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ARTICLE

Cationic β-cyclodextrin-modified hybrid magnetic microspheres as chiral selectors for selectively chiral absorption of dansyl amino acids

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Cite this: DOI: 10.1039/xoxxoooooox

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

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Chiral selectivity functionalized magnetic microspheres show great potentiality in enantiomeric separations. In this study, a novel class of chiral magnetic selectors was developed by immobilization of vinylimidazolium-β-cyclodextrin chloride (VIMCD-Cl) on 3-methacryloxypropyltrimethoxysilane-modified iron oxide magnetic microspheres through a radical polymerization. The prepared chiral materials have regularly three-dimensional core-shell architectures with an average particle size of about 580 nm and a high magnetization saturation of about 51 emu g^{-1}. Fourier transform-infrared spectra (FT-IR), thermogravimetric analysis (TGA) and elemental analysis confirmed that VIMCD-Cl was successfully polymerized on the surface of magnetic microspheres. The prepared functional magnetic materials were then applied in the selectively chiral absorption of three dansyl amino acids using the microbatch technology. The results indicated that VIMCD-Cl immobilized magnetic microspheres (VIMCD-MNPs) possessed good enantioselectivities toward the three dansyl amino acids, and showed stronger interactions with the L-enantiomers during the chiral adsorption process. Furthermore, these functionalized chiral magnetic materials possess an excellent recyclability and can be used as effective chiral magnetic selectors for chiral separations.

1. Introduction

Amino acids are essential components of many physiological active substances such as peptides and proteins, and exist in most of foods, seeds, body fluids and tissues. The two enantiomers of amino acids possess significant differences in their biological or physiological activities because of their disparate physical and chemical properties in living systems.[1] Chiral analysis of amino acids is of great significance in life science, especially in the food and pharmaceutical industries. Several separation methods, including chromatography[2,3], crystallization[4], membrane separation[5] and nanomaterials based microbatch methodology[6-10], have been developed for chiral recognition. Among them, the microbatch technology developed by several research groups[11-19], was applied in enantioselective recognition of racemic compounds by a chiral solid support and has been extensively employed for evaluation and screening of a variety of solid chiral selectors as available chiral stationary phases (CSPs). Using the microbatch methodology for chiral recognition can rapidly evaluate the enantioselectivity of the solid chiral selectors in a short analysis time with minimum chiral selector and solvent consumption. Roussel et al. evaluated and screened of six polysaccharide CSPs by selectively chiral recognition of 15 test-racemates using microbatch technology[12].

In recent years, magnetic nanoparticles (MNPs) immobilized with appropriate chiral discrimination agents were effective candidates for enantiomeric separation of chiral biomolecules because of their fast magnetic responsiveness, unique sizes, biocompatibility as well as facile surface modification. The unique magnetic properties afford the chiral materials fast separation from racemic mixtures by applying an external magnetic field. Our previous study has demonstrated the successful preparation of macrocyclic antibiotics and proteins functionalized magnetic microspheres as chiral magnetic selectors and their potential applications in chiral separation of racemates.[20-22]

β-cyclodextrin (β-CD) is a cyclic oligosaccharide that composed of seven D-(+)-glucopyranose units connected by α-1,4 linkages. It contains a hydrophobic interior cavity and a

hydrophilic exterior surface. The unique cavity structure endows β-CD with the forming of host-guest inclusion complex with a variety of chiral and achiral molecules, and makes it as one of the most effective chiral selectors for enantiomeric recognition. The native β-CD has a relatively limited host-guest recognition capability in enantioseparations. Cationic-modified β-CD derivatives with high enantioselectivity and resolution, which was first used as chiral additive in mobile phase by Roussel et al.[23], have been demonstrated to be powerful chiral selectors for chiral separation of multiple racemates because of their superior chiral recognition abilities caused by the cationic and hydrophobic cavity of β-CD. The additional electrostatic interaction between cationic charged β-CD and oppositely charged analyte enantiomers improves the chiral resolution capability. Recently, a series of ionic-liquids featured cationic charged β-CD derivatives used as chiral additives in CE or chiral stationary phase in HPLC have been developed for enantioseparations.[24-30] In view of the excellent characteristics of magnetic nanoparticles, MNPs combing these chiral selectors are simple and powerful for the selectively chiral absorption of racemates.

