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Core–shell molecularly imprinted particles

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ABSTRACT

Molecularly imprinted polymers (MIPs) have been utilized as recognition elements for a wide range of analytes due to their high stability and remarkable mechanical properties. However, the traditional MIPs suffered some limitations for the practical applications. To broaden the application scope, multifunctional core–shell MIPs (CS-MIPs) have attracted increasing attentions in various fields such as separation, sensing and imaging. This review mainly discusses the recent developments of CS-MIPs with a non-imprinted core (Core@MIP particles) and CS-MIPs with a non-imprinted shell (MIP@Shell particles). In addition, other novel miscellaneous CS-MIPs with a hollow-core, a semi-shell, or an empty-shell are summarized. The challenges and prospects of the CS-MIPs are also presented to identify research gaps and prospective trends in design and applications of multifunctional CS-MIPs in analytical science.

1. Introduction

In many cases, selective recognition of the targets in a complex sample is extremely needed prior to instrumental analysis. For this purpose, specific nature receptor-ligand interactions have been widely implemented as the recognition elements in practical analysis. However, the nature receptors (e.g., antibodies and enzymes) suffer the risks of fragility and high cost. To avoid these limitations, synthetic receptors have been increasingly used to replace the biological recognition units nowadays. Among the synthetic receptors possessing specific recognition capability, molecularly imprinted polymer (MIP) has been considered as one of the most popular materials [1].

The concept of molecular imprinting was introduced in 1972 by Wulff and Sarhan [2], where MIPs were synthesized using a covalent imprinting method. In 1981, Mosbach et al. presented another approach of non-covalent imprinting, which involved the formation of a host-guest complex via hydrogen bonds, ionic interactions, hydrophobic interactions, and metal-ion interactions [3]. Because of facile synthesis of MIPs using non-covalent imprinting method, molecular imprinting gained extremely attraction in analytical chemistry.

Fig. 1 demonstrates the synthesis process of MIPs, which mainly consists of the following three steps: i) formation of a complex between the functional monomers and the template molecules through covalent or non-covalent interactions; ii) polymerization

Abbreviations: AB, (4-Acrylamidophenyl)(amino)methaniminium acetate; ABTS, 2,2′-Azino-bis-(3-ethylbenzothiazoline-6-sulfonicacid)diammonium salt; ATRP, Atom transfer radical polymerization; BHb, Bovine hemoglobin; BPA, Bisphenol A; CDB, Cumyl dithiobenzoate; Core@MIP particles, CS-MIPs with a non-imprinted core; CRPP, Controlled/"living" radical precipitation polymerization; CS-MIPs, Core–shell molecularly imprinted polymers; CuAAC, Cu(I)-catalyzed azide-alkyne cycloaddition; 2,4-D, 2,4-Dichlorophenoxyacetic acid; EbAM, *N*,*N*′-ethylene-bis(acrylamide); EGDMA, Ethylene glycol dimethacrylate; FITC, Fluorescein isothiocyanate; GDMA, Glycerol dimethacrylate; GlcA, Glucuronic acid; GMA, Glycidyl methacrylate; GMMA, Glycerol monomethacrylate; GPTMS, (3-Glycidoxypropyl) trimethoxysilane; Hb, Human hemoglobin; h-Core@MIP particles, MIPs with a non-imprinted hollow-core; HEMA, 2-Hydroxyethyl methacrylate; HPLC, High-performance liquid chromatography; IF, Imprinting factor; LOD, Limit of detection; MAEL, 2-*O*-meth-acryloyloxyethoxyl-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranoside; MAM, Methacrylamide; MAPASA, 4-[(4-Methacryloyloxy)phenylazo]benzenesulfonicacid; MAzoPy, 4-[(4-Methacryloyloxy)phenylazo]pyridine; MBA, *N*,*N*′-methylene bisacrylamide; MIP@e-Shell particles, MIPs with an empty-shell; MIP@Shell particles, CS-MIPs with a non-imprinted shell; MIP@s-Shell particles, Janus MIPs with a non-imprinted semi-shell; MOFs, Metal-organic frameworks; MWCNTs, Multi-walled carbon nanotubes; NANA, *N*-acetylneuraminic acid; NIPAm, *N*-isopropylacrylamide; NPs, Nanoparticles; PDA, Polydopamine; PEG, Polyethylene glycol; PGMA, Poly(-glycidyl methacrylate); PP, Precipitation polymerization; QDs, Quantum dots; RAFTPP, Reversible addition-fragmentation chain transfer precipitation polymerization; RSD, Relative standard deviation; SERS, Surface enhanced Raman scattering; SPE, Solid-phase extraction; SSA, Specific surface area; TBA, Thrombin-binding aptamers; TEA, Triethylamine; TMB, 3,3′,5,5′-Tetramethylbenzidine; UCNPs, Upconversion nanoparticles.

