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# PAPER

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# 1. Introduction

Chiral recognition and enantioseparation of molecules play important roles in numerous fields, such as medicines, synthetic chemistry, food additives, and agrochemicals.<sup>1-3</sup> Individual enantiomers of chiral drugs usually exhibit significantly different pharmacological activities, toxicities, metabolic effects and rates due to the high degree of stereoselectivity of enzymatic reactions and other biological processes.<sup>4,5</sup> β-Adrenergic blocking agents (β-blockers), as a type of representative chiral drugs, are widely used for the treatment of angina, cardiac arrhythmias, hypertension, myocardial infarction and glaucoma.<sup>6-9</sup> They are commonly marketed and administered as racemic mixtures. The pharmacological activities usually reside in the *S*-enantiomer owing to its higher stereoselective affinity

# A chiral magnetic molybdenum disulfide nanocomposite for direct enantioseparation of *RS*-propranolol<sup>†</sup>

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We herein report a novel chiral magnetic molybdenum disulfide nanocomposite (MMoS<sub>2</sub>/PNG-CD) with a high enantioselectivity and excellent thermosensitivity and magnetism. The prepared MMoS<sub>2</sub>/PNG-CD shows temperature-dependent chiral discrimination and enantioselectivity toward a chiral drug RSpropranolol (RS-PPL), which is based on the molecular recognition ability of beta-cyclodextrin ( $\beta$ -CD) and the thermosensitivity of poly(N-isopropylacrylamide) (PNIPAM). The synthesized MMoS<sub>2</sub>/PNG2-CD by using a monomer molar ratio of GMA to NIPAM of 2:1 demonstrates a high selectivity toward R-PPL over S-PPL due to the synergistic effect of the PNIPAM moieties and  $\beta$ -CD hosts. The thermo-induced volume phase transition (VPT) of the introduced PNIPAM moieties significantly affects the inclusion constants of the  $\beta$ -CD/R-PPL complex, and thus the loading and desorption of R-PPL on the MMoS<sub>2</sub>/ PNG2-CD. The enantioselectivity at temperatures below the lower critical solution temperature (LCST) of the PNG- $\beta$ -CD grafting chains is much higher than that at temperatures above the LCST. As a result, the regeneration of the MMoS<sub>2</sub>/PNG2-CD is easily achieved via simply changing the operating temperature. Moreover, the regenerated MMoS<sub>2</sub>/PNG2-CD can be readily recovered from the RS-PPL solution under an external magnetic field for reuse. Such a multifunctional molybdenum disulfide nanocomposite with a high enantioselectivity and excellent thermosensitivity and regenerability is promising to serve as a high-performance nanoselector for direct resolution of various  $\beta$ -blocker drugs.

> toward  $\beta$ -receptors, while the *R*-enantiomer is pharmacologically inactive or even toxic in some cases.<sup>6-8</sup> RS-Propranolol (RS-PPL), as an important  $\beta$ -blocker, is extensively utilized in treating cardiovascular diseases, such as angina pectoris, arrhythmia, myocardial infarction, and dysfunctional labor and anxiety.8,9 But the two isomers of PPL usually show significantly distinct pharmacodynamics and pharmacokinetics. For example, the metabolism and elimination of S-PPL is faster than those of R-PPL, and the activity of S-PPL is 100 times higher than that of the R-PPL since the β-blocker activity relies on the Senantiomer.8,9 Hence, effective identification and resolution of RS-PPL to obtain single isomers is of importance and highly desirable. To date, various techniques have been developed for enantioseparation of β-blockers including highthe performance liquid chromatography (HPLC),6,9,10 gas chromatography (GC),<sup>11</sup> thin layer chromatography (TLC),<sup>12</sup> capillary electrochromatography (CEC),13,14 and capillary electrophoresis (CE).15-17 However, they are generally laborious, high cost and complicated in operation, thus hampering their practical applications. By contrast, direct resolution of RS-PPL by using chiral magnetic nanoselectors (CMNSs) is a feasible strategy to obtain single isomers due to its simplicity in operation, inexpensiveness, and easy manipulation.18-22 The key of this method is to develop high-performance CMNSs.

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The currently existing CMNSs obtained mainly via surface modification of magnetic nanomaterials using various chiral molecules or materials, such as lipases,23 polynorepinephrine,7 cellulose,<sup>24</sup> bovine serum albumin (BSA),<sup>25</sup> chiral metal organic frameworks (MOFs),<sup>26</sup> and β-cyclodextrin (β-CD) and its derivatives.27,28 Those CMNSs have been widely verified to own high enantioselectivity toward a variety of enantiomeric compounds. However, organic solvents or inorganic salts are required to release the loaded enantiomers from those CMNSs to realize the regeneration of the nanoselectors, which seems to be complicated and environmentally unfriendly.18-20,22,29-31 Poly(N-isopropylacrylamide) (PNIPAM) is a popular smart polymer that can occur reversible volume phase transition (VPT) in water as the surrounding temperature changes across its lower critical solution temperature (LCST) of  $\sim$ 32 °C, thus showing excellent thermosensitivity.32 β-CD is a cyclic polysaccharide and consists of seven glucose units characteristic of a hydrophobic cavity, in which a large number of guests can be loaded to form inclusion complexes based on van der Waals forces, hydrophobic interactions, hydrogen bonding interactions,33 hence demonstrating high chiral discrimination and enantioselectivity. Besides, the incorporation of β-CD into PNIPAM chains allows the fabrication of a PNIPAM-β-CD smart polymer that simultaneously possess chiral recognition and thermosensitive properties. Most importantly, the thermo-induced VPT of the PNIPAM components in response to temperature variations can remarkably affect the inclusion constants of β-CD and the loaded guest molecules in the PNIPAM-\beta-CD system.34,35 Inspired by which, we have recently developed a series of smart CMNSs via surface decoration of Fe<sub>3</sub>O<sub>4</sub> NPs,<sup>36,37</sup> Fe<sub>3</sub>O<sub>4</sub> NPsloaded graphene oxide nanosheets (MGO)<sup>38</sup> and carbon nanotubes (MCNTs)<sup>39</sup> with PNG-β-CD smart polymer chains. The PNG- $\beta$ -CD smart polymer chains are composed of poly(N-isopropylacrylamide-co-glycidylmethacrylate) (PNG) copolymer chains with appended rich β-CD hosts, which play a crucial role in effective chiral identification and resolution of various amino acids (AAs) enantiomers. The  $\beta$ -CD units serve as functional receptors or chiral selectors that can specifically recognize and bind L-enantiomer into their cavities to form  $\beta$ -CD/L-enantiomer inclusion complexes. The PNIPAM moieties in the PNG chains act as micro-environmental adjustors for regulating the inclusion constants of  $\beta$ -CD/L-enantiomer. Therefore, those nanoselectors exhibit high chiral recognition and enantioselectivity toward various AAs enantiomers. Most importantly, the desorption of the loaded L-enantiomers and the regeneration of the nanoselectors can be conveniently achieved via simply changing the operating temperature.