In this present work, we develop a novel class of chiral selective magnetic microspheres based on imidazolium cationic-modified β-CD derivatives for the selectively chiral absorption of charged racemates. Vinylimidazolium-modified β-CD tosylate (VIMCD-OTs) was synthesized by the nucleophilic substitution of 6-OTs-β-CD with vinylimidazole using a facile microwave-assisted synthesis methodology, and then converted into vinylimidazolium-modified β-cyclodextrin chloride (VIMCD-Cl) by anionic exchange of tosylate to chloride. The chiral magnetic materials were finally fabricated by immobilizing VIMCD-Cl on 3-methacryloxypropyltrimethoxysilane (MPS)-modified magnetic microspheres through a radical polymerization. Various characterization techniques were applied to demonstrate the successful preparation of the chiral materials. The chiral recognition abilities of the functionalized chiral magnetic microspheres were then evaluated by the selectively chiral absorption of dansyl amino acids racemates using microbatch technology. The chiral recognition mechanism of the chiral magnetic selectors is also discussed.

2. Experimental section

2.1 Materials

β-CD was purchased from Tianji Guangfu Fine Chemical Research Institute (Tianjin, China) and recrystallized three times from water. 1-vinylimidazole was obtained from Sigma-Aldrich (St. Louis, MO, USA). Amberlite IRA-900 resin (Cl) was supplied from Alfa Aesar (Heysham, England). Tetraethyl orthosilicate (TEOS), 3-methacryloxypropyltrimethoxysilane (MPS), ethyleneglycol dimethacrylate (EGDMA), p-toluenesulfonyl chloride (TsCl), dansyl chloride (Dns-Cl) and all the racemic amino acids used in the current study were procured from J&K Scientific (Beijing, China). Copper(II) sulfate pentahydrate ($CuSO_4·5H_2O$), 2,2'-Azobisisobutyronitrile (AIBN) and all other chemicals were of analytical grade, which were obtained from Beijing Chemical Reagent Co. Ltd (Beijing, China), and used without further purification.

2.2 Synthesis of mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin (6-OTs-β-CD)

The key intermediate 6-OTs-β-CD was synthesized starting from native β-CD by tosylation of the primary hydroxy at its 6-position with tosyl group according to the previous reports.[31] Typically, 20 mL of NaOH aqueous solution (8.21 M) was added dropwise to a suspension containing 500 mL of H_2O and 60.0 g of β-CD to obtain a homogeneous solution. Subsequently, 10.08 g of TsCl diluted in 30 mL acetonitrile was added dropwise over 20 min and white precipitates were immediately generated. After the mixtures were stirred at room temperature for 2 h, the precipitate was removed by suction filtration. The filtrate was then adjusted to the pH of 8-9 with 10% hydrochloric acid and followed by suction filtration. The filter residue was collected and recrystallized three times from hot water to obtain the white solids (7.23 g) with a yield of 10.6%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.75 (d, 2H, $=CH_{ortho}$), 7.45 (d, 2H, $=CH_{meta}$), 5.60-5.85 (m, 14H, OH-2,3), 4.75-4.89 (m, 7H, H-1), 4.21-4.58 (m, 6H, OH-6), 3.45-3.75 (overlapped with solvent, 28H, H-3,5,6), 3.15-3.47 (overlapped with solvent, 14H, H-2,4), 2.41 (s, 3H, CH_{3Ts}). Elemental analysis (%): calculated for $C_{49}H_{76}O_{37}S$ C: 45.65, H: 5.94, S: 2.49; Found: C: 44.66, H: 6.15, S: 2.29.

2.3 Synthesis of 6^A-(3-vinylimidazolium)-6-deoxy-β-cyclodextrin chloride (VIMCD-Cl)

A nucleophilic substitution of 6-OTs-β-CD with vinylimidazole by microwave irradiation was performed to yield the desired vinylimidazolium-modified β-CD tosylate (VIMCD-OTs), which was then converted into VIMCD-Cl by anionic exchange. Briefly, 2 g of 6-OTs-β-CD was dissolved in 3.12 mL of vinylimidazole with vigorous stirring. The homogeneous solution was then transferred into the microwave reactor (Discover SP, CEM, Matthews, NC, USA) and reacted at 90℃ for 1 h with a power of 80 W. The product was precipitated and washed with acetone three times, and finally dried to give a white solid (1.8 g). Next, an aqueous solution of VIMCD-OTs (2 g) was slowly passed through a packed column of amberlite IRA-900 (Cl) resin. The effluent was collected and distilled by rotary evaporation. The precipitate was washed with acetone and finally dried under vacuum to afford a white solid (1.85 g) with the total yield of 78.6%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.48 (s, 1H, =CH-2im), 8.23 (s, 1H, =CH-5im), 7.88 (s, 1H, =CH-4im), 6.02-6.05 (d, 1H, OH-2), 5.61-5.95 (m, 13H, OH-2,3), 5.41-5.49 (m, 1H, $=CH_{vinyl}$), 4.98-5.05 (d, 1H, H-1), 4.78-4.92 (m, 7H, H-1, $=CH_{2vinyl}$), 4.30-4.62 (m, 6H, OH-6, $=CH_{2vinyl}$), 4.02-4.10 (m, 1H, OH-6), 3.16-3.93 (overlapped with solvent, 40H, H-2,3,4,5,6), 3.01-3.11 (m, 1H, H-5), 2.79-2.88 (m, 1H, H-4). Elemental analysis (%): calculated for

