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Fabrication and characterization of novel tentacle-type adsorbent for resolution of chiral drugs

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Novel tentacle-type chiral adsorbent based on silica gels modified with β-cyclodextrin (β-CD) and polyvinyl alcohol(PVA) is synthesized by surface grafting technique. The adsorption behavior of chiral pharmaceuticals using the resulting adsorbents is investigated. In the study, FT-IR and thermogravimetric analysis (TGA) are employed to characterize the chemical and physical properties of the adsorbent; mandelic acid (MA) serves as model solute to evaluate the sorption capacity and selectivity of the adsorbent. The experimental results show that the novel tentacle-type adsorbent is possessed of larger equilibrium adsorption capacity and better selectivity over the conventional one and could be as potential chiral stationary phase (CSPs).

tentacle-type adsorbent, adsorptive selectivity, chiral resolution, MA

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Chirality is a fundamental feature of many pharmaceutical molecules, which plays an important role for disease treatment. Because of possessing many advantages such as high efficiency, low toxic side effect, small dosage, and so on, chiral pharmaceuticals have provoked great interest and become the orientation of future drug development in recent years [1]. However, enantiomers of chiral pharmaceuticals have shown different pharmacological activity or toxicity [2]. Therefore, separation of chiral pharmaceuticals has become an extremely important and challenging unit operation in the pharmaceutical industry. Up to now, there are so many techniques employed to separate the chiral drugs, such as diastereomer crystallization [3], membrane separation [4], chromatographic chiral separation [5,6] and so on. Among all of these techniques, liquid chromatography (LC) packed with chiral stationary phase (CSPs) is very attractive because it possesses excellent enantioselectivities in a wide range of enantiomers. For this technique, the CSPs are the central unit that relates strongly to the chromatographic performance [7–9]. At present, increasing research efforts have been focused on the fabrication of the novel adsorbent possessing of better enantioselectivity, stability and capacity and their potential application in industry.

For chromatography of CSPs, chiral ligand serves as one of the most important factors that impacts on the chiral resolution. Cyclodextrin (CD), that is a chiral polymer, has been widely used for the separation of enantiomers and other isomers owing to its special ring structure [10,11]. However, conventional chiral adsorbent is modified with one layer of chiral ligands on the surface of the carrier, which results in a monolayer adsorption of chiral drugs in the resolution process [12,13]. Due to the density limit of ligands, it usually results in the insufficient resolution capacity, and is not suitable for preparative scale resolution of chiral pharmaceuticals [14]. To resolve the problem, a surface grafting technique has been developed to increase the density of ligands in many adsorption materials recently [15–17]. For instance, the long polymer chains with multiple functional groups were grafted onto the pore surface of the materials to form the tentacle-type adsorbents, which was expected that the multi-layer adsorption for the target from the surface to three-dimensional space would exhibit high resolution capacity. The tentacle-type modification has been successfully applied to the adsorption of the metal ions

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[18] and protein separation [19], and the results showed that the adsorption performance has been improved remarkably, especially for separation capacity.

The chiral pharmaceutical molecules possess smaller size, better stability, and lower mass transfer resistance in the absorption process over the biological macromolecules. Based on the above-mentioned features, tentacle-type chiral adsorbent would be more adequate for the chiral pharmaceuticals resolution. Moreover, the flexible structure of the long-chain polymer can reduce effectively the steric hindrance during the adsorption process, which helps to the target adsorption onto the chiral adsorption sites. In addition, polyvinyl alcohol (PVA) is well known for its processability, strength and long-term temperature and pH stability [20]. Unfortunately, this tentacle-type chiral adsorbent has been scarcely any applied to separate chiral drugs. Inspirited by these, to obtain high-capacity of chiral drugs, a novel tentacle-type adsorbent based on the pore surface of silica gel particles grafted with PVA macromolecules and *β*-cyclodextrin (*β*-CD) were prepared, which was named *β*-CD-PVA-SiO_2. This novel tentacle-type adsorbent was expected to possess better enantioselectivity, stability and capacity due to the multiple functional groups on PVA. To highlight the novel adsorbents (*β*-CD-PVA-SiO_2), the traditional ones (*β*-CD-SiO_2) were also prepared in this study. The ligand densities on two types of chiral adsorbents were determined by infrared spectrum and thermogravimetric analysis. And adsorption properties of the chiral adsorbents were investigated using mandelic acid as model solute.

