Rapid Extraction of Bisphenol A by Dispersive Liquid-Liquid Microextraction based on Solidification of Floating Organic
(Pengekstrakan Pantas Bisfenol A dengan Pengekstrakan Mikro Cecair-Cecair Serakan berdasarkan Pemejalan Organik Terapung)

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ABSTRACT

Bisphenol A is an endocrine disruptor with widespread applications, especially in the production of polycarbonate and epoxy resins. Dispersive liquid-liquid microextraction based on solidification of floating organic technique has been developed for the extraction of bisphenol A from water and soft drink. The 1-undecanol has been applied as the extraction solvent because of its low density and melting point and high affinity to the analyte. The technique offered rapid and simple analysis as the 1-undecanol was homogeneously dispersed in the sample solution to speed the extraction and the collection of extraction solvent was simplified by centrifugation, cooling and melting steps.

Keywords: Bisphenol A; dispersive liquid-liquid microextraction based on solidification of floating organic; high performance liquid chromatography-fluorescence detection; water

ABSTRAK

Bisfenol A ialah suatu pengganggu endokrin yang mempunyai aplikasi meluas, khususnya dalam pengeluaran polikarbonat dan resin epoksi. Teknik pengekstrakan mikro cecair-cecair serakan berdasarkan pemejalan organik terapung telah dibangunkan untuk mengekstrak bisfenol A daripada air dan minuman ringan. 1-undekanol telah digunakan sebagai pelarut pengekstrakan disebabkan ketumpatan dan takat leburnya yang rendah dan tarikannya yang kuat terhadap analit. Teknik ini menawarkan analisis yang pantas dan senang kerana 1-undekanol menyerak dengan homogen di dalam larutan sampel untuk mempercepatkan pengekstrakan dan pengumpulan pelarut pengekstrakan telah dipermudahkan melalui langkah pengemparan, penyejukan dan peleburan.

Kata kunci: Air; bisfenol A; kromatografi cecair prestasi tinggi-pengesanan pendarfluor; pengekstrakan mikro cecair-cecair serakan berdasarkan pemejalan organik terapung

INTRODUCTION

Sample preparation is a crucial step in producing a clean sample to reduce instruments maintenance, improve detection sensitivity and selectivity. The classic liquid-liquid extraction (LLE) or solvent extraction is the most frequently applied sample preparation technique as it involves simple operation and offers selective and exhaustive extraction. Solid phase extraction (SPE) has appeared as an alternative sample preparation technique to LLE since 1970 when the popularity of LLE was diluted by the development of disposable based-SPE. The SPE provides multiresidue analysis with improved selectivity and sensitivity because various types of sorbents have been introduced. When the first miniaturized LLE, single drop micriextraction (SDME) was developed in 1996 (Liu & Dasgupta 1996), both LLE and SPE have been categorized as less supportive to green analysis due to their high consumption and disposal organic solvents and chemicals throughout the sample preparation process. Microextraction techniques, namely SDME, liquid

phase microextraction (LPME), dispersive liquid-liquid microextraction (DLLME) and solid phase microextraction (SPME) have been demonstrated to facilitate analyte enrichment and minimize the use of organic solvents and chemicals.

The microextraction techniques are non-exhaustive extractions and therefore they are time-dependent. The minimal extraction solvent or sorbent applied in a single attempt is not sufficient to completely extract the analytes. However, this weakness is also the competitive advantage of microextraction techniques, where the minimal solvent or sorbent employed enhances the analyte enrichment. Dispersive liquid-liquid microextraction (DLLME) that first developed in 2006 applies dispersive concept to overcome the long extraction time problem encountered in the microextraction techniques (Rezaee et al. 2006). The DLLME utilized evenly distributed extraction solvent drops to elevate the analytes transfer by simple solvent partition (Zang et al. 2009), which succeeding rapid extraction in 10 min time without agitation. This was then

followed by the development of dispersive liquid-liquid phase microextraction based on solidification of floating organic (DLLME-SFO) in 2008 to overcome the limitations of DLLME that employed toxic and environmentally unfriendly organic solvents (Leong & Huang 2008). DLLME-SFO applies less toxic solvent that solidify at low temperature to simplify the collection of the extract. Between, a home-designed glass vial with conic top has been applied to demonstrate DLLME based on low density solvent, which complements the original DLLME and DLLME-SFO (Saleh et al. 2009). The technique eliminates the use of toxic solvent with higher density and expensive solvent with low meting point that consumed in original DLLME and DLLME-SFO, respectively.

