with the established method, the LOD and the LOQ of the three kinds of compounds were 0.8 μg/kg and 2.5 μg/kg; different concentrations of the three kinds of standard phenolic compounds solutions were added to milk powders to test the method recovery rate, and the results showed that the recovery rate of 4-nonylphenol, 4-octylphenol, and BPA were of 68.5–89.2%, 64.8–87.0%, and 97.8–110.0%, respectively, and the relative standard deviation (RSD) was 4.3–12.1%. The total ion flow charts of these three kinds of phenolic compounds analyzed in the milk powders and with addition of the internal standard are shown in Figures 3 and 4, respectively.

Comparing with these analytical methods, the detection limits of dimethyl phthalate, diethyl phthalate, dibutyl phthalate, diethylhexyl phthalate, and di-*n*-octyl phthalate were 0.042, 0.0037, 0.0097, 0.045, and 0.23 μg/L, respectively.

Table 3: Analysis results of 4-OP, 4-NP, and BPA in 60 infant milk powder samples.

Sample numbers	BPA results (μg/kg)
1	—
2	1.7
3	1.3
4	1.0
5	1.6
6	—
7	—
8	—
9	—
10	1.9
11	—
12	1.2
13	2.3
14	3.7
15	0.9
16	1.4
17	8.0
18	1.8
19	—
20	—
21	—
22	—
23	—
24	—
25	14.0
26	1.7
27	1.6
28	3.0
29	—
30	2.1
31	2.0
32	—
33	1.8
34	1.3
35	—
36	—
37	1.6
38	0.9
39	1.3
40	1.7
41	1.2
42	—
43	1.6
44	1.1
45	—
46	—
47	—
48	—
49	3.0
50	—
51	1.3
52	3.1
53	—
54	1.9
55	1.6
56	—
57	—
58	1.2
59	3.4
60	0.8

*4-OP and 4-NP could not be detected.

The method was applied for the determination of the five phthalate esters in river, lake, tap, and drinking water, and the relative standard deviations were from 1.4% to 14.0%; recoveries of five phthalate esters were 90.8%–107.0% [17]. Also, Schecter et al. [16] reported that the BPA levels ranged from 0.23 to 65.0 ng/g (w/w) and were not associated with type of food or packaging but did vary with pH value. The LOD and LOQ were of 0.05 and 0.11 ng/g (w/w) based on 15 g (w/w) (sample intake), respectively, and the limits of detection was 0.20 ng/g wet weight (w/w).

3.7. Sample Analysis. Sixty samples of different brands were bought and analyzed by the method above, and the results are shown in Table 3. There are 10 brands of infant milk powders, and the first one has 8 samples from two corporations (4 + 4), the second brand has 6 samples, the third one has 7 samples from three manufacture factories (1 + 5 + 1), the fourth brand has 14 samples from four factories (6 + 5 + 2 + 1), the fifth brand has 9 samples from two factories (7 + 2), and then the last five brands have 6, 5, 2, 2, 1 samples, respectively. There were no 4-OP and 4-NP detected in all the 60 samples, and concentrations of BPA were from 0.8 to 14 μg/kg in 35 samples of the total 60 samples, which indicated the existence of BPA in formula milk powders, and the 35 samples came from 9 brands. The U.S. Environmental Protection Agency (EPA) and European Food Safety Authority (EFSA) have a BPA reference dose/tolerable daily intake (TDI) of 50 μg/kg/day [21, 22]. Children ages 1.5–6 years have been reported to have BPA intake ranging from 0.043 to 14.7 μg/kg/day, whereas children ages 6–19 years have BPA intake ranging from 0.311 to 0.348 μg/kg/day [16]. As per the results tested in the samples, the maximal concentration of BPA is 14 μg/kg, and a 20 kg child will consume 14 μg/d (0.05 kg per day) or 28 μg/d (0.1 kg per day), which is lower than the TDI of EPA or EFSA. Considering other food resources packed by plastics or other conditions, it is better to analyze or reduce the utilization of plastics packages.