Molybdenum disulfide (MoS<sub>2</sub>) nanosheet, a two-dimensional (2D) transition-metal dichalcogenide material, has attracted widespread interest for the past two decades due to its unique properties, such as large specific surface area, lamellar structure, low manufacturing cost, and simple fabrication.<sup>40-45</sup> This enables it to have significant potentials in a variety of fields including energy storage and conversion,<sup>40,45</sup> sensors,<sup>40,42</sup> opto-electronic devices,<sup>40,43</sup> and drug carriers.<sup>44</sup> Especially, the large specific surface area makes it be an ideal substrate for binding PNG-β-CD chains. Besides, *via* depositing certain amount of

 $Fe_3O_4$  NPs on the PNG- $\beta$ -CD-decorated MoS<sub>2</sub> nanosheets to achieve multifunctional nanocomposite will possess not only high enantioselectivity, but also excellent thermosensitivity and magnetism.

We herein report a PNG- $\beta$ -CD-modified magnetic MoS<sub>2</sub> nanocomposite (MMoS<sub>2</sub>/PNG-CD) and explored its potential as a chiral nanoselector for direct enantioseparation of RS-PPL. The MMoS<sub>2</sub>/PNG-CD was prepared via a multistep reaction process including solvothermal reaction, surface-initiated atom transfer radical polymerization (SI-ATRP) and a ring-opening reaction. The fabricated MMoS<sub>2</sub>/PNG-CD simultaneously possesses chiral identification and enantioselectivity toward RS-PPL based on the molecular recognition of  $\beta$ -CD and the thermosensitivity of the PNIPAM moieties. Effects of the operating temperature, the initial RS-PPL concentration and the molar ratio of glycidylmethacrylate (GMA) to NIPAM on the separation efficiencies of RS-PPL were systematically investigated. The results indicate that the operating temperature and the RS-PPL concentration strongly affect the resolution efficiencies of RS-PPL. Moreover, those parameters were rationally optimized to achieve the optimal separation efficiency of RS-PPL. Besides, the desorption of the loaded R-PPL molecules and the renewability of the MMoS<sub>2</sub>/PNG-CD were easily realized via simply changing the operating temperature. Such a multifunctional MoS<sub>2</sub> nanocomposite developed herein that possesses a high chiral recognition and enantioselectivity, excellent thermosensitivity and regenerability, is promising to serve as a high-performance nanoselector for direct enantioseparation of various β-blocker drugs.

# 2. Experimental

#### 2.1. Materials

Sodium molybdate dihydrate (Na<sub>2</sub>MO<sub>4</sub>·2H<sub>2</sub>O, 99%) and thioacetamide (C<sub>2</sub>H<sub>5</sub>NS, 98%) were purchased from Aladdin Chemicals (Shanghai, China). Poly(acrylic acid) (PAA,  $M_{\rm w}$  = 1800) was obtained from Sigma-Aldrich Chemicals (Shanghai, China). Iron(iii) chloride hexahydrate (FeCl<sub>3</sub>·6H<sub>2</sub>O, 99%), sodium acetate anhydrous (CH<sub>3</sub>COONa, 99%), dopamine hydrochloride (DA, 98%) and RS-PPL (99%) were bought from Alfa chemicals (Shanghai, China). Tris(hydroxymethyl)aminoethane (Tris, 99.5%), 2-bromoisobutyrylbromide (BiBB, 98%), 2,2'-bipyridine (bpy, 99%), GMA (96%) and NIPAM (98%) were obtained from Tokyo Chemicals Industry (TCI, Japan). NIPAM was purified by recrystallization with a mixture of hexane/ acetone (50/50, v/v) before use. Cuprous bromide (CuBr, 99%) and  $\beta$ -CD (99%) were purchased from Kelong Chemicals (Chengdu, China). Ethylenediamine-modified β-CD (EDA-β-CD) was synthesized according to the ref. 46 and 47 Deionized water (18.2 MΩ, 25 °C) from a Milli-Q plus purification system (Millipore) was used throughout the experiments. All other chemicals were analytical grade and used as received.

#### 2.2. Synthesis of MoS<sub>2</sub> nanosheets

 $MoS_2$  nanosheets were synthesized *via* a simple hydrothermal reaction.<sup>45</sup> Briefly, 0.3 g of  $Na_2MO_4 \cdot 2H_2O$  and 0.6 g of  $C_2H_5NS$ 

were dissolved in 40 mL water by ultrasonication for 30 min. Then the obtained solution was transferred in a Teflon-lined stainless-steel autoclave (100 mL) and reacted at 220 °C for 24 h. After natural cooling, the black precipitate was separated by centrifugation (8500 rpm, 15 min) and washed several times with water, and finally dispersed in 50 mL water for the subsequent use.

#### 2.3. Synthesis of MMoS<sub>2</sub>

The Fe<sub>3</sub>O<sub>4</sub> NPs-loaded MoS<sub>2</sub> nanosheets (MMoS<sub>2</sub>) were synthesized according to the ref. 45 with some modification (Fig. 1a and b). In brief, 15 mL of MoS<sub>2</sub> dispersion (100 mg MoS<sub>2</sub>) was mixed with 30 mL of water/ethanol (v/v = 1:2) for 1 h under ultrasonication. Then, 0.5 g of FeCl<sub>3</sub>·6H<sub>2</sub>O, 0.75 g of CH<sub>3</sub>-COONa and 100 mg of PAA were added under mechanical stirring for 30 min. After that, the mixture was transferred in a Teflon-lined stainless-steel autoclave (100 mL) and allowed to react at 200 °C for 10 h. After natural cooling, the black precipitate was separated with a permanent magnet and washed several times with water, and then dispersed in 20 mL water for the subsequent use.

