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Original Paper

Hybrid silica polymeric monolith-based in-tube microextraction and CE for determination of bisphenol A in beverages

On-line concentration techniques in capillary electrophoresis, including stacking and sweeping, have a weak tolerance towards complex real samples. A phenyl-functionalized hybrid silica monolithic polymeric capillary column (id 530 μm) was prepared by *in-situ* co-condensation of phenyltriethoxysilane (PTES) and tetraethoxysilane (TEOS). In order to enhance the stability of a monolithic column within a wide-bore capillary, a novel and simple frit-preparation method for wide-bore capillaries was first introduced by immobilizing a short length of capillary of suitable outer diameter at the end of the monolithic capillary column during condensation of the sol-gel solution. The monolithic column was used for the extraction of bisphenol A (BPA) from cola samples, and the interfering compounds can be removed from the samples with 40% ACN solution (v/v) as eluent. The pretreated samples were further concentrated and separated using large-volume stacking and sweeping micellar electrokinetic chromatography. The method was successfully applied to the determination of bisphenol A spiked in cola, yielding a detection limit of 1.8 ng/mL. Close correlation coefficients and acceptable method reproducibility were obtained for bisphenol A over a linear range of 0.005–0.200 μg/mL.

Keywords: Bisphenol A / Hybrid silica monolithic column / Microextraction

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1 Introduction

Recently, endocrine disrupting chemicals (EDCs) have been found in the environment and can adversely affect animals and human [1, 2]. EDCs of either natural or synthetic origin have the ability to interfere with the normal functioning of the endocrine system and the reproductive system. Bisphenol A (BPA), used as stabilizing material or antioxidant for numerous types of plastics [3], has been discharged directly or indirectly into the environment, contaminating the atmosphere, water, and soil. It has also been shown that BPA is leached from lacquer-coated cans [4] and baby feeding bottles [5] due to hydrolysis of the polymer during thermal treatment. BPA is slightly toxic and has a low potential for bioaccumulation in aquatic organisms. It has been demonstrated to exhibit estrogenic activity [4, 6] and is classified as an endocrine disrupter in many countries. It is very important to monitor BPA in drinking water or beverage samples.

Numerous methods have been developed to identify trace BPA in various matrices. However, they are based primarily on GC and LC methods [7–14]. Capillary electrophoresis (CE), a family of high-resolution separation techniques, can be advantageous over HPLC in terms of simplicity, resolution, and economy. Despite these advantages, CE suffers from poor concentration sensitivity as a consequence of the limited sample volume and short path length when using conventional UV absorbance detection. In CE with absorbance detection it is difficult to measure sub-micromolar levels of analytes. Therefore, it is necessary to develop sample preconcentration methods. Concentration methods include electrokinetic and chromatographic techniques [15]. Sample stacking is the simplest technique for on-line sample concentration. The concentrating effect basically relies on the change in electrophoretic velocities when the analytes reach the interface between the sample zone and background solution zone [16–18], which is related to the difference of these zones in conductivity [19]. In sweeping MEKC, the pseudostationary phases entrap and accumulate the ana-

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Abbreviations: BPA, bisphenol A; **EDCs,** endocrine disrupting chemicals; **PTES**, phenyltriethoxysilane; **SPME**, solid-phase microextraction; **TEOS**, tetraethoxysilane

lytes as they pass the sample zone [20]. The concentration effect relies on the affinity of the analyte toward the pseudostationary phases that enter the sample solution zone [19, 21, 22]. Although stacking and sweeping are the simple on-line concentration techniques in capillary electrophoresis, they have a weak tolerance towards complex real samples. Anion- or cation-selective exhaustive injection is not suitable for the injection of neutral or weakly ionized compounds. Therefore, sample pretreatment is often necessary for the analysis of real samples and enrichment of analytes.

