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Selective molecular adsorption using electrospun nanofiber affinity membranes

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Abstract

Molecularly imprinted nanoparticles were encapsulated into polymer nanofibers with a simple electrospinning method. The composite nanofibers form non-woven mats that can be used as affinity membrane to greatly simplify solid phase extraction of drug residues in analytical samples. Upward 100% of propranolol-imprinted nanoparticles can be easily encapsulated into poly(ethylene terephthalate) nanofibers, ensuring the composite materials to have a high specific binding capacity. As confirmed by radioligand binding analysis, the specific binding sites in the composite materials remain easily accessible and are chiral-selective. Using the new composite nanofiber mats as solid phase extraction materials, trace amount of propranolol (1 ng mL^{-1}) in tap water can be easily detected after a simple sample preparation. As validated in this study, there is no problem of template leakage from the composite nanofibers. Without the solid phase extraction, the existence of propranolol residues in water cannot be confirmed with even tandem HPLC–MS/MS analysis.

Keywords: Molecular imprinting; Electrospinning; Nanoparticle; Nanofiber; Affinity membrane; Propranolol

1. Introduction

Nanomaterials are receiving increasing attention as their small physical size can bring in improved and even new functions, which are impossible to achieve with bulk materials. To realize further advance, methodologies to introduce specific molecular recognition capabilities into nanomaterials are required. Among the different synthetic strategies, molecular imprinting is probably the most straightforward for the purpose of producing nano- and micro-structured materials that have pre-designed molecular recognition capabilities (Chronakis et al., 2006a,b; Conrad et al., 2003; Huang et al., 2004; Yan and Kapua, 2001; Yang et al., 2004).

Frequently, molecularly imprinted polymers (MIPs) are prepared by co-polymerization of functional monomer with cross-linking monomer in the presence of a template molecule. Following removal of template, specific binding sites complimentary to the template structure are obtained. MIPs for a wide range of molecules have been reported, some of them have showed high affinity and specificity comparable to biological antibodies (Andersson et al., 1995; Ramström et al., 1996; Vlatakis et al., 1993). Due to their favorable molecular recognition capability and stability, potential applications of MIPs have been investigated in broad areas, such as ligand binding assays (Ansell, 2004), liquid chromatography (Takeuchi and Haginaka, 1999), solid-phase extraction (Lanza and Sellergren, 2001), sensors (Haupt and Mosbach, 2000) and catalytic chemical reactions (Wulff, 2002). In addition to exploring new applications, we, and others have been studying new synthetic strategies to prepare MIP beads using simple precipitation polymerization method (Boonpanggrak et al., 2006; Carabias-Martínez et al., 2005; Castell et al., 2006; Ho et al., 2005; Jiang and Tong, 2004; Li et al., 2003; Puoci et al., 2004; Sambe et al., 2006; Sun and Fung, 2006; Tamayo et al., 2003; Wang et al., 2003; Wei et al., 2006; Ye et al., 1999, 2000, 2002; Zhang et al., 2006), especially

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Table 1
Molecularly imprinted nanoparticles and microspheres used in this study

Polymer beads[a]	Identity	Propranolol (mmol)	MAA[b] (mmol)	DVB[b] (mmol)	TRIM[b] (mmol)	Size (μm)[c]
Imprinted nanoparticles	mipT2	0.53	1.31	0	2.02	0.13
Non-imprinted nanoparticles	refT2	0	1.31	0	2.02	0.39
Imprinted microspheres	mipDT1	0.53	1.31	1.31	1.52	1.2
Non-imprinted microspheres	refDT1	0	1.31	1.31	1.52	1.4
Imprinted microspheres	mipD2	0.53	1.31	5.25	0	2.4
Non-imprinted microspheres	refD2	0	1.31	5.25	0	2.4

[a] The imprinted polymers were synthesized by precipitation polymerization using (*R*,*S*)-propranolol as template. For details, see Yoshimatsu et al. (2007).
[b] Abbreviations. MAA: methacrylic acid, DVB: divinylbenzene, TRIM: trimethylolpropane trimethacrylate.
[c] Average diameter measured by SEM.

for producing spherical particles within the size range of 100 nm to 3 μm in diameter (Yoshimatsu et al., 2007). As shown in several recent publications, MIP nanoparticles prepared by precipitation polymerization have proven very valuable antibody substitutes in non-separation assays (Hunt et al., 2006; Ye and Mosbach, 2001) and in microfluidic separations (Schweitz et al., 2000; Spégel et al., 2001).