#### 2.4. Synthesis of MMoS<sub>2</sub>/PDA-Br

The magnetic MoS<sub>2</sub> macroinitiator (MMoS<sub>2</sub>/PDA-Br) was synthesized via a two-step reaction process (Fig. 1b-d). First, the PDA-coated MMoS<sub>2</sub> (MMoS<sub>2</sub>/PDA) was prepared according to our recent work.37-39 In detail, 100 mg of MMoS2 was dispersed in 100 mL Tris-HCl buffer solution (pH = 8.6) in a three-necked flask (150 mL). The Tris-HCl buffer solution was prepared by dissolving 0.26 g of Tris in a mixture solution of ethanol/water (30/70, v/v, 100 mL). Then, 10 mL of DMF dissolved 0.2 g of DA was added dropwise under ultrasonication and allowed the reaction to continue under stirring at 25 °C for 6 h. The black product of MMoS<sub>2</sub>/PDA was collected with the permanent magnet and washed several times with water, and then dispersed in 30 mL water for subsequent use. The PDA layer provides the MMoS<sub>2</sub> with rich catechol and imine functional groups. This offers an ideal platform for immobilizing rich Br atom on the MMoS<sub>2</sub> via a nucleophilic substitution reaction between the acyl bromide group in BiBB and the -NH2 and -OH

groups on the PDA layer. In detail, 100 mg of MMoS<sub>2</sub>/PDA was mixed with 20 mL of DMF in a three-necked flask and stirred at 450 rpm for 10 min under N<sub>2</sub> atmosphere and ice bath. Then, 1 mL of triethylamine was added and continued to stir for another 10 min. After that, 20 mL DMF solution contained 0.8 mL BiBB was added dropwise. After reaction for 12 h, the obtained MMoS<sub>2</sub>/PDA-Br product was collected by a magnet and washed with water several times, and then dispersed in 30 mL water for the further use.

#### 2.5. Synthesis of MMoS<sub>2</sub>/PNG

The PNG chains-grafted MMoS<sub>2</sub> (MMoS<sub>2</sub>/PNG) was synthesized *via* a SI-ATRP using NIPAM and GMA as the monomers, MMoS<sub>2</sub>/ PDA-Br as the macroinitiator (Fig. 1d and e). Detailly, 100 mg of MMoS<sub>2</sub>/PDA-Br and various GMA and NIPAM dosages, which represent the molar ratios of 1:1 ( $V_{\text{GMA}} = 0.85 \text{ mL}, m_{\text{NIPAM}} =$ 0.6827 g), 2 : 1 ( $V_{\text{GMA}}$  = 1.70 mL,  $m_{\text{NIPAM}}$  = 0.6827 g), 3 : 1 ( $V_{\text{GMA}}$ = 2.565 mL,  $m_{\text{NIPAM}}$  = 0.6827 g), and 4:1 ( $V_{\text{GMA}}$  = 3.39 mL,  $m_{\rm NIPAM} = 0.6827$  g), denoted as the MMoS<sub>2</sub>/PNG1, MMoS<sub>2</sub>/ PNG2, MMoS<sub>2</sub>/PNG3, and MMoS<sub>2</sub>/PNG4 samples, respectively, were added in the mixture of methanol/water (15/5, v/v, 20 mL) in a dry Schlenk flask (50 mL) under N2 atmosphere and magnetic stirring for 20 min. Next, CuBr (0.04 g) and bpy (0.12 g) were added and the mixture was stirred for another 30 min. After three freeze-pump-thaw cycles deoxygenation, the reaction was allowed to last at 55 °C for 6 h. The MMoS<sub>2</sub>/PNG serial products were obtained and washed with water several times, and then dried in vacuum at 30 °C for 24 h for the subsequent use.

#### 2.6. Synthesis of MMoS<sub>2</sub>/PNG-CD

The  $\beta$ -CD-modified MMoS<sub>2</sub>/PNG (MMoS<sub>2</sub>/PNG-CD) was synthesized as follows (Fig. 1e and f). MMoS<sub>2</sub>/PNG (0.08 g) and EDA- $\beta$ -CD (0.75 g) were firstly dispersed in dry DMF (15 mL) under ultrasonication for 30 min. Then the reaction was proceeded at 60 °C for 36 h, and the black MMoS<sub>2</sub>/PNG-CD product was collected with a magnet and washed with DMF and water several times, and lyophilized. The MMoS<sub>2</sub>/PNG-CD serial products synthesized using the MMoS<sub>2</sub>/PNG1, MMoS<sub>2</sub>/PNG2, MMoS<sub>2</sub>/PNG3, and MMoS<sub>2</sub>/PNG4 were denoted as the MMoS<sub>2</sub>/



Fig. 1 Schematic illustration of the synthesis process of MMoS<sub>2</sub>/PNG-CD.

PNG1-CD, MMoS<sub>2</sub>/PNG2-CD, MMoS<sub>2</sub>/PNG3-CD, and MMoS<sub>2</sub>/PNG4-CD, respectively.

#### 2.7. Direct resolution of RS-PPL

Direct resolution of RS-PPL using MMoS<sub>2</sub>/PNG-CD was performed as follows. MMoS<sub>2</sub>/PNG-CD (50 mg) was added in 15 mL *RS*-PPL solution ( $C_0 = 0.5$  mM). Then the dispersion was stirred at 25 and 55 °C (below and above the LCST of PNG-β-CD). Next, the enantiomers-loaded MMoS<sub>2</sub>/PNG-CD was enriched on the wall of vials with a magnet at the predetermined time intervals, and a 150 µL supernatant solution was taken out and filtrated with a microporous membrane  $(0.22 \ \mu m)$  for the subsequent HPLC measurement. Quantitative analysis of the separation of RS-PPL by the MMoS<sub>2</sub>/PNG-CD was conducted with a HPLC system (Agilent 1200, USA) equipped with a variable wavelength detector (DAD, Agilent Technologies), and the obtained data were analyzed with a HPLC-1200 ChemStation software. Sample tests were carried out with a symmetry shield RP18 column (3.9 imes 150 mm, 5  $\mu$ m, Waters, USA) at 25 °C under a 225 nm UV detector wavelength and 20  $\mu$ L injection volume ( $\nu = 0.8$ mL min<sup>-1</sup>) for the mobile phase. The mobile phase was a mixture of ethanol/ammonium acetate (5/95, v/v, pH 4.5). All the separation experiments were conducted at least twice to guarantee the data accuracy.