Compared with solid-phase extraction and liquid-liquid extraction, solid-phase microextraction (SPME), including in-tube SPME, is the most promising sample preparation technique [23–25]. This method not only saves sample preparation time, reduces solvent and sample consumption, but also can lower the detection limit. The enrichment ability and extraction selectivity of SPME depend mainly on the properties and the phase ratio of coating materials. The polymeric monolithic material can be easily synthesized *in situ* and provides tunable monolithic structures and tailored functional groups for specific purposes. Moreover, the monolithic porous structure offers convective mass transfer procedure and high specific surface area [26], which is preferable in extraction processes. The monolithic column has emerged as a popular alternative to the packed capillary column due to the simplicity of their preparation as well as the diverse surface chemistry. Recently, both organic polymer [27–30] and silica-based [31] monoliths have also been used as SPME media.

Silica-based monolithic columns are typically prepared directly inside the capillary via a sol–gel process and the surface is subsequently modified by silanization to anchor the stationary phases under rigorously anhydrous conditions. The preparation procedure is tedious. As an alternative, a hybrid organic-inorganic silica monolithic column can be easily prepared in a single step by co-condensation of the functional monomer to generate a desirable chromatographic surface [32–35]. Recently, an octyl-functionalized hybrid silica monolithic column synthesized via co-condensation of tetraethoxysilane and *n*-octyltriethoxysilane has been developed for in-tube SPME coupled to capillary HPLC [36]. The size of through-pores as well as the carbon content can be adjusted by changing the ratio of TEOS to functional monomer in the polymerization mixture. Another kind of hybrid silica-based monolith with sulfonic acid groups was applied to purify and enrich the target analytes in human urine [37]. In addition, a novel bimodal porous *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane-silica monolithic capillary was prepared and used as microextraction column for aluminum fractionation [38].

In this work, a phenyl-functionalized hybrid silica monolithic column (id 530 μm) for in-tube solid-phase microextraction was prepared in a single step by sol–gel technology. A novel frit-preparation method for wide-bore capillary was reported for the first time. The in-tube microextraction conditions for BPA spiked in water and beverages were optimized. Consequently, on-line preconcentration methods, including stacking and sweeping, combined with off-line solid-phase microextraction, were investigated for the CE analysis of BPA in cola.

2 Experimental

2.1 Chemicals and materials

Tetraethoxysilane (98%, TEOS) was purchased from the Chemical Plant of Wuhan University (Wuhan, China) and used directly without further purification. Phenyltriethoxysilane (98%, PTES) and *n*-dodecylamine (98%) were purchased from ABCR GmbH & Co. KG (Karlsruhe, Germany). HPLC-grade methanol and acetonitrile (ACN) were supplied by Yuwang Chemical Plant (Zibo, Shandong Province, China). All other chemicals used in the experiment were of analytical grade and were obtained from Shanghai Reagent Factory (Shanghai, China). Water used in all of the experiments was doubly distilled and purified by a Milli-Q system (Millipore, Milford, USA). All capillaries were purchased from Yongnian Optic Fiber Plant (Hebei, China).

2.2 Preparation of hybrid monolithic capillary column with frit

The hybrid monolith was *in-situ* synthesized inside a fused silica capillary (id 530 μm × od 690 μm) according to a previously described procedure with some modifications [33, 35]. In order to clean the inner surface and expose the maximum number of silanol groups thereon, the capillary was first flushed with 1 M NaOH for 0.5 h, and then, after sealing both ends, placed in a water bath at 60°C for 2 h. After that, it was rinsed with water, 0.1 M HCl, water, and methanol for 0.5 h each. Subsequently, the capillary was dried at 115°C under nitrogen gas flow for 4 h prior to the next step. The prepared precursor solution, containing TEOS (80–90 μL) and PTES (70–75μL), was mixed with the porogen solution, consisting of methanol (230 μL) and 0.2 M HCl solution (40 μL), in a vial. After thorough vortexing, the solution was placed in a water bath at 60°C for 3 h. Following ultrasonication for 15 min at 0°C, *n*-dodecylamine (15 mg) was added to the solution. After vigorous vortexing, the resulting homogeneous mixture was sucked into a 15 cm length of the pretreated capillary to a length of about 14 cm, then a short (5 mm) length of capillary (200 μm id × 320 μm od) was inserted into the end of the 530 μm id capillary. With both ends sealed by rubber, the capillary was submerged in a water bath at 40°C overnight. Subsequently,

the column was taken out and rinsed with methanol and ACN for 1 h each. Finally, the monolithic column was flushed with 50% ACN solution and 50% methanol solution for 1 day each, then conditioned with H_2O prior to use.