4. Conclusion

A detection method for 3 kinds of phenolic compounds of endocrine disruptors (4-NP, 4-OP, and BPA) in infant milk powders by solid-phase extraction combined with GC-MS method was established. The LOD and LOQ of the 3 kinds of compounds were 0.8 μg/kg and 2.5 μg/kg, respectively, with the RSD of 4.3–12.1%. The recovery rates of 4-NP, 4-OP, and BPA were of 68.5–89.2%, 64.8–87.0%, and 97.8–110.0%, respectively. In accordance with the established method, 60 kinds of infant milk powders in the market of Hangzhou were analyzed for the survey of 4-NP, 4-OP, and BPA, and the results showed that there were no 4-NP and 4-OP analyzed in all the samples, and concentrations of BPA were from 0.8 to 14 μg/kg in 35 samples of the total 60 samples, which is lower than the TDI value of 50 μg/kg/day of EPA and EFSA calculated according to a 20 kg child consuming 0.1 kg milk powder, but considering other different foods contacted with the plastics containing BPA, it is necessary to control the overall BPA possible consumed.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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References

[1] R. W. Tyl, C. B. Myers, M. C. Marr et al., "Two-generation reproductive toxicity study of dietary bisphenol-A in CD-1 (Swiss) mice," *Toxicological Sciences*, vol. 104, no. 2, pp. 362–384, 2008.

[2] C. M. Markey, E. H. Luque, M. Munoz de Toro, C. Sonnenschein, and A. M. Soto, "In uteroexposure to bisphenol A alters the development and tissue organization of the mouse mammary gland," *Biology of Reproduction*, vol. 65, no. 4, pp. 1215–1223, 2001.

[3] B. G. Timms, K. L. Howdeshell, L. Barton, S. Bradley, C. A. Richter, and F. S. Vom Saal, "Estrogenic chemicals in plastic and oral contraceptives disrupt development of the fetal mouse prostate and urethra," *Proceedings of the National Academy of Sciences*, vol. 102, no. 19, pp. 7014–70193, 2005.

[4] W. V. Welshons, K. A. Thayer, B. M. Judy, J. A. Taylor, E. M. Curran, and F. S. Vom Saal, "Large effects from small exposures: I. mechanisms for endocrine-disrupting chemicals with estrogenic activity," *Environmental Health Perspectives*, vol. 111, no. 8, pp. 994–1006, 2003.

[5] P. Dagmar and C. M. Margit, "Determination of bisphenol A in canned fish by sol–gel immunoaffinity chromatography, HPLC and fluorescence detection," *European Food and Research Technology*, vol. 224, no. 5, pp. 629–634, 2007.

[6] T. Suzuki, Y. Nakagawa, I. Takano, K. Yaguchi, and K. Yasuda, "Environmental fate of bisphenol A and its biological metabolites in river water and their exo-estrogenic activity," *Environmental Science & Technology*, vol. 38, no. 8, pp. 2389–2396, 2004.

[7] P. Hohenblum, O. Gans, W. Moche, S. Scharf, and G. Lorbeer, "Monitoring of selected estrogenic hormones and industrial chemicals in ground waters and surface waters in Austria," *Science of the Total Environment*, vol. 333, no. 1–3, pp. 185–193, 2004.

[8] R. Jeannot, H. Sabik, E. Sauvard, T. Dagnac, and K. Dohrendorf, "Determination of endocrine-disrupting compounds in environmental samples using gas and liquid chromatography with mass spectrometry," *Journal of Chromatography A*, vol. 974, no. 1-2, pp. 143–159, 2002.

[9] R. J. W. Meesters and H. F. Schroder, "Simultaneous determination of 4-nonylphenol and bisphenol A in sewage sludge," *Analytical Chemistry*, vol. 74, no. 14, pp. 3566–3574, 2002.