Bisphenol A (BPA) was first synthesized in 1905 and applied as a monomer in the production of polycarbonate in 1953 (Clagett & Shafer 1985). It is a building material in the manufacturing of polycarbonate and epoxy resin that are commonly used in the food and beverage packaging containers because of its durability and heat stability. BPA was classified as an endocrine disruptor when it was found disturbing hormonal balance in human and animals even at concentration below 1 ngL^{-1} (Chen et al. 2002; Fisher et al. 1999; Kang et al. 2006; Kim et al. 2001; Steinmetz et al. 1997; Vandenberg et al. 2007; Watts et al. 2003; Welshons et al. 2006).

Determination of BPA in food and beverages has been frequently reported due to the leaching of BPA from the polycarbonate and epoxy resin based-packaging containers, especially when the containers are aging, repeatedly used or subjected to heat (Bae et al. 2002; Cooper et al. 2011; Kubwabo et al. 2009; Le et al. 2008). Determination of BPA residues with SPE was frequently reported (Cao et al. 2009; Gallart-Ayala et al. 2011; Grumetto et al. 2008; Madrakian et al. 2015; Maragou et al. 2006) mainly because the SPE is simple, sensitive and able to process multi samples at one time. The modification of SPE and LLE into the microextraction formats have greatly reduced the organic solvent used in the analysis. Both microextraction techniques, SPME (Chang et al. 2005; Li et al. 2006) and DLLME (Cunha et al. 2012; Salgueiro-González et al. 2012) that applied solventless format and dispersive concept, respectively, have enhanced the analytes enrichment and shortened the analysis time.

In this work, DLLME-SFO was studied for the extraction of BPA from both water and soft drink. The technique simplifies and shortens the routine analysis and can be applied by the consumers and manufacturers for the monitoring of the BPA residues. In addition, the proposed technique requires smaller sample size and it is time-effective as compared with SPE-DLLME-SFO demonstrated by Sadeghi et al. (2016). The proposed technique, DLLME-SFO also offers higher sensitivity for the analysis of BPA when the quantification is performed using high performance liquid chromatography coupled with ultraviolet detection, instead of using capillary electrophoresis (Alshana et al. 2013).

MATERIALS AND METHODS

REAGENTS AND CHEMICALS

HPLC grade acetone, acetonitrile and methanol, AR grade sodium hydroxide, hydrochloric acid and 1-undecanol were purchased from Merck (Darmstadt, Germany). Bisphenol A (BPA) was supplied by Dr. Ehrenstorfer GmbH (Augsburg, Germany). A standard stock solution of BPA (500 mgL^{-1}) was prepared by dissolving 0.005 g of BPA in methanol. Serial working solutions in the range of 1 to 10 mgL^{-1} were prepared from the stock solution prior to use. All the solutions were stored at 0°C in darkness when not in use.

CHROMATOGRAPHIC CONDITIONS

All analyses were carried out using high performance liquid chromatography (HPLC)-fluorescence detection (FD) (Shimadzu, Kyoto, Japan) equipped with fluorescence detection (FD) a C18 column (4.6 × 250 mm, 5 µm) purchased from Agilent. The separation was performed using isocratic mobile phase acetonitrile-water (60:40) (v/v) at column temperature of 30°C. The flow rate, injection volume and detection wavelengths were fixed at 1.0 mL/min, 10 µL and 275/305 nm of excitation/emission wavelengths, respectively.

DLLME-SFO

A total of 3 mL sample was placed in a 5 mL centrifuge tube. A pre-mixed solvents consisted of 10 µL of 1-undecanol (extraction solvent) and 200 µL of acetonitrile (disperser solvent) was rapidly injected into the sample with a 1 mL disposable syringe. The resulting cloudy solution was left at room temperature for 1 min to allow for the analytes partitioning. The tube was then centrifuged at 4000 rpm for 5 min. The tube was then transferred into a beaker containing crushed ice to solidify the extraction solvent droplet (10 µL) that floated on the top layer. The solidified extraction solvent droplet was scooped into a vial and left at room temperature. The melted extraction solvent was diluted with another 10 µL of methanol prior to the HPLC-FD analysis.

PREPARATION OF SAMPLES

The water and soft drink samples were obtained from local enterprise shops. A drinking water sample and two cola samples with different brands were selected to study the linearity and relative recovery. The cola samples were degassed for 20 min in an ultrasonic bath prior to extraction. The samples were extracted using optimized DLLME-SFO procedure without pre-filtration steps.