2.3 Apparatus

All CE experiments were carried out on a Beckman P/ACE™ instrument from Beckman Coulter (Fullerton, CA, USA) equipped with a photo diode array detector (190–600 nm), automatic injector, fluid-cooled column cartridge, and Gold Data Station. The separations were performed in an uncoated fused-silica capillary of 60 cm × 50 μm id (effective length, 50 cm).

The in-tube SPME device for this study is similar to that described in Feng's report [39]. The overall system consists of a regular plastic syringe (1 mL), a plastic pinhead (one part of the whole syringe), the hybrid monolithic capillary tube (id 530 μm × 14 cm), and a hand-assisted syringe pump (Unimicro Anal. Tech. Co., Shanghai, China). The hybrid monolithic capillary was inserted into the metallic needle, and the space between the outer surface of capillary and the inner surface of the metallic needle was sealed with adhesive, while the other end of the pinhead was coupled seamlessly to the syringe barrel.

2.4 Samples and buffers

Stock solutions of 0.10 and 0.01 mg/mL BPA were prepared in methanol. The samples for extraction were prepared by diluting the stock solution of BPA to the appropriate concentrations with H_2O or cola (CocaCola Co., Wuhan, China). The samples for CE were prepared by evaporating the eluates of the extracted samples almost to dryness and then redissolving them in solutions containing low concentrations of H_3PO_4 and SDS. Stock solutions of 0.5 M H_3PO_4 and 0.4 M SDS were prepared in purified water. Non-micellar buffers (H_3PO_4 200 mM, ACN 10–30%, v/v) were prepared by diluting stock solutions of H_3PO_4 with water and ACN. Micellar buffers (H_3PO_4 200 mM, SDS 50 mM, ACN 10–30%, v/v) were prepared by diluting the stock solutions of H_3PO_4 and SDS with water and ACN.

2.5 SPME and CE experiments

The overall SPME procedure consisted in preconditioning, sample loading, washing, and desorption. A syringe pump employed for delivery automatically provided smooth and regular movement of the syringe plunger in a highly reproducible manner. For preconditioning, the hybrid monolithic column was rinsed with 0.2 mL of methanol by the syringe pump, and then rinsed with 0.2 mL of purified water. After that, the sample solution was pumped through the hybrid monolithic column at approximately 0.02 mL/min. Subsequently, 0.2 mL of purified water was flushed to remove the residual sample solution. For desorption, the hybrid monolithic column was eluted with ACN solution (30–75%, v/v) at a flow rate of about 0.02 mL/min. The eluates were collected in segments for subsequent analysis by CE. To avoid contamination, separate syringes were used for injection sample, buffer, and desorption solution, respectively.

The capillary for CE was rinsed with methanol solution (1:1, methanol/H_2O, v/v) and purified water for 5 min at 103.5 kPa (15 psi), respectively, then conditioned by rinsing with non-micellar buffer (H_3PO_4 200 mM, ACN 10–30%, v/v) between consecutive analyses. CE analyses were carried out by applying a voltage of −15 kV while both ends of the capillary were immersed in micellar buffer (H_3PO_4 200 mM, SDS 50 mM, ACN 10–30%, v/v). The temperature was kept at 25°C and the detection wavelength was set at 192 nm.

3 Results and discussion

3.1 Preparation of monolithic polymeric capillary column (id 530 μm) with frit

The recently introduced hybrid organic–inorganic silica monolithic column represents an attractive direction in chromatography. Various silane co-precursors containing functional groups could be directly incorporated in the reaction mixture with the aid of catalysts and appropriate solvents [32, 33, 35, 40]. In our experiment, two sol–gel precursors, PTES and TEOS, were used for the preparation of monolithic columns *via* a two-step catalytic sol–gel process [33]. The phenyl groups were incorporated into the monolithic materials through the neutral amine assembly pathway [40]. The high permeability and specific surface area of porous monolithic polymeric column are very important for highly efficient extraction. It is thought that PTES plays an important role in phase separation and size-control of the hybrid silica skeleton and macropores of resultant gels. The composition of the polycondensation mixture was optimized to attain a compromise between mechanical strength and permeability for a capillary with id 530 μm. The optimized PTES/TEOS ratio in the experiment was 73:87 v/v while the total volume of these precursors was 160 μL and the volumes of methanol and HCl (0.2 M) were fixed at 230 and 40 μL, respectively.