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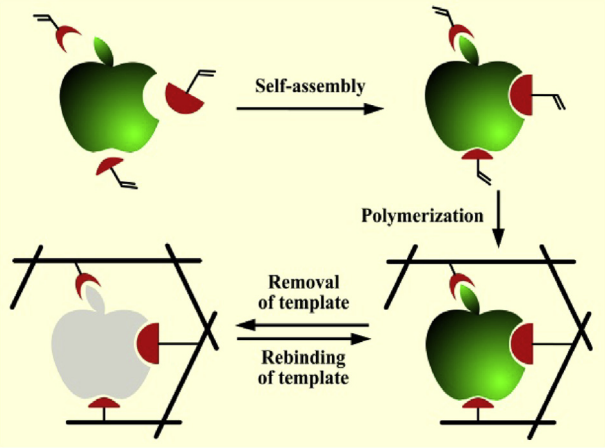

Fig. 1. Schematic depiction of the synthesis of molecularly imprinted polymers (MIPs).

of the functional monomers in the presence of polymeric cross-linking reagent; iii) removal of the template molecules from the polymer matrix to generate three-dimensional cavities that are sterically and chemically complementary to the target analytes.

Traditional MIPs were usually prepared by bulk polymerization, where the template molecules, functional monomers, initiators and cross-linking reagents were mixed with a porogen solvent. After the polymerization, polymers were ground, crushed and sieved to the desired MIPs with a certain particle size. However, the traditional MIPs displayed several shortcomings: irregular shapes with low reproducibility, difficult elution of the template molecules, large mass transfer resistance and poor selectivity. To overcome these disadvantages, other approaches such as suspension polymerization, emulsion polymerization and precipitation polymerization (PP) have been developed to prepare MIP particles with regular shapes [4–6].

Among the MIP particles with different shapes, core–shell MIP (CS-MIP) particles play a significant role in design and construction of different analytical sensors or devices by integrating the MIPs with other functional components (either core or shell materials). Generally, CS-MIP particles can be classified into two categories: i) CS-MIP particles with a non-imprinted core substrate and a MIP shell (Core@MIP particles) and ii) CS-MIP particles with a MIP core and a non-imprinted shell layer (MIP@Shell particles).

Recent literatures indicate that both the Core@MIP and the MIP@Shell particles showed interesting potential and platform for expanding the application field of molecular imprinting. Up to date, only a small amount of review articles on Core@MIP particles are available, where the applications of the Core@MIP particles in solid phase extraction (SPE), chemical sensing and controlled drug release have been reviewed [5–7]. As for the MIP@Shell particles, to the best of our knowledge, this kind of materials have not been summarized elsewhere.

Therefore, in the present review, a brief summary of the Core@MIP particles is discussed from other angles (based on the goals for introduction of the non-imprinted core components). The novel applications of the Core@MIP particles are further updated. Moreover, the construction and applications of MIP@Shell particles are summarized. Our special attention is paid to the challenges and prospects of MIP@Shell particles with different functional shell layers. In addition, the applications of other miscellaneous CS-MIPs (e.g., MIPs with a non-imprinted hollow-core, Janus MIPs with a non-imprinted semi-shell, and MIPs with an empty-shell) are also highlighted in this review.

2. CS-MIPs with a non-imprinted core (Core@MIP particles)

Utilizing different functional materials as the core substrates, the size distribution, separation efficiency, specific surface area, and detection sensitivity of the Core@MIP particles could be improved significantly [5]. Therefore, SPE separation and chemical sensing are the common applications of Core@MIP particles [6,7]. However, we will not dedicate a section on it since which have recently been discussed [5–7]. In the present article, a brief summary of the Core@MIP particles will be updated according to different goals for the introduction of core components (the details are seen in Table 1).

2.1. For immobilizing key molecules

The Core@MIP particles, which are usually prepared by surface molecular imprinting technique, confine almost all the binding sites on the surface of the core particles [8]. During surface imprinting, modification of the core components with templates, functional monomers or other key molecules plays a crucial role in production of a well-controlled MIP shell.

Immobilization of templates on the supported core component through covalent interactions [9–11] and non-covalent interactions

Table 1
Function of core particles and application of the Core@MIP particles.

Goal for introduction of core	Core particle	Analyte	Application	Ref
Template immobilization	Fe_3O_4@SiO_2	BHb	SPE	[13]
Monomer immobilization	Au	Thrombin	Control enzyme activity	[14]
Monomer and template immobilization	SiO_2-FITC	Monosaccharide	Cell imaging	[10]
	Fe_3O_4	Glycoprotein, Glycan	SPE	[11]
RAFT reagent immobilization	Polystyrene	Lysozyme	SPE	[16]
	SiO_2	Sialic acid	Cell imaging	[17]
Increase of mass transfer kinetic	Divinylbenzene	Thiabendazole	HPLC separation	[27]
Enhancement of specific surface area	MOF-5	Metolcarb	SPE	[28]
	MIL-101	Metolcarb	sensor	[29]
	HKUST-1	BHb	Sensor	[30]
	MWCNTs/SiO_2	Triclosan	SPE	[32]
	PGMA	2,4-D	SPE	[34]
Provision of enzyme-like catalytic ability	Fe_3O_4/CeO_2/Au	TMB, ABTS, DA	Enzyme mimicking	[37]
	TiO_2	Chlorophenols	Enzyme mimicking	[38]
Introduction of radiation signal	InP/ZnS QDs	GlcA, NANA	Cell imaging	[42,45]
	SiO_2@FITC	Monosaccharide	Cell imaging	[10]
Creation of catalytic micromotor engine	PEDOT/Pt-Ni	Avidin-FITC	Nano/micromachine MIP transporter	[46]
	PEDOT/Pt-Ni	Phycocyanin	Nano/micromachine MIP transporter	[47]