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Highly selective dummy molecularly imprinted polymer as a solid-phase extraction sorbent for five bisphenols in tap and river water

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ABSTRACT

A simple and fast method for both dummy template selection and polymer composition optimization is proposed here. A series of dummy templates for bisphenols imprinting were screened by running them on a non-imprinted polymer (NIP) column with porogen solvent as mobile phase. The tested dummy templates mainly involved bisphenol S (BPS), bromobisphenol A (TBBPA), bisphenol F (BPF), bisphenol E (BPE), bisphenol B (BPB), bisphenol AF (BPAF), 2,2′,6,6′-tetramethyl-4,4′-sulfonyldiphenol (BS-TM) and 4,4′-diaminodiphenylmethane (DADPM). Different monomers and porogens were also investigated for BPS and DADPM using the same method. BPS dummy template was finally selected with acetonitrile and 4-VP as porogen and monomer. The resulting dummy molecularly imprinted polymer (DMIP) achieved superior affinities for BPF, BPE, BPA, BPB and BPAF with imprinting factors 14.5, 13.8, 8.7, 5.7 and 4.2, respectively. An efficient method based on BPS-DMIP-SPE coupled with HPLC-UV was developed for selective extraction of BPF, BPE, BPA, BPB and BPAF in water samples. The method showed excellent recoveries (89.4–102.0%) and precision (RSD 0.3–4.8%, $n = 5$) for tap and river water samples spiked at three concentration levels each (40, 200 and 1000 ng L^{-1}). The detection limits ranged between 2.2 and 3.8 ng L^{-1} with a sample volume of 500 mL. The result demonstrated the superiority of the optimized method for selective extraction of BPs in water samples at the ng L^{-1} level.

1. Introduction

Bisphenol A (BPA) is a weak estrogenic chemical that is widely used as an intermediate in the production of polycarbonate plastic resin and epoxy resin [1]. It has been reported that BPA can induce a decrease in daily sperm count and fertility [2], disrupt chromosome alignment [3] and affect sexual maturation [4] or synaptogenesis [5] in humans. These potential health risks have raised serious concerns over its use in some consumer products and strict regulations have been implemented to minimize its adverse effects [6–8]. Subsequently, a series of structural analogs as the substitutes of BPA emerged, such as bisphenol B (BPB), bisphenol E (BPE), bisphenol F (BPF), bisphenol AF (BPAF), and bisphenol S (BPS). However, these substitutes also share the similar dilemma of acute toxicity, genotoxicity, and estrogenic activity with BPB reported to be even more toxic than BPA [9–11].

BPA is present ubiquitously in various environmental matrices and human samples such as air, surface water, waste water, sewage sludge, sediments, house dust, foodstuffs, urine, blood, and breast milk [1,12–14]. While related reports about the occurrence of other bisphenol analogs are scarce. One study reported the occurrence of BPF in surface water, sewage, dump water and sediments [15]. BPS, BPA and BPF have been reported to be present in surface water at 6.71–250.30 ng L^{-1} level [16]. The ultra trace amounts of BPF were reported in two kinds of soft drinks [17] while BPA, BPS, and BPF were the major contributors accounting for >98% of the total BPs found in the indoor dust samples from the United States and several Asian countries [18].

The ultra low concentrations and complex nature of environmental samples are the bottlenecks for analysis of BPs in real samples [19]. Pretreatment and enrichment processes are indispensable for their analysis even by LC–MS or LC–MS/MS. A series of solid-phase extraction (SPE) cartridges have been used for BPs such as reversed-phase (C18) [20], hydrophilic–hydrophobic balance (HLB) [21] and mixed-mode cationic exchange (MCX) cartridges [16,22]. Although traditional SPE sorbents have high capacities and

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can trap a wide range of analytes, they suffer from low efficiencies due to their low selectivity toward a specific target molecule. It can cause ion suppression and enhancement during LC–MS analysis or a drop in sensitivity of HPLC analysis [23]. These problems necessitate the development of an effective sample pretreatment approach featuring high selectivity, sensitivity, precision and accuracy.

Molecular imprinting is a rapidly developing technique for the preparation of polymers with excellent molecular recognition properties, promoting its applications in molecular imprinted solid-phase extraction (MISPE) [24,25]. BPA-imprinted polymers have been prepared using various methods, such as surface imprinting on silica [26] and magnetic particles [27–29], precipitation polymerization [30,31], supercritical polymerization [32] or spherical polymers by using microfluidic device [33]. All of these MIPs were prepared using target molecule as template. However, the possible leakage of template molecules even after exhaustive washing steps can have a serious impact on the accuracy of analytical method [34]. This becomes one of the major areas of concern in recent sample pretreatment methods employing MISPE [35].

The use of a dummy template offers an easy way to circumvent this problem as any leakage will be different from the analyte [36]. Structurally related analogs, fragments [37–43] and isotope labeled compounds[44] such as 4,4-dihydroxybiphenyl (DHBP), BPE, BPF, BPB, TBBPA, 2,6-bis(trifluoromethyl)benzoic acid (BTFB), *p-tert*-butylphenol (PTBP), 4,4-methylenebisphenol (MBP) and [^{2}H16]bisphenol A (BPA-d16) have been used as dummy templates for BPs imprinting. However, most of those dummy molecularly imprinted polymers (DMIPs) could be used for high sensitive detection of only a single compound, but not for a group of BPs [45]. Nevertheless, the main drawback of template analog imprinted polymers is the resulting inferior molecular recognition ability compared to those prepared using analytes as templates. On the other hand, despite the excellent molecular recognition ability of isotope imprinted polymer, it still has serious limitations such as the use of expensive isotopic templates and mass spectrometric (MS) detection. Therefore, the selection of a dummy template for BPs with higher class selectivity, lower toxicity and cost is a very crucial step which can affect the final result and outcome of MISPE procedure.