The porous monolithic capillary columns without frits are usually prepared via *in-situ* polymerization in capillaries with inner diameter lower than 250 μm. Recently, polymer monolithic capillary columns with id 530 μm have been reported by Feng *et al*. [30]. However, the stabil-

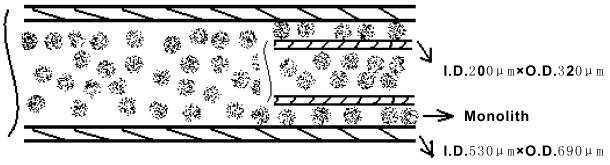

Figure 1. Frit preparation.

ity of the column bed would decrease with increasing capillary inner diameter, and the conventional frit-preparation technique performed by sintering silica at the end of capillary column with small inner diameter is not suitable for capillaries with inner diameter of 530 μm. It is therefore important to establish a simple frit-preparation method for wide-bore capillary. In this paper, we first proposed a novel frit-preparation method suitable for wide-bore capillary by immobilization of a short length of capillary at the end of monolithic column during the condensation of sol-gel solution (as shown in Fig. 1). In the extraction experiments, it is found that the hybrid monolithic column with frit can endure alternate rinsing with organic or aqueous solution for a total solution volume of more than 60 mL, while the column without frit could only endure less than 20 mL. These results show that the simple frit-preparation method can significantly enhance the mechanical stability of column bed.

3.2 Optimization of on-line concentration in CE

3.2.1 Choosing the sample matrix

Sample stacking is performed by preparing the sample in a matrix having a resistance considerably higher than that of the background solution. The concentrating effect basically relies on the change in electrophoretic velocities when the analytes reach the interface between the sample zone and the background solution zone. Because BPA is weakly deprotonated, SDS and phosphate acid should be added to the sample solution prior to CE injection. The effect of the composition of sample matrix on stacking efficiency is investigated. Figure 2 illustrates the relationship between peak area and phosphoric acid concentration in the sample containing 4 mM SDS. The peak area increases to a maximum value as the concentration of phosphoric acid increases to 10 mM, and then decreases with further increase in acid concentration. The effect of SDS concentration on stacking efficiency was also investigated, while the concentration of phosphoric acid was kept at 10 mM. As shown in Fig. 3, the peak area reaches the maximum value at an SDS concentration of 4 mM. However, the peak shapes will deteriorate if the SDS concentration further increases.

It is known that the CMC of SDS decreases with increasing ionic strength of the sample solution [41], which means there would be more BPA in the neutral form and stronger interaction between BPA and micelles with

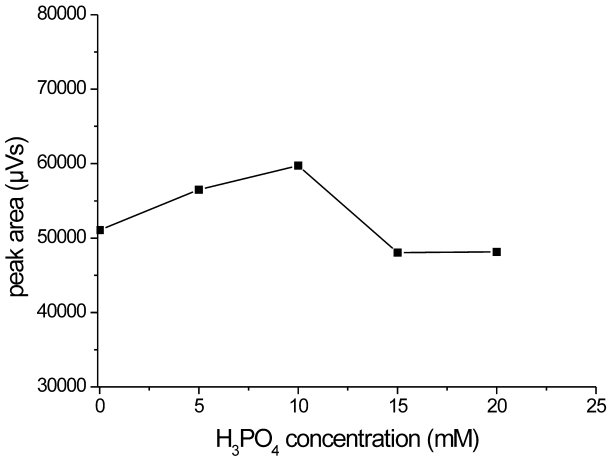

Figure 2. Effect of different concentrations of phosphoric acid in sample matrix on the stacking of BPA. Sample matrix: SDS 4 mM, BPA 1 μg/mL. Injection: H_2O 60 s/6.9 kPa (1 psi) and sample 90 s/6.9 kPa (1 psi). Non-micellar buffer: H_3PO_4 200 mM, ACN 20% (v/v). Micellar buffer: H_3PO_4 200 mM, SDS 50 mM, ACN 20% (v/v). Applied voltage: −15 kV.