$C_{47}H_{75}O_{34}N_2Cl$ C: 45.25, H: 6.06, N: 2.25, Cl: 2.84; Found: C: 43.21, H: 6.32, N: 2.16, S: 0.0018.

2.4 Preparation of MPS modified magnetic microspheres (MPS-MNPs)

Fe_3O_4 MNPs was synthesized through a typical solvothermal process according to our previous report.[20] Silica-coated MNPs (SiO_2-MNPs) was prepared by hydrolysis and condensation of TEOS via a versatile sol-gel process. Briefly, 1 g of Fe_3O_4 MNPs was ultrasonically dispersed in a solution containing 60 mL of H_2O, 200 mL of ethanol and 5 mL of $NH_3 \cdot H_2O$. Subsequently, 1.5 mL of TEOS diluted in 40 mL ethanol was added dropwise over 30 min. The mixture was vigorously stirred and reacted at room temperature for 8 h. After separation with a magnet, the resulting product was washed and finally dried under vacuum for further use. To generate the functional sites for attachment of VIMCD-Cl, MPS-MNPs was synthesized by the surface modification of SiO_2-MNPs with MPS using a microwave-assisted synthesis method. Typically, 1.2 g of SiO_2-MNPs was dispersed in a 10% (v/v) MPS toluene solution by ultrasonication. The mixture was then vigorously stirred in the microwave reactor and reacted at 100℃ and 100 W for 5 h. The synthesized MPS-MNPs was washed with ethanol and finally vacuum dried at 50℃ for 3 h.

2.5 Fabrication of the chiral magnetic microspheres (VIMCD-MNPs)

The chiral materials were prepared by the co-polymerization of MPS-MNPs with monomers (EGDMA and VIMCD-Cl) in the presence of AIBN initiator. Typically, the as-synthesized MPS-MNPs were ultrasonically suspended in a solution containing 40 mL of methanol, 100 μL of EGDMA and 0.15 g of VIMCD-Cl. After addition of AIBN, the mixture was polymerized at the boiling temperature for 24 h with distilling 15 mL of the solvent out of the reaction system under a nitrogen atmosphere. After cooling down to room temperature, the synthesized chiral materials were washed with ethanol several times and finally dried in a vacuum oven at 50℃ for 3 h.

2.6 Chiral absorption of dansyl amino acids racemates by VIMCD-MNPs

The microbatch technology was applied in evaluation of the chiral recognition capabilities of the synthesized chiral magnetic microspheres with three dansyl amino acids as test-racemates. Capillary electrophoresis (CE) was carried out to determine the ratio of enantiomers left in the supernatant after the racemic solution interaction with VIMCD-MNPs. All of the dansyl amino acids used in the current study, including dansyl DL-valine (Dns-Val), dansyl DL-phenylalanine (Dns-Phe) and dansyl DL-leucine (Dns-Leu), were synthesized according to the previous report.[32] Typically, 100 mg of VIMCD-MNPs was washed with acetate buffer three times and then re-dispersed in 5 mL of racemic solution (0.5 mg mL^{-1}, 50 mM acetate buffer, pH 6.0). The suspension was vigorously stirred and then separated with a magnet. The supernatant was collected for CE analyses. The detailed synthetic protocol for synthesis of VIMCD-MNPs and its applications in selectively chiral absorption of dansyl amino acids are presented in Fig. 1.