RESULTS AND DISCUSSION

OPTIMIZATION OF DLLME-SFO

The extraction parameters, namely type of disperser solvent, volume of extraction solvent, extraction time and sample pH were optimized in order to increase the analyte enrichment. The optimization was carried out using deionized water samples spiked with 10 μgL^{-1} of BPA.

SELECTION OF DISPERSER SOLVENT

The miscibility of the disperser solvent in the aqueous sample solution and organic extraction solvent is the main criteria in selecting a disperser solvent (Rezaee et al. 2006). The miscibility of the aqueous-organic system ensures the large contact surface area between the analyte and extraction solvent thus enhancing analyte diffusion. Three disperser solvents, namely acetonitrile (ACTN), methanol (MeOH) and acetone (ACE) were investigated in this study. Figure 1 indicates that ACTN showed the highest extraction efficiency as compared to MeOH and ACE. The ACTN with high polarity and low viscosity succeeded the rapid miscibility and even dispersion of the extraction solvent in the sample solution and resulted high efficiency extraction.
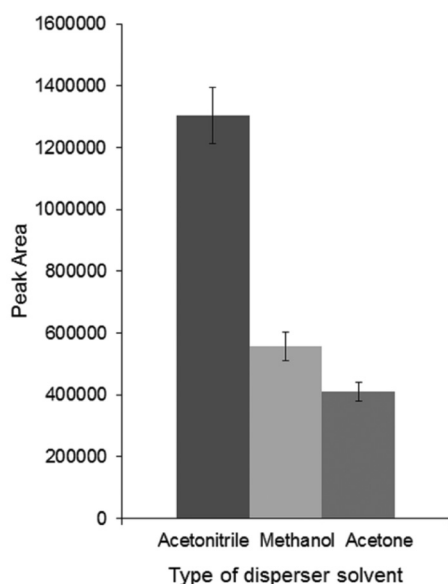

FIGURE 1. Effect of disperser solvents on DLLME-SFO of BPA from spiked deionized water sample (*n*=3 in each case). Error bars represent the standard deviation

EFFECT OF EXTRACTION SOLVENT VOLUME

In this study, 1-undecanol was applied as the extraction solvent because it fulfills the criteria, which include low volatility, low toxicity, low solubility in water, low melting point in the range of 10 to 30°C, and high affinity for the organic compounds (Leong & Huang 2008). Extraction solvent in the range of 10 to 50 μL was examined. Figure 2 shows that the extraction solvent with the smallest volume,

10 μL has significantly enhanced the BPA enrichment. Higher volume tended to dilute the extracted analyte and they are not beneficial to the green analysis. Therefore, 10 μL of 1-undecanol was applied in the subsequent experiments.
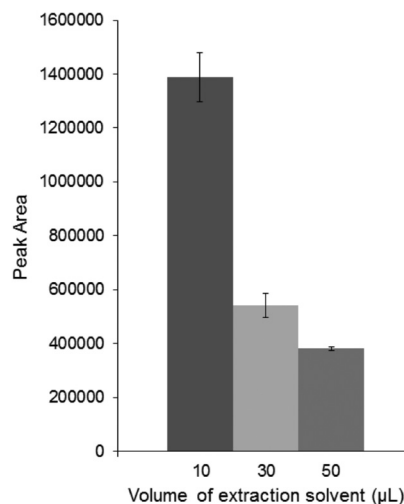

FIGURE 2. Effect of extraction solvent volume on DLLME-SFO of BPA from spiked deionized water sample (*n*=3 in each case). Error bars represent the standard deviation

EFFECT OF EXTRACTION TIME

The DLLME-SFO is a time-dependent system because it demonstrates non-exhaustive extraction. The extraction time of DLLME is defined as the time interval between the injection of the mixture containing both disperser and extraction solvents and the time before applying centrifuge (Berijani et al. 2006). The extraction time was examined in the range of 1 to 5 min in this study. Figure 3 indicates that the extraction equilibrium was achieved within a minute and the cloudy solution formed was stable to allow for the fast diffusion of the analytes to the extraction solvent. This was because the surface area between the analytes and the extraction solvent was large and thus resulting in rapid analyte diffusion (Jahromi et al. 2007). However, the cloudy solution was not stable when the extraction time was extended to 3 and 5 min, which then causing low extraction efficiency (Yan et al. 2011). Therefore, 1 min of extraction time was applied in the following experiments.