To verify the thermosensitive resolution of *RS*-PPL was due to the formation of  $\beta$ -CD/*R*-PPL complexes and the incorporation of PNIPAM moieties, the control trials were performed by the  $\beta$ -CD-free MMoS<sub>2</sub>/PNG and the PNIPAM-free MMoS<sub>2</sub>/PG-CD with the same procedure as mentioned above. The separation of *RS*-PPL was evaluated with an enantiomeric excess (ee%) from the peak areas of two isomers in permeates and calculated based on the equation:

$$ee\% = (S_{\rm S} - S_{\rm R})/(S_{\rm S} + S_{\rm R}) \times 100\%$$
 (1)

where  $S_S$  and  $S_R$  represent the corresponding peak areas of *S*and *R*-PPL in the filtrate measured by HPLC, respectively.

Besides, since  $\beta$ -CD were tethered in the PNG chains *via* an epoxy ring-opening reaction of the -NH<sub>2</sub> group in EDA- $\beta$ -CD and the epoxy groups in PGMA moieties. The dosage of GMA monomer will certainly affect the binding amount of  $\beta$ -CD significantly, thus the separation efficiencies of *RS*-PPL. Therefore, effect of the molar ratios of GMA to NIPAM ( $n_{\text{GMA}}: n_{\text{NIPAM}}$ = 1:1, 2:1, 3:1 and 4:1) on the separation efficiencies of the resulted MMoS<sub>2</sub>/PNG*i*-CD products (*i* = 1, 2, 3, and 4) were also studied. Besides, to investigate the effect of the initial *RS*-PPL concentration on the resolution performance of the MMoS<sub>2</sub>/ PNG-CD, the *RS*-PPL concentration varied from 0.1 to 1 mM while sustaining the other conditions invariable during the separation experiments. To explore the reusability of the nanoselector, the used MMoS<sub>2</sub>/PNG-CD was washed with hot/ cold water in turn by ultrasonication for the next cycle.

#### 2.8. Characterization

Transmission electron microscope (TEM) images were obtained with a JEM-2010 microscope (JEOL, Japan) at an accelerating

voltage of 120 kV. The samples were prepared by drop-casting a dilute solution of particles onto carbon-coated copper grids, followed by air drying. High-resolution transmission electron microscopy (HRTEM) images were obtained on a field-emission electron microscope (FEI Talos F200x, USA) equipped with a Super X energy spectrum. X-ray photoelectron spectroscopy (XPS) measurements were performed on a Thermo Fischer ESCALAB 250Xi (USA). Structural information of the samples was obtained by X-ray diffractometer-6100 diffractometer (Shimadzu, Japan). Fourier transform infrared spectrometry (FT-IR) analysis was conducted on an IR 200 spectrometer (Thermo Nicolet, USA) using KBr pellets. Thermogravimetric analysis (TGA) was performed on a Mettler TGA/SDTA851e° instrument (Switzerland) at a heating rate of 5 °C min<sup>-1</sup> from 30 to 700 °C under N<sub>2</sub> atmosphere. The magnetism of the samples was measured with a vibrating sample magnetometer (VSM) on a model 2000 physical property measurement system (Quantum design) at room temperature.

### 3. Results and discussion

#### 3.1. Fabrication and characterization of materials

The synthesis process of the material is schematically illustrated in Fig. 1. MoS<sub>2</sub> nanosheets with a large specific surface area were used as the substrate for binding PNG-β-CD smart polymer chains. Fe<sub>3</sub>O<sub>4</sub> NPs were firstly deposited on the  $MoS_2$ nanosheets to endow them with magnetic separability (Fig. 1a and b) then the PDA functional layer is coated on the  $MMoS_2$  to offer the nanosheets rich active sites (-NH<sub>2</sub> and -OH groups) (Fig. 1b and c), and plentiful of Br atoms were introduced on the MMoS<sub>2</sub> via a nucleophilic substitution reaction between the acyl bromide group in BiBB molecule and the -NH2 and -OH groups on the PDA layer (Fig. 1c and d). The PNIPAM moieties were introduced in the PNG-\beta-CD to facilitate the MMoS<sub>2</sub> with thermosensitive resolution ability and convenient regenerability via simply changing the operating temperature. Rich β-CD hosts were bound to the PNG via an epoxy ring-opening reaction of epoxy groups in PGMA and the -NH<sub>2</sub> group in EDA-β-CD to endow the MMoS<sub>2</sub> nanocomposite with high enantioselectivity toward various chiral compounds (Fig. 1e and f).

Effect of the amount of Fe<sub>3</sub>O<sub>4</sub> NPs deposited on the MoS<sub>2</sub> on the separation performances of the MoS<sub>2</sub> functional nanocomposite was also investigated by the different samples synthesized with various FeCl<sub>3</sub>·6H<sub>2</sub>O dosages (0.2, 0.5, and 1.0 g), since the Fe<sup>3+</sup> concentration in the feed reactants strongly affects the loading amount of Fe3O4 NPs. As observed in Fig. S1a,<sup>†</sup> the samples synthesized with a smaller (0.2 g) or a larger dosage of  $FeCl_3 \cdot 6H_2O(1.0 \text{ g})$  (denoted the MMoS<sub>2</sub>-0.2 and MMoS<sub>2</sub>-1.0, respectively) show undesirable magnetism. The MMoS<sub>2</sub>-0.2 exhibits a poor magnetic separability owing to that a low Fe<sup>3+</sup> concentration in the reactant leads to a small loading amount of Fe<sub>3</sub>O<sub>4</sub> NPs. Therefore, it was difficult to be collected by a magnet even after 24 h. For a larger dosage (1.0 g), the prepared MMoS2-1.0 exhibits poor water dispersibility (Fig. S1b<sup>†</sup>). Rapid enrichment of the sample particles on the vial wall is observed. The undesirable aggregations of the MMoS<sub>2</sub>-1.0 will dramatically reduce the specific surface area of the

MMoS<sub>2</sub> substrate, and thus the grafting density of PNG-β-CD as well as the binding amount of  $\beta$ -CD, and finally the separation efficiencies of RS-PPL. Therefore, the MMoS<sub>2</sub>-0.5 sample with a relatively high specific surface area and a satisfactory magnetism was chosen as the substrate for the subsequent grafting reactions. Besides, at a small FeCl<sub>3</sub>·6H<sub>2</sub>O dosage, the typical Fe–O peak at 584 cm<sup>-1</sup> from the Fe<sub>3</sub>O<sub>4</sub> NPs on the MoS<sub>2</sub> is observable and the peak intensity is quite weak (Fig. S2<sup>†</sup>). While with increasing the dosage to 1.0 g, the Fe-O peak shifts from 584 to 536 cm<sup>-1</sup> and becomes much stronger. This indicates that a larger FeCl<sub>3</sub>·6H<sub>2</sub>O dosage causes a larger loading amount of Fe<sub>3</sub>O<sub>4</sub> NPs on the MoS<sub>2</sub>. Higher loading amount will inevitably decrease the specific surface area of the MMoS<sub>2</sub> substrate, and thus the grafting density of PNG-β-CD as well as the binding amount of  $\beta$ -CD, and finally the resolution efficiencies of RS-PPL. Therefore, the MMoS<sub>2</sub>-0.5 sample with a compromising performance of specific surface area and magnetic property (abbreviated  $MMoS_2$ ) was employed for the following grafting of PNG-CD functional polymer chains.