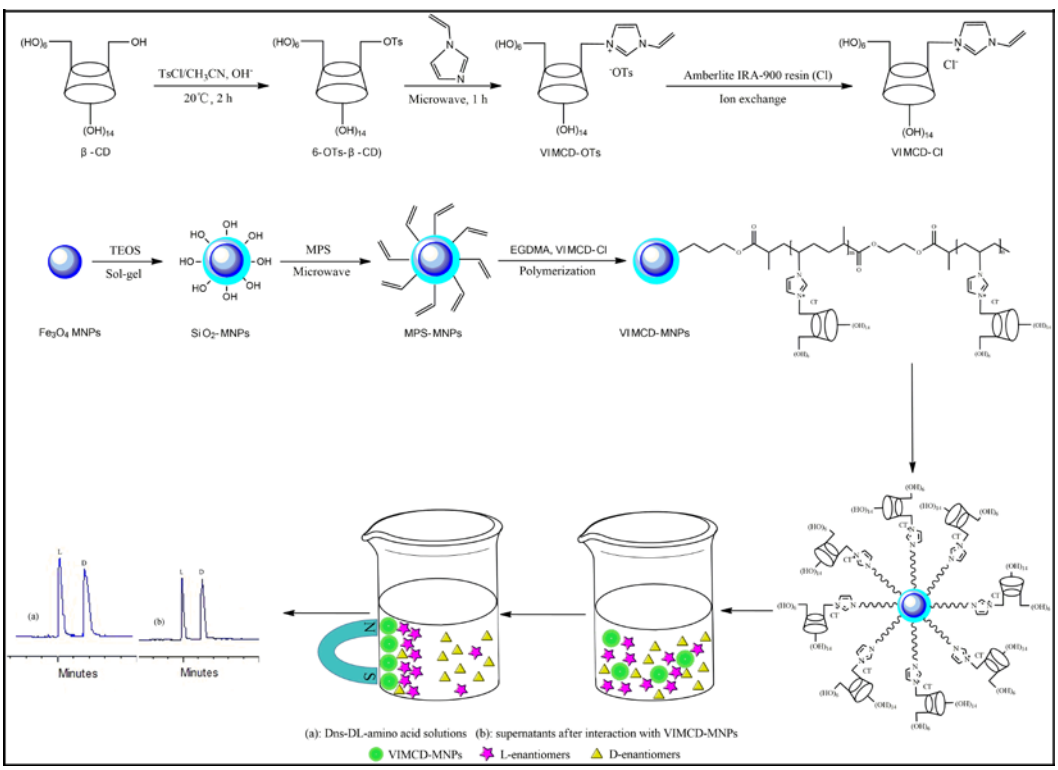

Fig. 1 Schematic illustration for synthesis of VIMCD-MNPs, and its application in selectively chiral absorption of dansyl amino acids.

2.7 Characterization

Transmission electron microscopy (TEM, Philip Tecnai 20, Amsterdam, Netherlands) was used to determine the size of the synthesized magnetic materials. The morphology of the chiral magnetic microspheres was observed using a Zeiss SUPRA55 scanning electronic microscopy (SEM, Oberkochen, Germany). X-ray diffraction (XRD) patterns were collected on a Rigaku Ultima3 diffractometer (Tokyo, Japan) using Ni-filtered Cu Kα radiation at 40 kV and 40 mA. Fourier transform-infrared (FT-IR) spectra were recorded on a Nicolet spectrometer (Thermo Fisher Scientific, Waltham, MA, USA) from 4000–400 cm^{-1} using a KBr pellet. Thermogravimetric analysis (TGA) curves were measured using a Mettler Toledo (Columbus, OH, USA) 1100SF thermogravimetric analyzer with a heating rate of 10 °C min^{-1} from 25–1000 °C under N_2. The magnetic properties of the prepared materials were determined on a Lake Shore 7410 vibrating sample magnetometer (VSM, Westerville, OH, USA). The chemical structures of the synthesized β-CD derivatives were confirmed by ^{1}H-NMR spectra using a Bruker Avance-400 spectrometer. Elemental analysis (Vario EL cube, Elementar, Hanau, Germany) was applied to determine the organic compositions of the synthesized β-CD derivatives and the functionalized magnetic microspheres. CE experiments were carried out on a Beckman Coulter MDQ system (Beckman, Fullerton, CA, USA), equipped with a photodiode array detector. The CE separation conditions were set as follows: fused-silica capillaries with total length 60.2 cm (effective length 50.2 cm, 50 μm i.d.); applied voltage, 20 kV; running buffer, 20 mM ammonium acetate (containing 4 mM $CuSO_4$, 8 mM L-Val and 20 mM SDS) at pH 9.0; sample injection, 0.5 psi for 10 s.