[10] S. Meier, J. Klungsoyr, S. Boitsov, T. Eide, and A. Svardal, "Gas chromatography–mass spectrometry analysis of alkylphenols in cod (*Gadus morhua*) tissues as pentafluorobenzoate derivatives," *Journal of Chromatography A*, vol. 1062, no. 2, pp. 255–268, 2005.

[11] B. Shao, H. Han, D. Li, Y. Ma, X. Tu, and Y. Wu, "Analysis of alkylphenol and bisphenol A in meat by accelerated solvent extraction and liquid chromatography with tandem mass

spectrometry," *Food Chemistry*, vol. 105, no. 3, pp. 1236–1241, 2007.

[12] N. C. Maragou, E. N. Lampi, N. S. Thomaidis, and M. A. Koupparis, "Determination of bisphenol A in milk by solid phase extraction and liquid chromatography–mass spectrometry," *Journal of Chromatography A*, vol. 1129, no. 2, pp. 165–173, 2006.

[13] B. Shao, H. Han, X. Tu, and L. Huang, "Analysis of alkylphenol and bisphenol A in eggs and milk by matrix solid phase dispersion extraction and liquid chromatography with tandem mass spectrometry," *Journal of Chromatography B*, vol. 850, no. 1-2, pp. 412–416, 2007.

[14] R. Carabias-Martinez, E. Rodriguez-Gonzalo, and P. Revilla-Ruiz, "Determination of endocrine-disrupting compounds in cereals by pressurized liquid extraction and liquid chromatography–mass spectrometry: Study of background contamination," *Journal of Chromatography A*, vol. 1137, no. 2, pp. 207–215, 2006.

[15] L. K. Sorensen, "Determination of phthalates in milk and milk products by liquid chromatography/tandem mass spectrometry," *Rapid Communications in Mass Spectrometry*, vol. 20, no. 7, pp. 1135–1143, 2006.

[16] A. Schecter, N. Malik, D. Haffner et al., "Bisphenol A (BPA) in U.S. food," *Environmental Science & Technology*, vol. 44, no. 24, pp. 9425–9430, 2010.

[17] M. X. Li, J. H. Wu, W. Zeng, and Z. L. Ma, "Determination of phthalate esters in water by single-drop microextraction coupled with gas chromatography," *Chinese Journal of Analytical Chemistry*, vol. 34, no. 8, pp. 1172–1174, 2006.

[18] P. G. Wu, X. D. Pan, L. Y. Wang, X. H. Shen, and D. J. Yang, "A survey of ethyl carbamate in fermented foods and beverages from Zhejiang, China," *Food Control*, vol. 23, no. 1, pp. 286–288, 2012.

[19] R. Feng, X. J. Yu, M. L. Ni et al., "Determination of five kinds of bisphenol A nonylphenol and octyl phenolic compounds in solid phase extraction column by isotope dilution-liquid chromatography tandem mass spectrometry," *Environmental Chemistry*, vol. 31, no. 9, pp. 1456-1457, 2012, in Chinese.

[20] Y. M. Niu, J. Zhang, S. J. Zhang, and B. Shao, "Determination of bisphenol A, nonylphenol and octylphenol in animal food by isotopic dilution liquid chromatography tandem mass spectrometry," *Chinese Journal of Analytical Chemistry*, vol. 40, no. 4, pp. 534–538, 2012.

[21] The European Food Safety Authority, "Opinion of the scientific panel on food additives, flavourings, processing aids and materials in contact with food on a request from the commission related to 2,2-BIS(4-HYDROXYPHENYL) PROPANE (bisphenol A)," *EFSA Journal*, vol. 4, no. 11, pp. 1–75, 2006.

[22] L. N. Vandenberg, M. V. Maffini, C. Sonnenschein, B. S. Rubin, and A. M. Soto, "Bisphenol-A and the great divide: A review of controversies in the field of endocrine disruption," *Endocrine Reviews*, vol. 30, no. 1, pp. 75–95, 2009.