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Recent progress in molecularly imprinted media by new preparation concepts and methodological approaches for selective separation of targeting compounds

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ABSTRACT

For highly sensitive determination of trace-level compounds in environmental, biological, and food samples, a selective separation and concentration are usually required with a removal of contaminants before quantitative detection by spectroscopic detection techniques, such as mass spectrometry. In the last few decades, molecularly imprinted adsorbents have widely contributed to the separation and concentration in liquid-phase separations. In this study, the latest preparation procedures, such as the use of surface modifications, inorganic substrates, and monolithic materials, in the molecular imprinting techniques are summarized. Recent achievements of practical quantitative determination in a variety of fields by new methodological protocols with molecular imprinting are also reported.

Contents

1. Introduction

Achieving an artificial molecular recognition using biological functionalities of enzyme and antibody is one of the greatest challenges in the field of chemistry. These intelligent materials with molecular recognition ability would probably find applications in catalysis, sensors, and separations. In separation fields, a molecular template technique, named molecular imprinting, has been widely used in liquid chromatographic separations and solid-phase extraction (SPE) instead of typical affinity gels based on biomolecules. Molecular imprinting is the most attractive technique to obtain a specific material having the selective recognition ability for targeting compounds by simple preparation procedures. In brief, the molecularly imprinted polymer (MIP) is prepared by simple thermal- or photopolymerization. First, the self-assembled complex of template molecules and functional monomers, which can interact with the templates via hydrogen bonding, electrostatic

Abbreviations: SPE, solid-phase extraction; SPME, solid-phase microextraction; MIP, molecularly imprinted polymer; LC, liquid chromatography; MAA, methacrylic acid; DVB, divinylbenzene; GO, graphene oxide; EDMA, ethylene glycol dimethacrylate; LED, light-emitting diode; 4VP, 4-vinylpyridine; PSP, pseudo-stationary phase; EKC, electrokinetic chromatography; NP, nanoparticle; AAm, acrylamide; MBAA, *N,N'*-methylenebiscrylamide; CBZ, *N*-carbobenzyloxy group; LOD, limit of detection; LOQ, limit of quantification; GC, gas chromatography; TAGL, allyl 2,3,4,6-tetra-O-acetyl-glucopyranoside; PFVB, 1,2,3,4,5-pentafluoro-6-vinylbenzene; BPA, bisphenol A; IBP, ibuprofen; NPX, naproxen; KEP, ketoprofen; DFC, diclofenac; CA, clofibric acid; 2VP, 2-vinylpyridine; RAFT, reversible addition–fragmentation chain transfer; OFX, ofloxacin; FQs, fluoroquinolones; CS-NR-Mag-MIP, core–shell nanoring amino-functionalized superparamagnetic MIP; SAs, sulfonamides; d-μ-SPE, dispersive micro-SPE; UFLC–MS/MS, ultrafast liquid chromatography–tandem quadrupole mass spectrometry; MCNTs@MIP, MIP on the surface of magnetic carbon nanotubes; E1, estrone; E2, estradiol; E3, estriol; DES, diethylstilbestrol; p-GDMA, poly(glycerol monomethacrylate); TCM, Traditional Chinese Medicine; ECD, electron capture detector; MOFs, metal-organic frameworks.

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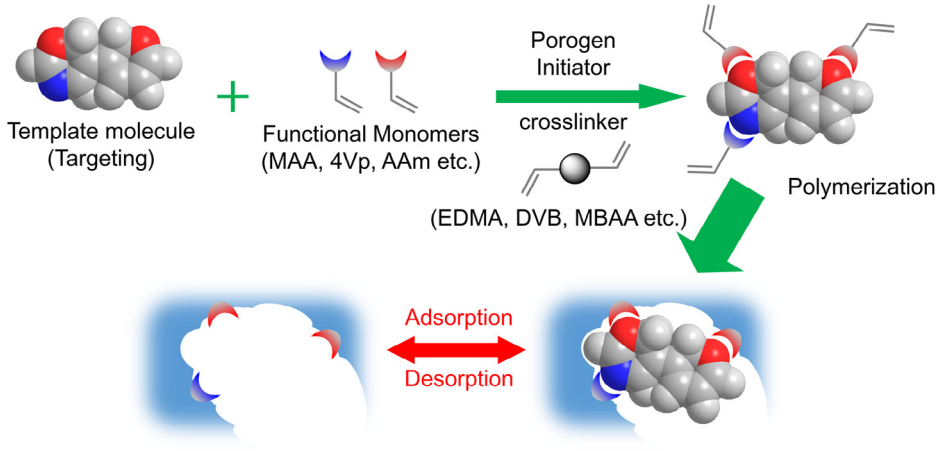

Fig. 1. Principle of a typical molecularly imprinting technique.

interaction, and hydrophobic interaction, is prepared using an excess of cross-linking agent and a large amount of porogenic solvents. Once the mixture attained a homogeneous state, polymerization is carried out with a certain amount of polymerization initiator. Because of their porous structure, MIPs usually have high adsorption capacity, and are suitable for separation media of liquid chromatography (LC) and SPE. The preparation of MIP via noncovalent intermolecular interactions is depicted in Fig. 1.