3. Results and discussion

3.1 Synthesis of vinylimidazolium-modified β-CD derivatives

In this current study, microwave-assisted synthesis technology was employed to synthesize vinylimidazolium-modified β-CD tosylate. Microwave-assisted synthesis is an attractive alternate technique to thermal heating. Compared with conventional heating synthesis, microwave-assisted synthesis shows several unique advantages such as selective heating, uniform temperature distribution and high levels of efficiency. These excellent properties enable it remarkably increase reaction rates, reduce preparation time and improve reaction yields. Using microwave-assisted synthesis to prepare imidazolium cationic modified β-CD derivatives can be fast and efficient. Elemental analysis was used to investigate the efficiency of synthesis of VIMCD-OTs by different heating methods. The data were as follows: C 45.88%, N 1.78%, S 1.67% for conventional heating method; C 45.01%, N 2.06%, S 2.08% for microwave-assisted synthesis process. Conventional heating process for synthesis of imidazolium-modified β-CD tosylate required as many as 48 h.[24-26] The microwave-assisted synthesis process just required 1 h to get a high yield. The reaction time required for synthesis of VIMCD-OTs using microwave-assisted synthesis method was obviously shorter than that using conventional heating method. The N content of VIMCD-OTs synthesized by microwave irradiation increased, suggesting that the microwave-assisted process improved the reaction efficiency over the conventional heating process. The strong polarity of imidazole caused the high efficiency of microwave absorption, and then resulted in the improved reaction yield. These results indicated that microwave-assisted synthesis was green and efficient for synthesis of imidazolium-modified β-CD derivatives.

3.2 Characterization of the prepared chiral magnetic microspheres

The size and morphology of the synthesized microspheres were observed by TEM and SEM. As shown in Fig. 2a, Fe_3O_4 MNPs had a uniform spherical structure with an average size of 450 nm. After coating with silica, a core-shell structure with the thickness of the silica layer of 50 nm was clearly observed (Fig. 2b). There was no obvious change in the particle size and morphology after surface grafting MPS, suggesting that an alkenyl monolayer was modified on the surface of SiO_2-MNPs (Fig. 2c). The images in Fig. 2d indicated that a typically three-dimensional structure with a thin polymer layer of about 15 nm in thickness was obviously detected because of the successful co-polymerization of EGDMA and VIMCD-Cl on MPS-MNPs. The SEM image also confirmed that a polymer layer was successfully coating on the surface of the particles to form the chiral magnetic microspheres (Fig. 3a).

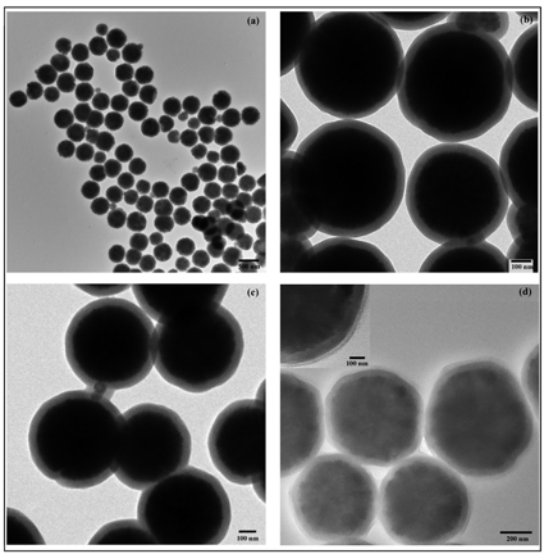

Fig. 2 TEM images of Fe_3O_4 MNPs (a), SiO_2-MNPs (b), MPS-MNPs (c) and VIMCD-MNPs (d).

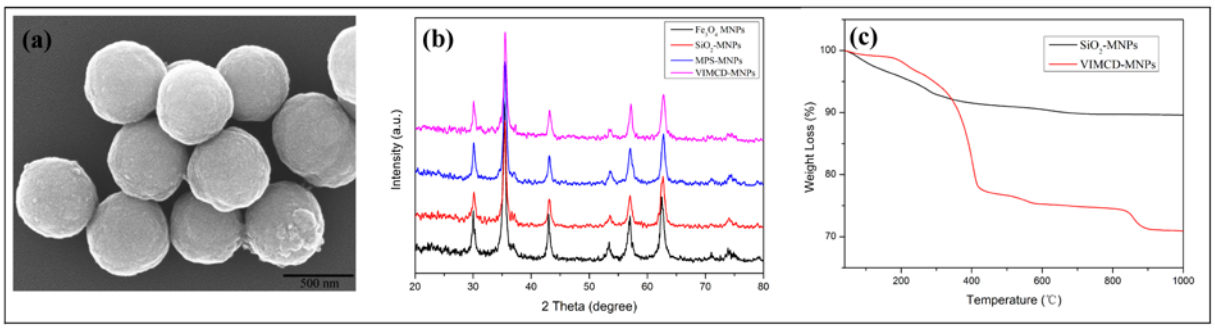

Fig. 3 SEM image of VIMCD-MNPs (a), XRD patterns of the synthesized magnetic microspheres (b), and TGA curves of Fe_3O_4 MNPs and VIMCD-MNPs (c).