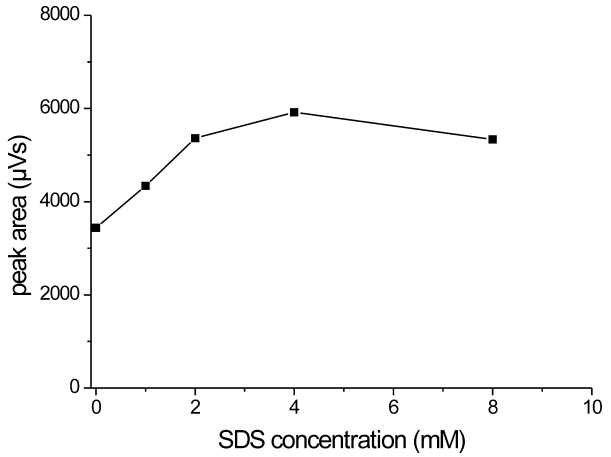

Figure 3. Effect of different concentrations of SDS in sample matrix on the stacking of BPA. Sample matrix: H_3PO_4 10 mM, BPA 0.10 μg/mL. Other conditions are the same as those in Fig. 2.

increasing acid concentration. However, as the acid concentration increased, there was a corresponding decrease in electric field strength in the sample matrix. This led to a reduction in stacking efficiency. The combination of these factors yielded an optimum stacking condition. Consequently, the eluates of the samples were adjusted to the matrices containing 4 mM SDS and 10 mM phosphoric acid prior to CE injection in the following experiments.

3.2.2 Injection length of sample zone and standard sample analysis

Chien [42] had demonstrated that a water plug introduced before large-volume sample injection in field-

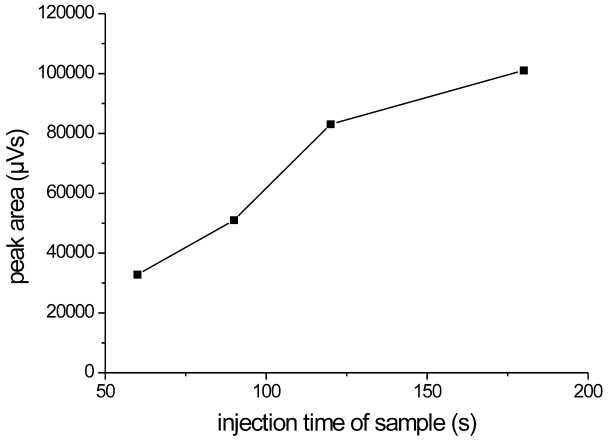

Figure 4. Effect of different injection lengths of sample on the enrichment of BPA with the injection of water being fixed at 60 s/6.9 kPa (1 psi). Sample matrix: SDS 4 mM, H_3PO_4 10 mM, and BPA 1.0 μg/mL. Buffers and applied voltage are the same as those in Fig. 2.

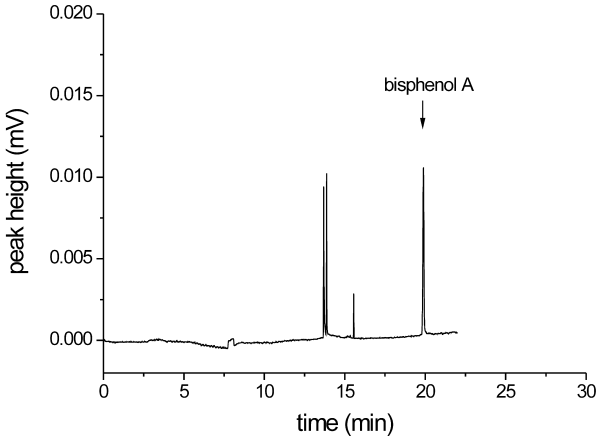

Figure 5. Separation of standard sample. Sample matrix: SDS 4 mM, H_3PO_4 10 mM, and BPA 1.0 μg/mL. Injection: H_2O 60 s/6.9 kPa (1 psi) and sample 90 s/6.9 kPa (1 psi). Non-micellar buffer: H_3PO_4 200 mM, ACN 20% (v/v). Micellar buffer: H_3PO_4 200 mM, SDS 50 mM, ACN 20% (v/v). Applied voltage: −15 kV.