EFFECT OF SAMPLE pH

The pH of the sample solution was examined to ensure the best extraction efficiency was obtained. Generally, organic extraction solvent has stronger affinity for the analyte that exists in the molecular form. The sample pH was adjusted in the range of pH 2 to pH 8 in this study. Figure 4 shows that the peak area of BPA increased when the sample pH was modified from pH 2 to pH 6. BPA is a weak acidic compound with logarithm of acid dissociation constant (pK$_a$) in the range of 9.6-10.2 (Yoon et al. 2003). The BPA
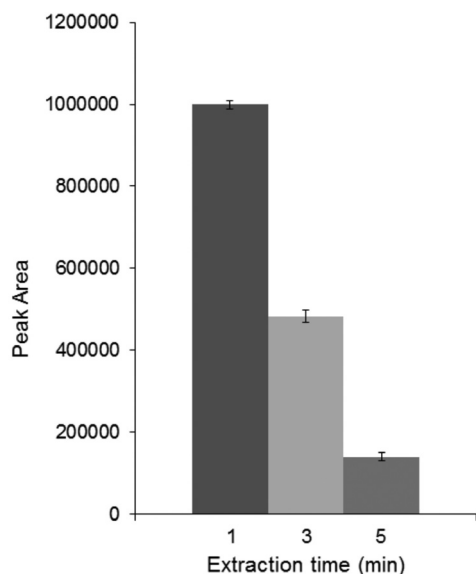
FIGURE 3. Effect of extraction time on DLLME-SFO of BPA from spiked deionized water sample (*n*=3 in each case). Error bars represent the standard deviation
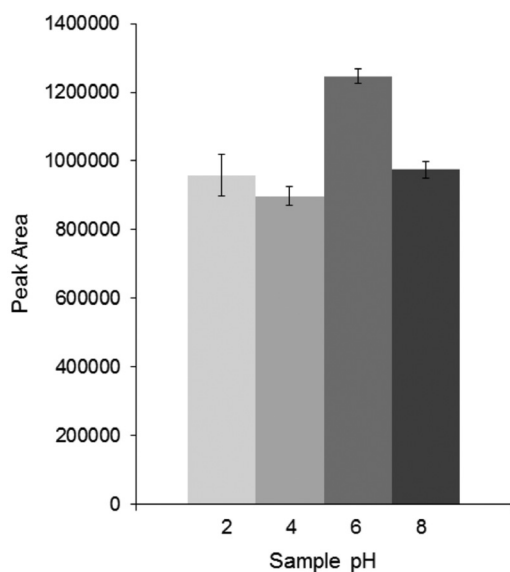

FIGURE 4. Effect of sample pH on DLLME-SFO of BPA from spiked deionized water sample (*n*=3 in each case). Error bars represent the standard deviation

existed in molecular form at pH < 9.6 and thus the results exhibited higher extraction efficiency in the range of pH 2 to pH 6. However, sample pH that was acidic than pH 6 was not a favorable pH for the extraction of BPA as the BPA might have been hydrolyzed and degraded (Zhao et al. 2014). The drop in peak area was also observed at pH 8. The difference between the pH and pK_a was less than 2 units and this was not facilitating the extraction of BPA since the BPA has started to dissociate and partially existed in anionic form.

VALIDATION OF DLLME-SFO

The method was validated for relative recovery, sample calibration, limit of detection (LOD) and limit of quantification (LOQ). Matrix matched calibration was performed as the detector responses obtained were different when the same amount of BPA was spiked in the deionized water and soft drink samples. It was clearly indicated by the slopes obtained, as shown in Table 1. The matrix matched calibration compensated the matrix effect that may cause signal suppression or enhancement (Zrostlíková et al. 2002). The linearity in the ranges of 0.05 to 200 µgL^{-1} and 0.1 to 200 µgL^{-1}, respectively, for deionized water and cola samples, correlation coefficients, $r \geq 0.9855$ and trace LODs in the range of 0.02 to 0.03 µgL^{-1} were obtained from the validation. The trace LODs suggests that the method was sensitive to support trace BPA analysis in the water and soft drink samples.

The relative recovery is the amount of analyte recovered from the matrix with reference to the matrix matched calibration. The relative recovery studies were performed by spiking both drinking water and cola samples to give final concentrations of 5 and 50 µgL^{-1}. Sample blank determinations were conducted and the samples were free from BPA. The results showed reproducible average relative recoveries ranging from 84.7 to 103.3% were obtained as indicated in Table 1. This show that samples with similar matrix has negligible effect on the method accuracy.