The crystal structures and phase purities of the prepared magnetic materials were analyzed by XRD. Fig. 3b shows that characteristic diffraction peaks for all the synthesized microspheres were well matched with the standard Fe_3O_4 (JCPDS 75-1609). The crystallite size of the particles at crystal indices (311) was about 18 nm according to the Debye-Scherrer equation. These results indicated that the functionalized magnetic microspheres consist of numerous small nanoparticles with a typical cubic structure. No distinct changes in characteristic peaks were observed after surface coating with silica and polymerization, suggesting that the modification did not change the crystal structures of Fe_3O_4.

The coating of VIMCD-Cl on MPS-MNPs was demonstrated by FT-IR, TGA and elemental analysis. Fig. 4 shows that the characteristic absorption peak at 588 cm^{-1} is assigned to the Fe-O stretching vibration. The absorption bands at 951 and 1086 cm^{-1} were characteristic of Si-OH and Si-O-Si stretching vibration. New absorptions of the $–CH_2$ stretching vibration at 2922 and 2853 cm^{-1} were clearly observed after medication of SiO_2-MNPs with MPS. After surface polymerization of EGDMA and VIMCD-Cl, new peaks at 2985, 2951 and 1725 cm^{-1} were attributed to the $–CH_3$ asymmetry stretching, $–CH_3$ symmetry stretching and C=O stretching of ester groups in EGDMA, respectively. The peaks at 2922, 1640, 1450, 1157 and 943 cm^{-1} respectively corresponds to the $–CH_2$ asymmetry stretching, C=N stretching vibration, $–CH_2$ deformation vibration, coupled C–C/C–O stretching vibration and R-1,4-bond skeleton vibration of β-CD, similar to the results reported in the literature.[33,34] These results indicated that EGDMA and VIMCD-Cl have been successfully coating on the surface of MPS-MNPs. And these were further confirmed by TGA (Fig. 3c). The TGA curves shows that a significant decrease in the mass of the chiral materials over the observed temperature because of the decomposition of organics, including MPS, EGDMA and VIMCD-Cl. Elemental analysis results from Table 1 show that the C content of the synthesized magnetic microspheres increased after silanization. The amount of MPS grafted on the silica-coated magnetic microspheres was about 106.7 μmol g^{-1}. A clearly increased in C and N content was observed after modification with a polymer layer, suggesting that the successful coating of VIMCD-Cl and EGDMA on the surface of MPS-MNPs.

The magnetic properties of the prepared materials were determined at room temperature by VSM. No obviously coercivity or remanence for all the magnetic samples was detected after the applied magnetic field was removed, indicating that the synthesized magnetic materials were superparamagnetic (Fig. 5). The magnetization saturation (Ms) values of the MNPs, SiO_2-MNPs, MPS-MNPs and VIMCD-MNPs were 89, 67, 62 and 51 emu g^{-1}, respectively. The magnetic responsiveness significantly reduced after modification because of the non-magnetic coatings, including silica, MPS, EGDMA and VIMCD-Cl. The prepared chiral magnetic materials still possess high magnetic response and could be sensitively controlled by applying an external magnetic field (Fig. 5 inset). The excellent magnetic responsiveness facilitates the chiral magnetic selector recycling from racemic solution, resulting in the fast phase separation in the microbatch methodology.

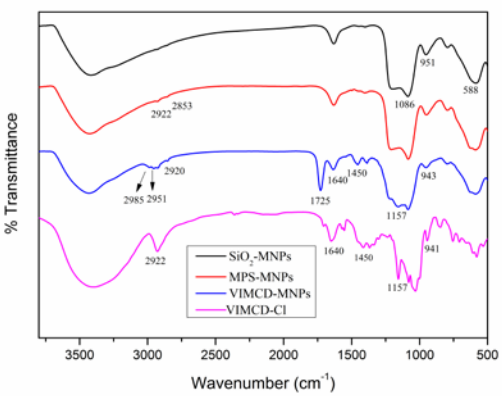

Fig. 4 FT-IR spectra of the synthesized SiO_2-MNPs, MPS-MNPs, VIMCD-MNPs and VIMCD-Cl.