1 Materials and methods

1.1 Chemicals

Silica gel (particle size, 5 μm) was purchased from the Ocean Chemical Co., Ltd. (Qingdao, China). *γ*-Aminopropyltrimethoxysilane and *γ*-glycidoxypropyltrimethoxysilane were provided by the Yongchang Chemical Company, Ltd. (Nanjing, China). *β*-Cyclodextrin (*β*-CD) and polyvinyl alcohol (PVA, molecular weight, 79 kDa) were obtained from Changzheng Chemical Co., Ltd. (Chengdu, China). The racemic mandelic acid (MA) and its enantiomers (R-MA and S-MA) were produced by Sigma (USA). *n*-Hexane and dehydrated alcohol (HPLC grade) were purchased from Fisher (Loughborough, UK). Other reagents were all of analytical grade received from local sources.

1.2 Preparation of silica gel functionalized with PVA

The silica gel functionalized with PVA (PVA-SiO_2) was synthesized as follows. Firstly, silica gel activated with hydrochloric acid [21], was soaked in the mixture of dry toluene and *γ*-aminopropyltrimethoxysilane. The suspension was refluxed with gentle stirring in an argon atmosphere for 24 h. After filtered and washed with dry toluene and acetone, the aminopropyl silica gel was obtained. Then, 5 g of aminopropyl silica gel was added to 50 mL of 0.02 mol L^{-1} glutaraldehyde solution containing 0.01 mol L^{-1} phosphate buffer solution (pH 6.2). After reacting for 4 h at room temperature, the intermediate was washed to neutral solution by water. Subsequently, it was dispersed in the 100 mL of solution containing 90 mL of PVA aqueous solution (5%, w/w) and 10 mL of hydrochloric acid (5 mol L^{-1}) and reacted for 3 h, and then PVA was grafted onto the silica gel surface through coupling. Finally, the product PVA-SiO_2 was washed by water and dried under vacuum at 80°C.

1.3 Synthesis of tentacle-type chiral adsorbent

In the procedure, 5 g of *β*-CD was firstly dissolved in 100 mL of dry DMF, and reacted with 0.4 g of NaH for 2 h at room temperature. After filtered, the resultant reacted with 2 mL of *γ*-glycidoxypropyltrimethoxysilane in an argon atmosphere for 5 h at 90°C, and further reacted with 4.0 g of PVA-SiO_2 by refluxing for 24 h at 120°C. After the reaction, the tentacle-type chiral adsorbent (*β*-CD-PVA-SiO_2) was obtained. The final products was washed successively with DMF, methanol, water, and acetone, and then dried in vacuum at 80°C.

As a reference, the non-grafted adsorbent was prepared by a similar procedure. Firstly, 5 g *β*-CD was dissolved in 100 mL dry DMF, and reacted with 0.4 g NaH for 2 h at room temperature. Then the products were filtered and reacted with 2 mL *γ*-glycidoxypropyltrimethoxysilane in an argon atmosphere for 5 h at 90°C. Finally, the results mixed with 4.0 g silica gel which was activated with hydrochloric acid for 24 h at 120°C, and the non-grafted adsorbent (*β*-CD-SiO_2) were obtained.

1.4 Characterization and evaluation of the chiral adsorbents

The adsorbents were characterized by FT-IR obtained using KBr (Spectrum One, Perkin-Elmer, USA) and Thermogravimetric analysis (TGA) performed on a TA instrument (TG 209F1, Netzsch, Germany), at a heating rate of 10°C min^{-1} and an air flow of 100 mL min^{-1}.

To highlight the tentacle-type chiral adsorbent, MA as model solute was applied to perform the static and dynamic adsorption experiments. Enantiomers of MA in different samples were analyzed on a programmable HPLC (CLASS-VP, LC-20AT, 15 μL injection loop, SPD-M20A detector, Shimadzu, Japan) packed with a chiral column OD-H (250 mm × 4.6 mm i.d.) at 254 nm, 25°C and a flow rate of 0.8 mL min^{-1}. The mobile phase consisted of the mixture of *n*-hexane and dehydrated alcohol (92∶8, v/v) containing 0.5% trifluoroacetic acid. Samples and mobile phases were filtered through a 0.45 μm filter membrane before injection. The software of origin 7.5 was utilized to determine the figures and the relevant parameters.