The morphology and microstructures of the functional  $MMoS_2$  nanocomposites were observed by TEM. As shown in Fig. 2a, the primitive  $MoS_2$  nanosheets character a 2D fold laminar structure. After solvothermal reaction,  $Fe_3O_4$  NPs with sizes of 20–50 nm are clearly observed on the  $MoS_2$  (Fig. 2b), which endow the nanosheets with convenient magnetic separability from enantiomeric solutions under an external magnetic field (EMF). The HRTEM image shows that the loaded  $Fe_3O_4$  NPs have a spherical structure and good dispersibility (Fig. S3a†). Further magnifying one of the particles, a clear and obvious lattice fringes is observed (Fig. S3b†). Measuring the distance between two adjacent planes in a specific direction

gives a value of 0.48 nm, corresponding to the lattice spacing of (111) planes of cubic magnetite. The cubic crystal lattice is determined by SAED, as shown in Fig. S3c.<sup>†</sup> The XRD pattern shows that the peaks at 18.3, 30.0, 35.5, 43.1, 53.4, 57.0, and 62.6° are marked by the indices (111), (220), (311), (400), (422), (511), and (440) of Fe<sub>3</sub>O<sub>4</sub> phases (Fig. S3d<sup>+</sup>). These peaks coincide with those of standard patterns (JCPDS no. 19-0629), confirming the formation of the cubic phase. Besides, XPS analysis provides detailed information on the chemical compositions of the MMoS<sub>2</sub>. As shown in Fig. S4,<sup>†</sup> the binding energy of Fe  $2p_{3/2}$ and Fe 2p<sub>1/2</sub> for Fe<sub>3</sub>O<sub>4</sub> is around 711.1 and 724.5 eV, respectively, which further confirm the particles are Fe<sub>3</sub>O<sub>4</sub> NPs.<sup>48</sup> After coating with a PDA layer on the surface, a thin organic matter of PDA is clearly observed on the MMoS<sub>2</sub> (Fig. 2c). After further modification with BiBB, the MMoS<sub>2</sub>/PDA-Br does not show a noticeable change in the surface microstructures due to the introduction of monolayer BiBB (Fig. 2d). When the PNG2 chains are grafted onto the MMoS<sub>2</sub> via a SI-ATRP reaction, black organic substance corresponding to the PNG2 chains are witnessed on the nanosheets (Fig. 2e). After the subsequent binding of  $\beta$ -CD in the PNG2, the morphology of the MMoS<sub>2</sub>/ PNG2-CD changes little, and only slight agglomeration of the sample is observed, indicating that the incorporation of  $\beta$ -CD has little effect on the morphology and microstructure of the sample (Fig. 2f). Those results indicate the successful synthesis of the MMoS<sub>2</sub>/PNG2-CD.

The successful fabrication of the MMoS<sub>2</sub>/PNG-CD is also verified by the FT-IR results. As displayed in Fig. 3a, for the MMoS<sub>2</sub>, two characteristic peaks at 572 and 1716 cm<sup>-1</sup> correspond to the stretching vibration of Fe–O and C=O stretching vibration of PAA stabilizers, respectively.<sup>49</sup> For the MMoS<sub>2</sub>/PDA,



Fig. 2 Typical TEM images of (a) MoS<sub>2</sub>, (b) MMoS<sub>2</sub>, (c) MMoS<sub>2</sub>/PDA, (d) MMoS<sub>2</sub>/PDA-Br, (e) MMoS<sub>2</sub>/PNG2, and (f) MMoS<sub>2</sub>/PNG2-CD.



Fig. 3 FT-IR spectra (a), TGA curves (b), and hysteresis loops (c) of MoS<sub>2</sub>, MMoS<sub>2</sub>, MMoS<sub>2</sub>/PDA, MMoS<sub>2</sub>/PDA-Br, MMoS<sub>2</sub>/PNG2 and MMoS<sub>2</sub>/PNG2-CD. The insets in (c) show the photographs of the MMoS<sub>2</sub>/PNG2-CD before (c1) and after (c2) magnetic separation.

the typical absorption peaks of 1400–1700 cm<sup>-1</sup> are ascribed to the stretching vibrations of N-H and benzene rings of PDA, indicating the coating of PDA layer on the MMoS<sub>2</sub>.<sup>37,39</sup> After anchoring BiBB molecules on the MMoS<sub>2</sub>/PDA, a weak characteristic peak of C=O stretching vibration at 1742 cm<sup>-1</sup> in BiBB is observed from the spectrum of the MMoS<sub>2</sub>/PDA-Br.<sup>37,39</sup> When the SI-ATRP reaction between GMA and NIPAM with a molar ratio of 2:1 occurs on the MMoS<sub>2</sub>/PDA-Br, the absorption peaks at 912 and 1734 cm<sup>-1</sup> owing to the C–O–C and C=O stretching vibrations in PGMA are all observed.37,39 Besides, the typical peak at 1660 cm<sup>-1</sup> due to the stretching vibration of C=O in PNIPAM moieties is also observed for the spectrum of the MMoS<sub>2</sub>/PNG. This indicates the successful grafting of PNG on the MMoS<sub>2</sub>/PDA.<sup>37,39</sup> For the MMoS<sub>2</sub>/PNG2-CD, the characteristic peaks at 1039 and 1157 cm<sup>-1</sup> come from the antisymmetric vibrations of the C–O–C and the C–C/C–O of β-CD, respectively. Moreover, the typical peak of the epoxy groups in PGMA at 912 cm<sup>-1</sup> disappears.<sup>37,39</sup> This indicates the successful synthesis of the MMoS<sub>2</sub>/PNG2-CD again.