amplified sample injection provided a high electric field at the tip of the capillary, and markedly improved the sample stacking procedure. In our experiments, a section of purified water (60 s/6.9 kPa (1 psi)) was also introduced before sample injection. The effect of increasing the length of the sample zone on the enrichment of BPA was investigated. As shown in Fig. 4, peak areas of BPA increase with an increase in the fraction of capillary filled with sample zone. However, a longer injection length might result in deterioration of peak shapes. Consequently, 90 s/6.9 kPa (1 psi) was chosen for sample injection in the following experiments.

The concentrations of phosphoric acid, SDS, and ACN in buffer were also optimized. The optimized conditions are summarized as follows: nonmicellar buffer contains 200 mM H_3PO_4 and 20% ACN (v/v), micellar buffer contains 200 mM H_3PO_4, 50 mM SDS and 20% ACN (v/v). The standard sample separated in MEKC under optimized conditions is shown in Fig. 5. Besides stacking, sweeping also participated in the on-line enrichment of BPA due to the reverse migrating micelles which come from the vial in the cathode.

3.3 Optimization of SPME conditions

3.3.1 Equilibrium extraction volume profile

In order to assess the extraction capacity of the hybrid silica monolithic column for BPA, the extraction volume profiles were constructed by increasing the volume of the extracted sample from 0.2 to 2.0 mL at an extraction flow rate of about 0.02 mL/min on extracting a sample solution containing 0.10 μg/L BPA. As shown in Fig. 6, a linear increase of the extracted amount is found with increasing extraction volume, and equilibrium has not been reached at an extraction volume of up to 2.0 mL, which indicates the great extraction capacity of this monolithic material toward BPA. In fact, the linear range of extraction volume profile is restricted by the on-line concentration method in CE.

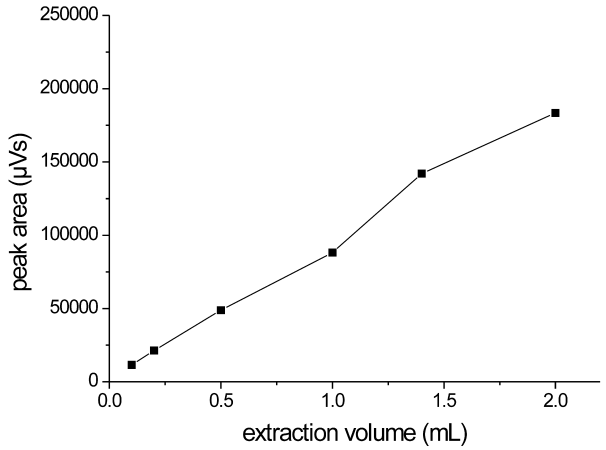

Figure 6. Extraction volume profile for BPA using SPME. SPME conditions: Sample, 0.10 μg/mL BPA in purified water; eluent, 75% ACN solution (v/v); extraction flow rate, 0.02 mL/min. CE conditions are the same as those in Fig. 5.

3.3.2 Effect of sample pH and flow rate on extraction

The pH of standard sample solutions was controlled by diluting BPA stock solution with 20 mM phosphate buffer solution. The effect of sample pH on extraction was investigated in the range from pH 3 to 8, and the peak areas of extracted BPA remained at the same values without too much variation. As the pH values are lower than the pK_a of BPA (9.6–11.3), the BPA molecule seldom loses