Until now, there are no general rules to select a dummy template for DMIP. Generally, dummy templates are selected only on the basis of molecular structures, and the final imprinting effect can not be predicted until the resulting DMIPs are obtained and tested, which makes such work really adventurous and time consuming. Hence, there is a dire need to summarize the basic rule for the selection of dummy template. In this way, the imprinting effect of one DMIP prepared using a certain dummy template can be anticipated and this may assist computational modeling [46].

For a long time, the properties of non-imprinted polymers (NIPs) have been overlooked. Since the imprinting effect is coming from the presence of a template molecule that enhance the pre-existing binding properties of a polymer, positive correlation has been found between the binding properties of non-imprinted and imprinted polymers for the non-covalent imprinting approach. Thus, the functional monomers and cross-linkers can be selected by screening a NIP library, making the optimization of polymer formulations faster and easier [47,48]. We propose here, a new alternative approach for selecting the dummy template for DMIPs. The non-imprinted polymers (NIPs) are used as packing materials in HPLC columns and the capacity factors of potential dummy templates are obtained using porogen solvents as the mobile phase. The template molecule which has the highest capacity factor can have the most significant imprinting effect. At the same time, the polymer composition can be optimized by preparing NIPs with varying polymer compositions and analyzing their effect on the capacity factors of the dummy template.

To verify this hypothesis, different DMIPs were prepared using BPS, TBBPA, BPF, BPA, BS-TM and DADPM as dummy templates and their properties were evaluated by chromatographic experiments. The results demonstrated that the capacity factors of template molecules on NIP columns were related to their imprinting factors. Bisphenol S was found to be the best dummy template with extraordinary class selectivity and low toxicity compared with the other BPs [9]. The BPS-DMIP was applied for the selective extraction and determination of BPA, BPF, BPE, BPB and BPAF in tap and river water samples with high recoveries, precision and accuracy.

2. Experimental

2.1. Reagents and chemicals

Bisphenol F (BPF), bisphenol S (BPS), bisphenol E (BPE), bisphenol A (BPA), bisphenol B (BPB), bisphenol AF (BPAF), 4,4′-diaminodiphenylmethane (DADPM), 4-*n*-nonylphenol (NP), 2,2′,6,6′-tetramethyl-4,4′-sulfonyldiphenol (BS-TM), dienestrol (DIEN), ethylene dimethacrylate (EDMA), methacrylic acid (MAA) and trifluoroacetic acid (TFA) were purchased from J&K Chemical Ltd. (Beijing, China). The initiator 2,2′-azobisisobutyronitrile (AIBN) and bromobisphenol A (TBBPA) were supplied by Aladdin Chemical (Shanghai, China). 4-vinylpridine (4-VP), 2,4,6-trichlorophenol (TCP) and 1,2-benzenediol (CAT) were obtained from Acros (NJ, USA). HPLC grade acetonitrile, methanol and formic acid were purchased from Fisher (Fair Lawn, NJ, USA). Analytical grade chloroform was purchased from Tianjin Bodi Chemical Engineering Co., Ltd. (Tianjin, China), and was purified by washing it with water, drying it over anhydrous sodium sulfate and then distilling it from calcium hydride.

2.2. Preparation of imprinted and non-imprinted polymers

Dummy molecularly imprinted polymers were prepared as follows: the dummy template (1 mmol), the functional monomer 4-VP (0.42 mL, 4 mmol) or MAA (0.35 mL, 4 mmol), the cross-linking monomer EGDMA (3.8 mL, 20 mmol), and the initiator AIBN (0.04 g) were dissolved in 5.6 mL porogen solvent (acetonitrile, methanol or chloroform) in a 10 mL thick walled glass tube. The pre-polymerization solution was sonicated and saturated with dry nitrogen for 15 min, the glass tube was then sealed under nitrogen and kept at 4 °C for 2 h. Afterwards the glass tube was placed in a water bath at 60 °C for 24 h. The obtained DMIP was crushed, ground, and sieved, and particles in the size range of 38.5–63.0 μm were collected. The particles were then allowed to sediment in acetone to remove the fine particles and the resulting DMIP was dried under vacuum at 60 °C for 24 h. The template was Soxhlet extracted for 48 h with methanol–acetic acid (9:1, v/v) and methanol. Non-imprinted polymers were prepared simultaneously using the same protocol in the absence of the template molecules.

2.3. Chromatographic evaluation of the polymers

The DMIPs and NIPs particles were suspended in methanol by sonication and then slurry packed into stainless steel HPLC columns (100 × 4.6 mm id) at 3000 psi using an air-driven fluid pump (Haskel, Burbank, CA, USA) with ethanol as the pushing solvent.

The chromatographic evaluation of the polymers were carried out using a Waters 515 HPLC pump equipped with a Waters 2487 dual wavelength absorbance detector at room temperature. The polymers binding affinities were studied using acetonitrile as the mobile phase. A 20 μL aliquot of the analyte (20 ppm) was injected for the analysis with a mobile phase flow rate of 1 mL min^{-1} and