Initially, from 1985 to 2000, the MIP-based adsorbents were used in the separation media for LC separations. In most of these studies, self-assembly between templates and functional monomers via hydrogen bonding was used. The most important achievement of MIP technologies was the effective separation of racemic compounds. Mosbach, Sellergren, and coworkers reported enantioseparations in LC using MIPs as the new biomimic material separation technique [1,2]. Shea and coworkers also achieved an effective separation of benzodiazepine and its related compounds [3]. Following the success of these attempts, molecular imprinting has been used as the separation media for a variety of compounds, such as drugs, toxins, pollutants, and biomolecules. Particularly, MIPs have been widely studied in drug analyses from 1990 onward [4–6]. As a result of these achievements, MIPs have been currently used in various fields, including pharmaceutical, medical, chemical engineering, and environmental assessment [7,8]. More than 1000 reports related to MIPs have been published every year. Only few attractive achievements of MIPs in liquid-phase separations are summarized in this study. In addition, both preparation procedures, rather than an authentic method, and effective methodological approaches for the selective separation/concentration of targeting compounds in real samples are presented.

2. Direct selective separations with MIP-based columns

A liquid chromatographic evaluation is useful to understand the retention selectivity of certain packing materials, because the differences in the retention strengths can be quantitatively estimated by altering Gibbs free energy (ΔG), which is calculated by chromatographic parameters such as retention factor and separation factor. Therefore, the comparison of retention selectivity is commonly used for the estimation of binding strength in MIPs as well as the aforementioned initial studies. As the preparation procedures are very simple, the MIPs are mostly prepared as bulk polymers, and then the crashed and classified polymer particles can be evaluated by LC after packing a simple slurry into an empty column. However, the separation efficiency of the column packed with uniform-sized particles is quite low.

In order to overcome this drawback, uniform-sized spherical particles and a monolithic material were used. Kubo et al. provided an effective separation and concentration of environmental pollutants for the uniform-sized particles using the multistep swelling and polymerization method [9]. Furthermore, the precipitation polymerization has recently been used for the preparation of the uniform-sized adsorbents and resulted in more effective separation efficiency in LC evaluations. For example, Haginaka and coworkers reported the preparation of MIPs for creatinine by modified precipitation polymerization using methacrylic acid (MAA) as a functional monomer and divinylbenzene (DVB) as a cross-linker. The MIP allowed the specific retention of creatinine, whereas the structurally related compounds, such as hydantoin, 1-methylhydantoin, 2-pyrrolidone, *N*-hydroxysuccinimide, and creatine, were not recognized. Furthermore, creatinine concentrations in human serum and urine were successfully determined by directly injecting the deproteinized serum and diluted urine samples into the MIP-based column [10].

In addition to the uniform-sized particles, the monolithic materials based on silica and organic polymers have recently attracted attention in MIP technologies. It is well known that the monolithic materials can be prepared in situ using a typical column and a capillary. In addition, the permeability and column efficiency are much higher than those of packed columns. These advantages make the monolith-based MIPs suitable for the direct selective separation in LC analyses. Although the monolithic materials are not suitable for MIPs because of their fragile and/or shrinkable properties during drying and changing the solvents, some successful reports on their application in column or capillary in situ preparation have been described.

Zheng et al. have recently summarized the achievements of the monolithic MIPs and discussed their advantages based on theoretical approaches [11]. As one of the current approaches regarding monolithic MIPs, Zhai et al. proposed a new type of MIP with a graphene oxide (GO)-conjugated polymer monolith in a capillary [12]. Furthermore, a method was developed for the sensitive determination of phloxine B in coffee bean using MIPs. The capillary monolithic column was prepared using GO, phloxine B, MAA, and ethylene glycol dimethacrylate (EDMA) as the support material, template, functional monomer, and cross-linker, respectively. Then, under the selected conditions, enrichment factors of over 90-fold were obtained and extraction on the monolithic column effectively cleaned up the coffee bean matrix with a laser-induced fluorescence detection.

Some researchers have successfully achieved effective enantioseparation using MIPs with unique approaches. Dong et al. described a novel pathway for the development of a new type of