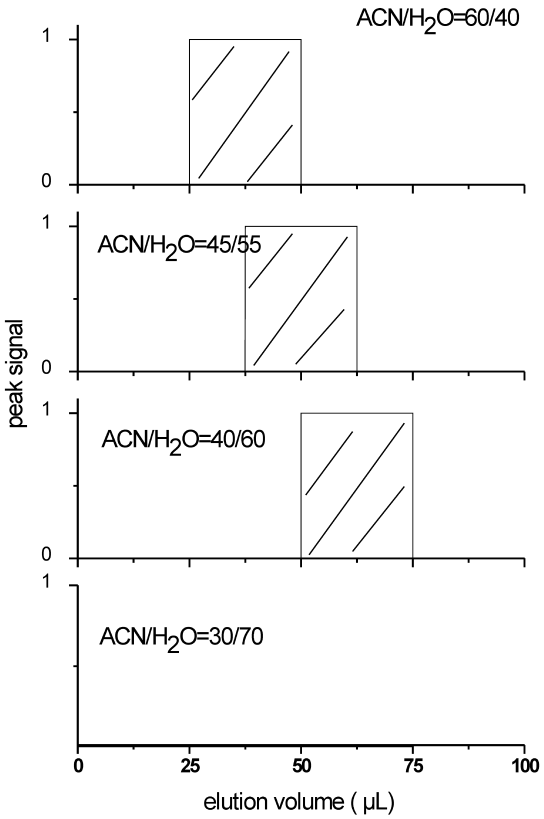

Figure 7. Effect of ACN content in elution on the desorption of BPA. Sample matrix for extraction: 0.20 μg/mL BPA in water. SPME conditions: Extraction volume, 1 mL; eluent, 30–75% ACN solution (v/v); sample, eluates collected at different elution volumes. CE conditions are the same as those in Fig. 5.

its proton and mainly exists as the neutral species under acid and neutral conditions. Its adsorption on the monolithic capillary column was mainly based on hydrophobic interaction with the phenyl pendant groups of the polymer. Therefore, the raw cola samples were directly used for the subsequent extraction without pH adjustment.

The flow rate of the sample solution was investigated in the range of 0.01–0.05 mL/min, and no obvious change in extraction efficiency was found. A higher flow rate was not favorable since an increase of flow resistance was found, which occasionally led to leakage of sample solution from the junction between the plastic pinhead and the syringe barrel. Therefore, 0.02 mL/min was selected. A higher flow rate may be adopted if the home-made SPME device is improved.

3.3.3 Effect of ACN concentration on desorption

The effect of ACN content in the eluent on the desorption of BPA was investigated. The results are shown in Fig. 7, from which it can be seen that BPA can be eluted completely in the eluate collected between 37.5 and 62.5 μL

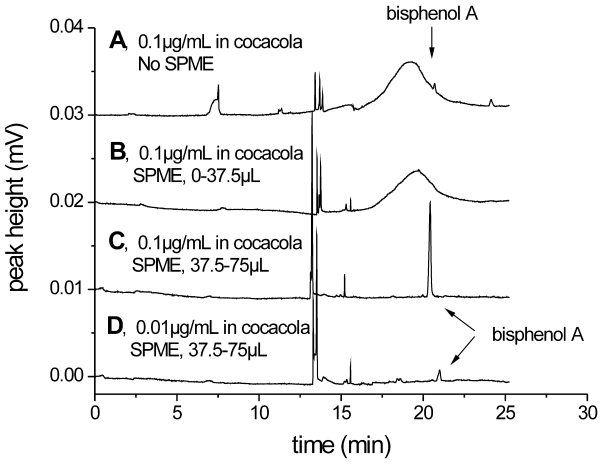

Figure 8. Separation of eluates collected at different elution volumes. SPME conditions: Sample, raw cola beverage spiked with BPA 0.10 and 0.01 μg/mL; extraction volume, 1.0 mL; eluent, 40% ACN solution (v/v). CE conditions: Sample A, raw cola beverage at elution volume from 0 to 37.5 μL (for B) and 37.5 to 75 μL (for C and D); other conditions are the same as those in Fig. 5.

(the dead volume is about 25 μL) with 45% ACN solution (v/v) as eluent and in the eluate collected between 50 and 75 μL with 40% ACN solution (v/v) as eluent, respectively. The retained volume increases with decreasing content of ACN in the eluent, which indicates that the extraction mechanism is mainly based on hydrophobic interaction. These facts imply that the weakly hydrophobic or ionic compounds in real samples can be removed in SPME with proper elution strategy.