Besides, the TGA results also confirm the successful fabrication of the MMoS<sub>2</sub>/PNG-CD. Fig. 3b shows the TG results of the MoS<sub>2</sub>, MMoS<sub>2</sub>, MMoS<sub>2</sub>/PDA, MMoS<sub>2</sub>/PDA-Br, MMoS<sub>2</sub>/PNG2, and MMoS<sub>2</sub>/PNG2-CD. The gradual increase in weight loss of each sample is mainly arisen from the decomposition of organic substances introduced on the MMoS<sub>2</sub>. For the MMoS<sub>2</sub>, a weight loss of 20.59% from 25 to 700 °C is owing to the evaporation of the physically adsorbed water and the decomposition of PAA stabilizers on the MMoS<sub>2</sub>. After PDA coating on the MMoS<sub>2</sub>, the weight loss increases by 5.65% attributed to the decomposition of PDA layer in the same temperature range. For the  $MMoS_2/PDA$ -Br, an additional weight loss of  $\sim 3.6\%$ compared with the MMoS<sub>2</sub>/PDA is thanks to the decomposition of BiBB attached in the PDA layer. After the grafting of PNG2 copolymer chains on the MMoS<sub>2</sub>/PDA-Br, the weight loss increases by  $\sim$ 27.16% due to the decomposition of PNG2 chains. The binding amount of PNG2 is 387.2 mg  $g^{-1}$  based on the weight loss data. After a ring-opening reaction between the epoxy groups in PGMA and the  $-NH_2$  group in EDA- $\beta$ -CD, rich  $\beta$ -CD hosts are tethered in the PNG2, giving rise to the formation of the MMoS<sub>2</sub>/PNG2-CD. An additional mass loss of ~25.58% in comparison with that of the MMoS<sub>2</sub>/PNG2 is owing to the decomposition of  $\beta$ -CD in the PNG2. The binding amount of  $\beta$ -CD is calculated to be 595.0 mg  $g^{-1}$ . Those results further confirm the successful fabrication of the MMoS<sub>2</sub>/PNG2-CD. The large binding of  $\beta$ -CD greatly benefits from incensing the enantioselectivity of the MMoS<sub>2</sub>/PNG2-CD toward RS-PPL.

The elemental analysis results of the  $MoS_2$  nanocomposites also verify the successful preparation of the  $MMoS_2/PNG$ -CD. As shown in Table 1, the element S in all samples come from  $MoS_2$ , and their content gradually reduces from the  $MMoS_2$  to the

Table 1         The elemental	analysis of th	ne functional	MoS <sub>2</sub> serial sa	mples
Sample	N (%)	C (%)	Н (%)	S (%)
$MMoS_2$	0.160	1.585	0.557	18.72
MMoS <sub>2</sub> /PDA	1.930	17.24	1.462	9.116
MMoS <sub>2</sub> /PDA-Br	2.495	21.61	1.241	6.275
MMoS <sub>2</sub> /PNG2	3.125	33.18	3.532	5.21
MMoS <sub>2</sub> /PNG2-CD	3.225	44.61	6.335	0.744

MMoS<sub>2</sub>/PNG2-CD due to the introduction of PDA layer, BiBB and PNG- $\beta$ -CD. The element N origins from PDA layer for the MMoS<sub>2</sub>/PDA, from PNIPAM moieties for the MMoS<sub>2</sub>/PNG2 and from EDA- $\beta$ -CD for the MMoS<sub>2</sub>/PNG2-CD. As seen from Table 1, the content of N, C, and H in the MMoS<sub>2</sub>/PDA sample increases significantly compared with that of the MMoS<sub>2</sub>, indicating the coating of PDA layer on the MMoS<sub>2</sub>. For the MMoS<sub>2</sub>/PNG2, the content of C and H increases obviously, showing the grafting of PNG2 chains on the MMoS<sub>2</sub>. The content of C and H increases evidently after a ring-opening reaction between the epoxy groups in PGMA and the -NH<sub>2</sub> group in EDA- $\beta$ -CD. This results imply the successful incorporation of  $\beta$ -CD into the PNG2, thus causing the formation of MMoS<sub>2</sub>/PNG2-CD.

Depositing certain amount of Fe<sub>3</sub>O<sub>4</sub> NPs on the MoS<sub>2</sub> endows them with convenient magnetic separability from the enantiomeric solution under an EMF. VSM technique was used to characterize the magnetism of the MoS<sub>2</sub> functional nanocomposite in this study. As shown in Fig. 3c, the magnetization saturation ( $M_s$ ) values of the MMoS<sub>2</sub>, MMoS<sub>2</sub>/PDA, MMoS<sub>2</sub>/PDA-Br, MMoS<sub>2</sub>/PNG2, and MMoS<sub>2</sub>/PNG2-CD are 27.03, 18.34, 15.74, 10.07 and 8.09 emu g<sup>-1</sup>, respectively. The gradual reduction in  $M_s$  values is mainly due to the introduction of non-magnetic organic substances including PAA stabilizers, PDA layer, BiBB, PNG2- $\beta$ -CD on the MMoS<sub>2</sub>. While the as-synthesized MMoS<sub>2</sub>/ PNG2-CD still shows excellent magnetism. Besides, the magnetic hysteresis loop of the sample measured in a small measurement range (-500-500 Oe) passes through the origin, and there are almost no residual magnetization and coercive force are observed (Fig. S5<sup>†</sup>), indicating that the synthesized  $MMoS_2/PNG2$ -CD is superparamagnetic. Moreover, the  $MMoS_2/PNG2$ -CD can be easily separated from the water within 3 min under an EMF (inset c2 in Fig. 3c), and redispersed in the water rapidly *via* slight shaking (inset c1 in Fig. 3c). Such excellent magnetism of the MMoS\_2/PNG2-CD makes it convenient recovery from the *RS*-PPL solution.

#### 3.2. Direct resolution of *RS*-PPL by MMoS<sub>2</sub>/PNG-CD

To verify that  $\beta$ -CD in the PNG- $\beta$ -CD play a crucial role in the chiral identification and resolution of RS-PPL, the separation of the  $\beta$ -CD-contained MMoS<sub>2</sub>/PNG2-CD and the  $\beta$ -CD-free MMoS<sub>2</sub>/PNG2 toward RS-PPL ( $C_0 = 0.5 \text{ mM}$ ) was firstly investigated at 25 °C. As observed from Fig. 4a, the MMoS<sub>2</sub>/PNG2-CD shows a high enantioselectivity toward RS-PPL, and the ee% can reach 19.64% after interaction for 28 h. As mentioned above,  $\beta$ -CD has a hydrophobic cavity, numerous guests can be accommodated in its cavity to form inclusion complexes via various interactions such as van der Waals forces, hydrophobic interactions, and hydrogen bonding interactions. Although Sand R-PPL can form complexes with B-CD since the hydrophobic naphthalene ring of both two enantiomers can permeate into the β-CD cavity, the 3D structures of S- and R-PPL with respect to the position of -OH group at the chiral center of the two enantiomers are significantly different.33,50 Compared with the S-enantiomer, the intermolecular hydrogen bonds between the -OH group of R-PPL and the second hydroxyl groups  $(-(HO)_s)$  of  $\beta$ -CD rims are formed more favorably,<sup>33</sup> thus giving