As the binding selectivity of MIPs can be tuned by using different template structures, it has been envisioned that one of the main applications of MIPs is in solid phase extraction for analytical sample preparation (Lanza and Sellergren, 2001). Provided that imprinted nanoparticles can be fixed on an appropriate support, their high loading capacity and fast binding kinetics should make them ideal affinity matrix for sample preparation in trace analysis. In a recent study, we demonstrated that MIP nanoparticles could be easily encapsulated into nanofiber membranes by a simple electrospinning method. The composite nanomaterials obtained displayed selective recognition capability for the original templates, theophylline and 17β-estradiol (Chronakis et al., 2006a,b).

The purpose of this study is to further verify that the binding sites in MIP nanoparticles can remain intact after encapsulation and, more importantly, the composite materials can provide efficient extraction of trace analytes from real samples. As a model system, we selected to use propranolol-imprinted nanoparticles for demonstration, not only because it represents a well-established example in precipitation polymerization (Schweitz et al., 2000; Spégel et al., 2001; Ye and Mosbach, 2001; Yoshimatsu et al., 2007), but also the analysis of propranolol residue in water has much practical relevance in environmental analysis. As an example, Sedlak and co-workers have used the enantiomeric ratio of residual propranolol in surface water to detect and document leaking sewers (Fono and Sedlak, 2005). The molecularly imprinted nanoparticles and microspheres used in this work were prepared using our recently published protocol (Yoshimatsu et al., 2007) and successively encapsulated into poly(ethylene terephthalate) (PET) nanofibers by electrospinning. The affinity nanofiber membranes were characterized by scanning electron microscopy (SEM) and radioligand binding analysis. Finally, extraction of aqueous propranolol from water using the nanofiber membrane was carried out, and the selective recovery of propranolol was verified by quantitative HPLC–MS/MS analysis.

2. Materials and methods

2.1. Materials

Atenolol (98%), metopronolol (+)-tartrate salt (97%), timolol maleate salt (98%), pindolol (98%) and acebutolol hydrochloride were purchased from Sigma (Gillingham, UK). (*R*,*S*)-Propranolol hydrochloride (99%), (*S*)-propranolol hydrochloride (99%) and (*R*)-propranolol hydrochloride (99%) were supplied by Fluka (Dorset, U.K.). (*S*)-[4-^{3}H]-propranolol (specific activity 555 GBq mmol^{-1}, 66.7 μM solution in ethanol) was purchased from NEN Life Science Products, Inc. (Boston, MA). Scintillation liquid, Ecoscint A was from National Diagnostics (Atlanta, GA). Poly(ethylene terephthalate) (PET) was purchased from Wellman International Ltd (Ireland). Analytical grade trifluoroacetic acid (TFA) and dichloromethane (DCM) were purchased from Sigma-Aldrich and used without further purification. Other solvents were of analytical grade. MIP nanoparticles and microspheres were prepared using our published protocols (Yoshimatsu et al., 2007). As controls, non-imprinted polymer (NIP) particles were prepared under identical conditions except for that no template was present during the polymerization. All the polymers prepared are uniform beads with different particle sizes, their identities and synthetic conditions are summarized in Table 1.

2.2. Electrospinning

Electrospinning of PET fiber was carried out at room temperature at a high voltage of 20 kV (HV Power Supply, Gamma High Voltage Research, Ormond, FL). The spinneret used in the experiments had an inner diameter of 0.8–0.9 mm. A copper wire was mounted in the spinneret and used as the positive electrode. A grounded aluminum foil was used as the counter electrode and mounted at a distance of 20 cm from the spinneret. Continuous PET fibers were collected on the aluminum foil in the form of a fibrous mat. To encapsulate MIP nanoparticles, the imprinted polymers were suspended in 1 mL of DCM and sonicated for 20 min. To the suspension was added TFA (1 mL), whereafter the mixture was stirred vigorously for 10 min. Finally, PET (200 mg) was added to the mixture and stirred for 3 h until complete dissolution. The suspension obtained contained 10% PET (w/w), and the nanoparticle content varied from 10% to 100% the weight