Table 1 Elemental analysis results for the functionalized magnetic micrspheres

Sample	C (%)	H (%)	N (%)
SiO_2-MNPs	1.98	0.86	0.061
MPS-MNPs	3.26	0.92	0.058
VIMCD-MNPs	10.85	1.26	0.293

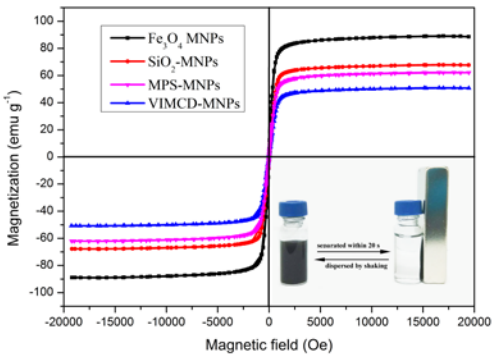

Fig. 5 Magnetization curves of the Fe_3O_4 MNPs, SiO_2-MNPs, MPS-MNPs and VIMCD-MNPs.

3.3 Chiral absorption of racemates using VIMCD-MNPs

The chiral recognition capacities of the synthesized VIMCD-MNPs for enantiomeric selectively absorption of dansyl amino acids were quantitatively evaluated by CE analysis of the supernatants. All the racemic solutions were mechanically agitated with the chiral materials and followed by magnetic decantation, the supernatants were collected and determined by CE. The results are shown in Fig. 6 and Table 2. Before treatment with VIMCD-MNPs, the peak areas of both two enantiomers for three dansyl amino acids were equal because of the equivalent amounts of D-enantiomers and L-enantiomers in their racemic solutions. After interaction with VIMCD-MNPs, the peak areas of both two enantiomers reduced. The decrease in the peak areas of L-enantiomers was much more than that of D-enantiomers. The results reveal that VIMCD-MNPs selectively discrimination of the two enantiomers and showed stronger interactions with the L-enantiomers than that of the D-enantiomers. According to the CE data, more amounts of L-enantiomers were adsorbed on chiral functionalized magnetic microspheres (*e.g.* 29% amounts of the L-enantiomers and 9% amounts of the D-enantiomers for Dns-DL-Phe), resulting in the relatively high concentration of D-enantiomers left in the supernatants with enantiomeric excess (Table 3). The enantioselectivity of VIMCD-MNPs was higher than 2.5, suggesting that VIMCD-MNPs shows high chiral recognition capacities toward dansyl amino acids and can be used as an efficient chiral magnetic selectors for potential application in enantiomeric separations. Various interactions including hydrophobic interactions, hydrogen bonding, π-π stacking effects and electrostatic interactions between VIMCD-MNPs and chiral analytes were responsible for the chiral recognition. All the three dansyl amino acids contain two or three aromatic rings and match the hydrophobic cavity of β-CD to form the host-guest inclusion complexes. The inclusion complexation between dansyl amino acids and VIMCD-MNPs plays important roles in the enantioselective adsoption process.[35-37] Additionally, VIMCD-MNPs could also interact with dansyl amino acids enantiomers through hydrogen bonding interactions resulting from the amino or carboxylate groups on the analytes and the hydroxy groups on the rims of the cavity in β-CD. Furthermore, the electrostatic interactions between the negatively charged carboxylate groups on the enantiomers and cationic imidazolium groups of VIMCD-Cl contributed most to the chiral discrimination.[38]

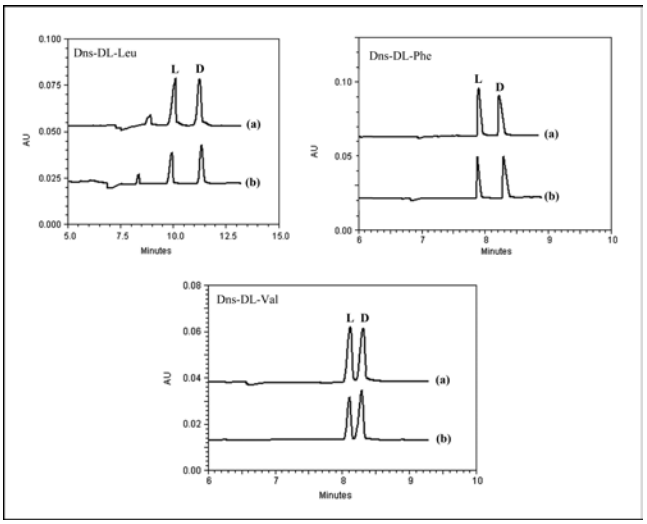

Fig. 6 CE separation of three dansyl amino acids in racemic solutions (a), in supernatants after interaction with VIMCD-MNPs (b).