Fig. 4 (a) Separation performances of the  $\beta$ -CD-contained MMoS<sub>2</sub>/PNG2-CD and the  $\beta$ -CD-free MMoS<sub>2</sub>/PNG2 toward *RS*-PPL at 25 °C. (b) Separation performances of the PNIPAM-contained MMoS<sub>2</sub>/PNG2-CD and the PNIPAM-free MMoS<sub>2</sub>/PG-CD toward *RS*-PPL at 25 and 45 °C. (c) Separation of *RS*-PPL by the MMoS<sub>2</sub>/PNG-CD serials samples synthesized with the different molar ratios of GMA to NIPAM. (d) Effect of the initial *RS*-PPL concentration on the separation performances of the MMoS<sub>2</sub>/PNG2-CD. (e) The reusability of the MMoS<sub>2</sub>/PNG2-CD. The concentration of *RS*-PPL in (a)–(c), and (e) is 0.5 mM.

rise to a higher selectivity of the MMoS<sub>2</sub>/PNG2-CD toward R-PPL over S-PPL at 25 °C. For the MMoS<sub>2</sub>/PNG2, since the absence of  $\beta$ -CD in the PNG2, therefore, it shows never a noticeable enantioselectivity toward RS-PPL. As observed in Fig. 4a, the maximal ee value is only 1.27% (diamond). Moreover, the operating temperature significantly affects the separation of RS-PPL (Fig. 4b). At the temperature lower than the LCST of the PNG-β-CD (such as 25 °C), the PNIPAM chains in the PNG-β-CD are hydrophilic and swollen. At this case, rich β-CD hosts can specifically recognize and bind R-PPL to form stable complexes since the inclusion constants of  $\beta$ -CD/R-PPL are large,<sup>37,39</sup> thus yielding a high enantioselectivity of the MMoS<sub>2</sub>/PNG2-CD. While at 45 °C, higher than the LCST, the ee value increases slowly and just reaches a small value (less than 2%) even prolonging the contact time up to 36 h (triangle, Fig. 4b). This is because that PNIPAM chains in the PNG-\beta-CD become hydrophobic and shrunken under this circumstance, effect of the steric hindrance from the shrinking and crowded PNIPAM chains results in a significant reduction in the inclusion constants of  $\beta$ -CD/R-PPL,<sup>34,35</sup> thus generating a low enantioselectivity of the MMoS<sub>2</sub>/PNG2-CD. This indicates that  $\beta$ -CD on the MMoS<sub>2</sub>/PNG2-CD play an important role in the enantioseparation of RS-PPL. The thermosensitive chiral recognition and enantioseparation of the MMoS<sub>2</sub>/PNG2-CD toward RS-PPL is ascribed to the incorporation of PNIPAM moieties into the PNGβ-CD.

As mentioned above,  $\beta$ -CD hosts play a pivotal role in the chiral recognition and enantioseparation of RS-PPL, which are bound in the PNG via a ring-opening reaction between the epoxy groups in PGMA and the  $-NH_2$  group in EDA- $\beta$ -CD. Therefore, upon keeping the usage of NIPAM invariable, the molar ratio of GMA to NIPAM  $(n_{\text{GMA}}/n_{\text{NIPAM}})$  will significantly affect the binding amount of β-CD in the PNG, and thus the hydrophilicity/hydrophobicity and the enantioselectivity of the MMoS<sub>2</sub>/PNG-CD. As observed in Fig. 4c, the ee value increases with increasing the  $n_{\rm GMA}/n_{\rm NIPAM}$  value from 1 to 2 at first, and then reduces gradually upon further enhancing from 2 to 4. The number of the epoxy groups in PNG increases with increasing the  $n_{\rm GMA}/n_{\rm NIPAM}$  value, thus a higher binding amount of  $\beta$ -CD in the PNG- $\beta$ -CD. A high binding amount of  $\beta$ -CD offers more active sites for interacting with R-PPL, thus causing a larger ee value. When the  $n_{\rm GMA}/n_{\rm NIPAM}$  value is larger than 2, the hydrophobicity of the MMoS<sub>2</sub>/PNG3 and MMoS<sub>2</sub>/PNG4 samples becomes stronger and stronger with increasing the GMA dosage. As a result, the reactive sites (epoxy groups) available in the PNG are relatively inadequate since the shrinkage of the PNG. Consequently, the PNG-β-CD chains become more hydrophobic, which worsens the dispensability of the  $MMoS_2/$ PNG3-CD and MMoS<sub>2</sub>/PNG4-CD in water (Fig. S6<sup>†</sup>). In this case, only small amount of β-CD on the MMoS<sub>2</sub>/PNG-CD can interact with R-PPL, thus leading to small ee values. As observed from Fig. 4c, the optimal  $n_{\text{GMA}}/n_{\text{NIPAM}}$  value for the synthesis of the

Table 2 Comparison of the resolution performances of the MMoS<sub>2</sub>/PNG-CD and other conventional methods<sup>4</sup>

Chiral selectors	Analyte	Interaction	Operation	Cost	Separation efficiency	Separation mode	Recyclability	Ref.
Chiral 3D HOIZA	2-Butanol and methyl-1- butano	Inclusion complexation	Complex	Low	ee = 8.4-98.2%	Direct	Yes	51
Ovomucoid chiral column	Carvedilol, pindolol and oxprenolol	Hydrogen bonds	Complex	High	$R_{\rm s} = 1.75 - 2.15$	Indirect	No	9
Chiral-mesoporous- polypyrrole NPs	Valine	Not mentioned	Complex	High	ee = 54%	Indirect	No	52
β-CD-modified AuNPs	DL-Val, Leu, Glu, Asp; chlorpheniramine, zopiclone and carvedilol	Inclusion complexation	Complex	High	$\alpha = 1.02$ –1.045	Indirect	No	53
β-CD-modified MWNTs, PS, TiO <sub>2</sub> , and Al <sub>2</sub> O <sub>3</sub>	Clenbuterol	Inclusion complexation	Complex	High	<i>α</i> = <b>1.023–1.034</b>	Indirect	No	54
Au(110) surface	Valine	S–Au, N–Au, and hydrogen bonds	Complex	High	Not mentioned	Indirect	No	55
CM-β-CD	Carteolol, atenolol, sotalol, metoprolol, esmolol and propranolol	Inclusion complexation and hydrogen bonds	Complex	High	$R_{\rm s} = 1.0-3.0$	Indirect	No	15
CM-β-CD, β-CD, and HP-β-CD	Betaxolol, sotalol, metoprolol, bisoprolol, bevantolol, and timolol	Not mentioned	Complex	High	$R_{\rm s} = 0.98 - 2.50$	Indirect	No	16
Ionic liquid cooperate with DM- β-CD and TM-β-CD	Pindolol, oxprenolol and propranolol	Hydrogen bonds, hydrophobic interactions and ion-dipole	Complex	High	α = 0.45-1.39	Indirect	No	17
MMoS <sub>2</sub> /PNG-CD	Propranolol	Inclusion complexation	Simple	Low	ee = 19.64%	Direct	Yes	This work