3.4 Analysis of BPA spiked in cola by SPME/MEKC

For comparison, the sample prepared in cola without extraction was first directly injected and separated. The corresponding electropherogram is shown in Fig. 8A, from which it can be seen that there are serious background interferences in cola, and the target peak is difficult to observe. Comparison of Fig. 8A and Fig. 5 indicates that the on-column concentration methods using stacking and micellar sweeping techniques have great difficulty in analyzing complex matrices. Although tea beverage samples spiked with some kinds of vanillic acids were separated by Huang *et al.* [43] using anion-selection exhaustive injection (ASEI) in sweeping micro-emulsion electrokinetic chromatography (MEEKC) without sample pretreatment, the interference resulting from the peaks of unknown compounds was still serious even if the samples were diluted prior to CE separation. Considering this, Wang *et al.* [44] used solid-phase extraction for the pretreatment of biological samples before large-volume stacking in CE. Therefore, it is necessary for the beverage samples to be subjected to pretreatment prior to sample stacking in CE.

The cola beverage sample spiked with BPA was extracted by the hybrid silica monolithic capillary column prior to injection. According to Section 3.3.3, 40% ACN solution (v/v) was chosen as eluent, and the eluates were collected in segments (from 0 to 37.5 μL and 37.5 to 75 μL). The collected eluates were evaporated almost to dryness, then SDS solution and phosphoric acid were added to the sample vials until the sample matrices contained 4 mM SDS and 10 mM phosphoric acid. These pretreated samples have been separated and the corresponding electropherograms are shown in Fig. 8B–D. It can be seen that some of the interfering components in samples adsorbed on the SPME column could be removed completely with only 37.5 μL of eluent. In fact, the main part of the interfering components in the samples was first removed during the extraction process due to the weak adsorption on the SPME column. According to Section 3.3.3, BPA could not be eluted until the elution volume exceeded 50 μL when 40% ACN solution (v/v) was used as eluent. This means that the interference can be eliminated by collecting the eluate selectively, which is proven by Fig. 8C and Fig. 8D. Thus, with 40% ACN solution as eluent, the initial eluate of 37.5 μL was discarded and the following eluate between 37.5 and 75.0 μL was collected for analysis by CE.

With the conditions stated in Fig. 8B–D, linearity, limit of detection, and relative standard deviations (RSD) of peak areas were calculated. The linear regression analysis equation is: $y = 905997x + 694$ (y is the peak area, μV.s; x is the concentration of BPA, μg/mL), $r = 0.999$ and LOD ($S/N = 3$) = 1.8 ng/mL. Linearity of response spans about two orders of magnitude (0.005–0.20 μg/mL). Reproducibilities of peak areas (RSD, $n = 5$) are 4.5% (0.20 μg/mL) and 5.8% (0.01 μg/mL), respectively. The recoveries of BPA are 96.6% (0.10 μg/mL) and 111.9% (0.01 μg/mL), respectively. The column-to-column reproducibilities, which are evaluated by calculating the RSD values of the recoveries of BPA extracted by columns prepared in different batches ($n = 3$), are 3.1% (0.10 μg/mL) and 7.2% (0.01 μg/mL), respectively. Recently, numerous methods based primarily on GC and LC methods have been developed to identify trace BPA in various matrices [7–14]. Although the limit of detection of BPA in cola acquired with CE in this paper is higher than that with SPME–GC–MS or SPME–HPLC–FD (fluorescence detector), it is close to that of BPA in lake water (2.9 ng/mL) with SPME–HPLC–UV [12].

4 Concluding remarks

In the present paper, a low-cost and sensitive method has been developed and validated for the analysis of trace bisphenol A (an endocrine disrupting chemical) in beverage samples. The phenyl-functionalized hybrid silica monolithic polymer was prepared in a wide-bore capillary column and used as an extraction medium. A novel frit was prepared to enhance the mechanic stability of monolithic capillary column. Prior to the CE analysis, an off-line in-tube SPME procedure was applied for extraction, concentration, and sample clean-up, then on-line concentration methods including large-volume sample stacking and sweeping were carried out to improve the detection sensitivity of bisphenol A in the beverage samples. In-tube SPME helps to reduce the interferences in sample matrices and promotes the application of large-volume sample stacking and micellar sweeping methods in CE for the analysis of real complex samples.

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