Table 2 Peak area analysis of three dansyl amino acids racemic solutions before and after interaction with VIMCD-MNPs by CE analyses

Samples	Peak Area	
	L-enantiomers	D-enantiomers
Dns-DL-Leu[a]	3.08×10^5	3.06×10^5
Dns-DL-Leu[b]	2.42×10^5	2.85×10^5
Dns-DL-Val[a]	1.18×10^5	1.16×10^5
Dns-DL-Val[b]	0.88×10^5	1.01×10^5
Dns-DL-Phe[a]	2.73×10^5	2.75×10^5
Dns-DL-Phe[b]	1.96×10^5	2.52×10^5

[a] the racemic solutions before treatment with VIMCD-MNPs;

[b] the supernatants after interaction with VIMCD-MNPs.

The effect of the interaction time between VIMCD-MNPs and dansyl amino acids on the efficiency of the enantiomeric recognitions was also studied. The adsorptions of L-enantiomers gradually increased with increasing the interaction time up to 30 min (Table 4). Further increases did not lead to the improvement of the enantioselectivity, suggesting that the chiral recognition capacity enhanced its maximum when the VIMCD-MNPs interacted with dansyl amino acids for 30 min. The results also indicated that the chiral discrimination interactions between VIMCD-MNPs and dansyl amino acids were stable, and the enantioselective adsorption process was in

themodynamic equilibrium after the interaction time lasted for 30 min.

Table 3 Results of the quantitative evaluation of the chiral recognition capabilities of VIMCD-MNPs by CE analyses

	Calibration equation		Correlation coefficient		Adsorptions (%) by VIMCD-MNPs		Enantioselectivity α value [a]	e.e. (%) in supernatants [b]
	L-enantiomers	D-enantiomers	R^2_L	R^2_D	Ads (L)	Ads (D)		
Dns-DL-Phe	$Y=1.05\times10^6X+1.04\times10^4$	$Y=1.05\times10^6X+1.27\times10^4$	0.9997	0.9997	28.8	8.8	4.19	12.3
Dns-DL-Leu	$Y=1.10\times10^6X+3.36\times10^4$	$Y=1.09\times10^6X+3.33\times10^4$	0.9991	0.9992	24.4	7.6	3.92	10.0
Dns-DL-Val	$Y=4.34\times10^5X+1.01\times10^4$	$Y=4.29\times10^5X+0.78\times10^4$	0.9996	0.9993	28.4	13.2	2.61	9.6

[a] The enantioselectivity α value was calculated by the formula: $\alpha = \frac{X_L\times(1-X_D)}{(1-X_L)\times X_D}$, where X_L and X_D represent the percentage of the L and D-enantiomers absorbed on VIMCD-MNPs.

[b] The enantiomeric excess was calculated by the formula: $e.e. = \frac{N_D-N_L}{N_D+N_L}\times100\%$, where N_L and N_D were respectively the amounts of the L and D-enantiomers left in the supernatants and can be obtained from the linear calibration equation quantified by CE analyses.

Table 4 Effect of interaction time on the chiral recognition ability of VIMCD-MNPs

Interaction time (min)	Adsorptions (%) by VIMCD-MNPs		Enantioselectivity (α)	e.e. (%) in supernatants
	Ads (L)	Ads (D)		
5	4.0	1.8	2.27	1.2
10	12.8	5.2	2.68	4.2
30	24.4	7.6	3.92	10.0
60	25.2	9.2	3.32	9.7

The reusability of the chiral magnetic materials was also investigated. After separation from racemic solution, all the used VIMCD-MNPs (total amount of 300 mg) were washed three times with acetate buffer and then dried under vacuum to give 283 mg of VIMCD-MNPs. These results indicated that the prepared chiral materials possess an excellent recyclability.

4. Conclusions

Vinylimidazolium-modified β-CD derivatives were synthesized by microwave irradiation for the first time, and were immobilized on the surface of MPS-MNPs to form novel chiral magnetic microspheres. The synthesized chiral materials were uniformly spherical with core-shell structures. They exhibited strong magnetic responsiveness and good superparamagnetism. The successful polymerization of VIMCD-Cl on the surface of MPS-MNPs was confirmed by TEM, FT-IR, TGA and elemental analysis. The chiral separation results indicated that VIMCD-MNPs showed excellent chiral recognition ability toward dansyl amino acids. Much stronger interactions were observed with the L-enantiomers than the D-enantiomers. The L-enantiomers had more adsorptions on the chiral functionalized magnetic materials in the chiral recognition. Additionally, the functionalized chiral magnetic microspheres could be completely separated and recycled from racemic solutions under an applied magnetic field. These chiral magnetic selectors are appropriate candidates for chiral discriminations and have potential application in chiral recognition of other kinds of racemates.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (Grant No. 21075008) and Beijing Natural Science Foundation (Grant No. 2132048).

Note and references

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