COMPARISON OF DLLME-SFO WITH OTHER METHODS

The analytical performance of the DLLME-SFO and other methods reported previously for the determination of BPA in water and beverage samples were summarized in Table 2. The sensitivities of the on-line solid phase extraction (SPE) (Gallart-Ayala et al. 2011), vortex-assisted liquid-liquid microextraction (VSLLME) (Yiantzi et al. 2010) and magnetic molecularly imprinted solid

TABLE 1. Validation data of the DLLME-SFO-HPLC-FD for the determination of BPA in drinking water and cola samples

Sample	Linearity range, µgL^{-1}	Regression equation	r	LOD, µgL^{-1}	Average of relative recovery± RSD, % (n=3)	
					Spiked at 5 µgL^{-1}	Spiked at 50 µgL^{-1}
Drinking water	0.05-200	y = 14453x + 315159	0.9855	0.02	84.7±6.5	103.3±7.2
Cola	0.1-200	y = 61777x + 55810	0.9971	0.03	93.0±8.8	87.4±5.1

TABLE 2. Comparison of the DLLME-SFO with other published methods for the determination of BAP in water and beverage samples

Analysis methods*	Matrix	Dynamic linear range, μgL^{-1}	LOD, μgL^{-1}	References
Hemimicelles magnetic SPE-LC-TMS	Soft drink	0.04-30	0.007	Yazdinezhad et al. 2013
Ionic liquid DLPME-HPLC-PDA	water	1-70	0.76	Sun et al. 2013
SBSE-GC-MS	Canned beverage	0.020-2.5	0.0025	Cacho et al. 2012
On-line SPE-LC-TMS	Cola	0.05-10	0.025	Gallart-Ayala et al. 2011
VALLME-HPLC-FD	water	0.05-100	0.02	Yiantzi et al. 2010
DLLME-HPLC-UV	water	0.5-100	0.07	Rezaee et al. 2009
Magnetic MISPE-HPLC-UV	water	0.1-40	0.014	Ji et al. 2009
DLLME-SFO-HPLC-FD	water	0.05-200	0.02	Present work
	Cola	0.10-200	0.03	

* Abbreviations: SPE = solid phase extraction; LC = liquid chromatography; TMS = tandem mass spectrometry; DLPME = dispersive liquid phase microextraction; PDS = photodiode array; SBSE = stir bar sorptive extraction; GC = gas chromatography; MS = mass spectrometry; VALLME = vortex-assisted liquid-liquid microextraction; HPLC = high performance liquid chromatography; FD = fluorescence detection; UV = ultraviolet detector; DLLME = dispersive liquid-liquid microextraction; SFO = solidification based on floating organic; MISPE = molecularly imprinted solid phase extraction

phase extraction (MISPE) (Ji et al. 2009) were comparable with DLLME-SFO. The on-line SPE combined both cleanup and quantification in a system which simplified the routine analysis, but the technique required excessive switching port for the automation. The magnetic MISPE offered specific and convenient extraction which overcame the time-consuming loading process in conventional SPE. However, the technique still required slightly high volume of organic solvent as it was not microextraction. The VSLLME eliminated the use of the disperser solvent and the sensitivity was surprisingly achieving trace level with only 1 min longer extraction time as compared to DLLME-SFO. DLLME utilized toxic halogenated solvent as the extraction solvent (Rezaee et al. 2009), which was not favored in the green analysis. The ionic liquid dispersive liquid phase microextraction (DLPME) (Sun et al. 2013) applied alternative ionic liquid to replace halogenated solvent, but the sensitivity was much lower which was not advantageous in the trace analysis. Hemimicelles magnetic SPE utilized nanoparticles as the sorbents that provided high surface area for the extraction of the BPA in the soft drink (Yazdinezhad et al. 2013). The approach did not apply microextraction format but successfully achieved ultra-trace LOD and simplified the collection of the sorbents. Stir bar sorptive extraction (SBSE) and DLLME-SFO were non-exhaustive systems. Both techniques were time-dependent. SBSE offered the lowest LOD as compared to others but required 3 h to achieve the equilibrium or extraction (Cacho et al. 2012). On the other hands, DLLME-SFO demonstrated LOD that was 10 times higher than SBSE's. However, DLLME-SFO has been proven to be a cost- and time-effective extraction technique as the techniques applies minimal amount of organic solvent and the dispersive approach has resulted in rapid analyte diffusion. In addition, the technique is simple and simultaneous multi-analysis could be performed to ease the routine analysis.

CONCLUSION

The study showed that DLLME-SFO-HPLC-FD is a simple and solvent-minimized approach which greatly shortens the analysis time and demonstrates high sensitivity and selectivity in analyzing the trace level of BPA in water and soft drink samples.

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