<sup>*a*</sup> PS, polystyrene; MWNTs, multi-walled nanotubes; CM- $\beta$ -CD, carboxymethyl- $\beta$ -cyclodextrin; HP- $\beta$ -CD, hydroxypropyl- $\beta$ -cyclodextrin; DM- $\beta$ -CD, 2,6-di-O-methyl- $\beta$ -cyclodextrin; TM- $\beta$ -CD, 2,3,6-tri-O-methyl- $\beta$ -cyclodextrin; ee, enantiomeric excess;  $R_s$ , separation resolution; and  $\alpha$ , separation factor.

MMoS<sub>2</sub>/PNG-CD with high enantioselectivity is 2. Therefore, the fabricated MMoS<sub>2</sub>/PNG2-CD was chosen to perform the material characterizations and the subsequent separation experiments. Incorporation of PNIPAM moieties into the PNG- $\beta$ -CD endows the MMoS<sub>2</sub>/PNG2-CD with excellent thermosensitivity (Fig. S7†), thus making the loaded *R*-PPL molecules release from the MoS<sub>2</sub> functional nanocomposite and the facile regeneration of the material. Therefore, the resolution of *RS*-PPL should be operated at temperatures below the LCST of the PNG2- $\beta$ -CD (25 °C) (circle, Fig. 4b), and the regeneration of the material can be operated at the temperature higher than the LCST (such as 45 ° C) (triangle, Fig. 4b).

The initial concentration of chiral compounds is another factor that significantly affects the separation performances of a nanoselector. Therefore, the effect of the initial RS-PPL concentration on the resolution performances of the MMoS<sub>2</sub>/ PNG2-CD was also investigated in this work. As observed in Fig. 4d, the ee value increases with increasing the RS-PPL concentration from 0 to 0.5 mM, and then gradually decrease at the concentration is over 0.5 mM. At low RS-PPL concentrations (lower than 0.5 mM), the number of  $\beta$ -CD is relatively excessive compared with that of R-PPL molecules. β-CD can bind more R-PPL to form  $\beta$ -CD/R-PPL complexes, thus yielding larger ee values. While upon further increasing the RS-PPL concentration, the number of  $\beta$ -CD become relatively insufficient than that of R-PPL, thus resulting in lower ee values. However, the MMoS<sub>2</sub>/PNG2-CD still show certain separation ability toward RS-PPL, and the optimal resolution concentration of RS-PPL is 0.5 mM.

On account of excellent magnetic and thermosensitive properties of the MMoS<sub>2</sub>/PNG-CD, it can easily recycled with an EMF and via simply changing the operating temperature. For this purpose, the R-PPL-loaded MMoS<sub>2</sub>/PNG2-CD was washed with hot/cool water (45 and 25 °C) alternatively under ultrasonication, and the adsorbed R-PPL molecules could be readily eluted from the material. As displayed in Fig. 4d, the used MMoS<sub>2</sub>/PNG2-CD shows good regenerability after consecutive five cycles. Although the ee value reduces slightly with an increase in the cycles, it can still reach 8.69%. The slight reduction in ee values is presumably arisen from that some parts of R-PPL molecules on the material were not desorbed. Moreover, certain amount of material suffered from weight loss during the washing process. Our developed MMoS<sub>2</sub>/PNG-CD when used for enantiomeric separations possesses some obvious advantages compared to those conventional methods (Table 2), such as simplicity in operation, inexpensiveness, relatively higher selectivity, and easy recyclability of the material, which indicates that the MMoS<sub>2</sub>/PNG2-CD is promising to serve as an excellent nanoselector for direct enantiomeric resolution of various β-blocker drugs.

# 4. Conclusions

In summary, a novel chiral magnetic molybdenum disulfide nanocomposite ( $MMoS_2/PNG-CD$ ) with a high enantioselectivity and excellent thermosensitivity and magnetism has been fabricated *via* a multistep reaction process. The resolution of

the prepared MMoS<sub>2</sub>/PNG-CD toward a chiral drug RS-PPL is systematically investigated. The obtained results indicate that  $\beta$ -CD on the MMoS<sub>2</sub>/PNG-CD play a crucial role in the chiral discrimination and enantioseparation of RS-PPL. The thermosensitive chiral recognition and resolution of RS-PPL by the MMoS<sub>2</sub>/PNG-CD is due to the incorporation of PNIPAM moieties into the PNG-\beta-CD chains. The molar ratio of GMA to NIPAM  $(n_{GMA}: n_{NIPAM})$  and the initial RS-PPL concentrations are two important factors that significantly affect the separation efficiencies of RS-PPL, the optional  $n_{\text{GMA}}$ :  $n_{\text{NIPAM}}$  value and the RS-PPL initial concentration are respectively 2 and 0.5 mM to achieve a satisfactory resolution efficiency. Besides, the used MMoS<sub>2</sub>/PNG-CD can be easily recovered under an external magnetic field and regenerated via simply changing the operating temperature. Such a multifunctional MoS<sub>2</sub> nanocomposite developed herein with a high enantioselectivity, excellent thermosensitivity and regenerability can serve as a high-performance nanoselector for direct enantioseparation of various β-blocker drugs.

# Author contributions

H. R. Yu and L. Lei: conceptualization, validation, investigation, software, data curation, formal analysis, writing – original draft; Y. L. Wang and X. Wang: investigation and data curation for the revised manuscript. T. Liang: methodology, investigation, funding acquisition, writing – review and editing, supervision; C. J. Cheng: conceptualization, funding acquisition, writing – review and editing.

# Conflicts of interest

The authors declare that they have no competing interests.

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