1.5 Static adsorption of MA on two types of adsorbents

(1) Measurement of kinetic adsorption curve. Briefly as follows, 0.2 g of absorbent was added into a conical flask containing 100 mL of aqueous R-MA or S-MA solution with an initial concentration (C_0) of 0.8 mg mL^{-1}. The suspension was incubated at the temperature of 20, 30 and 40°C, and stirred by a magnetic stirrer. Every interval, 1 mL of sample was periodically collected and centrifuged instantly to determine the MA concentration (C_t, mg mL^{-1}) in supernatant by using the HPLC technique, and then the sample was returned to the flask immediately. The adsorption amounts (Q, mg g^{-1}) of the MA on the adsorbents were calculated according to the eq. (1).

$$Q = \frac{V \times (C_0 - C_t)}{m}, \quad (1)$$

where V (mL) and m (g) stand for the solution volume and the weight of the absorbent, respectively.

(2) Measurement of adsorption isotherm with static method. In the procedure, 0.2 g of absorbent was placed into labeled conical flasks and mixed with 30 mL of R-MA aqueous solution of different concentrations (C_0) (0–0.8 mg mL^{-1}). Then the suspension was stirred by a magnetic stirrer in an incubator at the temperature of 20, 30 and 40°C for 24 h to ensure equilibrium. Finally, the suspensions were centrifuged and the R-MA concentrations (C_e) in supernatant were detected. The equilibrium adsorption capacity (Q_e, mg g^{-1}) of R-MA was calculated by the eq. (2).

$$Q_e = \frac{V(C_0 - C_e)}{m}, \quad (2)$$

where C_0 and C_e (mg mL^{-1}) stand for the initial and equilibrium concentration of R-MA, respectively. V (mL) and m (g) stand for the solution volume and the weight of the absorbent, respectively. The Langmuir isotherm was used to fit the equilibrium data by using the following equation:

$$Q_e = \frac{Q_m C_e}{K_d + C_e}, \quad (3)$$

where Q_m and K_d denote adsorption capacity and dissociation constant, respectively.

(3) Adsorption dynamics and elution experiments of MA on two types of adsorbents. Dynamic behaviors of β-CD-PVA-SiO_2 and β-CD-SiO_2 for MA were conducted by the adsorption dynamics and elution experiments. Briefly as follows, 2.0 g of absorbent was filled into a glass column with 10 mm of diameter, and formed the bed with 2.5 mL of volume. Then, the R-MA, S-MA or racemic MA solution with concentration of 0.8 mg mL^{-1} was allowed to flow gradually through the column at a rate of three bed volumes per hour (3 BV h^{-1}). Subsequently, the effluents with one bed volume were collected and analyzed to polt the dynamics adsorption curve and calculate the saturated adsorption amounts. Finally, elution experiments were performed by using hydrochloric acid solution (10%, v/v) as eluting agent at the flow rate of 0.5 BV h^{-1}. The eluent was collected and determined to calculate the elution ratio.

1.6 Adsorptive selectivity of two types of adsorbents

The selectivity of adsorption to the enantiomers of MA was performed to research the chiral resolution capacity of β-CD-PVA-SiO_2 and β-CD-SiO_2. In the procedure, 0.5 g of absorbent was suspended in 100 mL of racemic MA solution with an initial concentration (C_0) of 1.2 mg mL^{-1} in the conical flask. Then, the conical flask was stirred by a magnetic stirrer in an incubator at 20°C. Every 1 h, 1 mL of sample was periodically collected and treated as described in the front. The enantiomers of MA in supernatant were analyzed by HPLC to obtain the concentration of the R-MA and S-MA. In addition, to illustrate the practical value of the materials in chiral drug separation, the concentration of the product after the separation of racemic MA using the method described in experiment part 1.6 were used to evaluate the adsorptive selectivity. The enantiomeric excess (e.e.%) of the MA solution was calculated by the following equation:

$$ee\% = \frac{[S]-[R]}{[S]+[R]} \times 100\%, \quad (4)$$

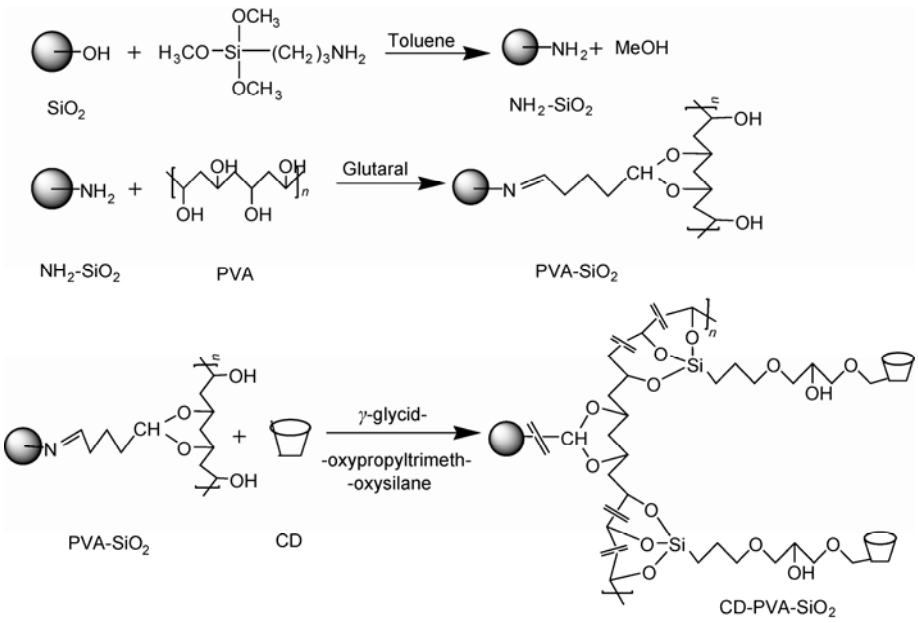
where [R] and [S] are the concentrations of the R-MA and S-MA in the solution.

2 Results and discussion

2.1 Preparing process and characterization

(1) FT-IR spectra. The preparing process of tentacle-type adsorbent CD-PVA-SiO_2 includes three steps as follows (Scheme 1). Firstly, after activated, a great deal of silanol groups reacted with γ-aminopropyltrimethoxysilane and formed the aminopropyl silica gel (NH_2-SiO_2). Then, glutaraldehyde was chosen as coupling agent to link the aminopropyl silica and functional macromolecular polyvinyl alcohol (PVA) to form the material with abundant hydroxy groups (PVA-SiO_2). Finally, the hydroxy groups and β-cyclodextrin (β-CD) were linked by γ-glycidoxypropyltrimethoxysilane and the tentacle-type material (CD-PVA-SiO_2) was obtained.

From the structure of CD-PVA-SiO_2 in Scheme 1, it could found that the new tentacle-type adsorbent may provide much more adsorption sites. In order to show the surface structure of the new tentacle-type adsorbent, FT-IR spectra of SiO_2, PVA-SiO_2, β-CD-PVA-SiO_2 were carried out and given in Figure 1. Comparing to the FT-IR spectra of SiO_2, the characteristic absorption peak of stretching vibration of C–H bond appeares at 2949 cm^{-1} (Figure 1(b)), and the characteristic absorption peak of stretching vibration of C–O bond are found at 1031 cm^{-1}, respectively. The



Scheme 1 Synthesis process of composite material CD-PVA-SiO_2.

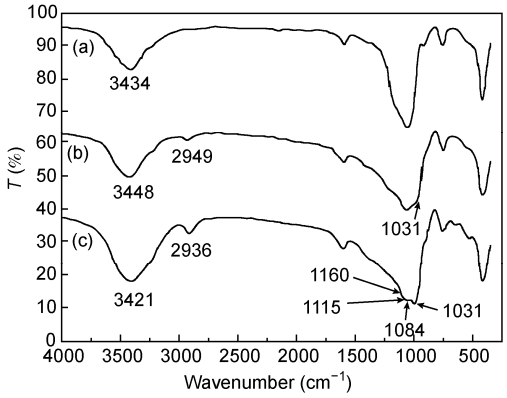


Figure 1 FT-IR spectra of (a) SiO_2, (b) PVA-SiO_2 and (c) β-CD-PVA-SiO_2.

appearances of these absorption bands show that PVA macromolecules have been grafted onto silica gel surface, and PVA-SiO_2 particles have formed. After the PVA-SiO_2 modified with β-CD, the FT-IR spectrum was recorded and is given in Figure 1(c). Here, the O–H stretching absorption band with the increased intensity is absorbed at 3421 cm^{-1} and this value shifts about 27 cm^{-1} to the lower wavenumbers compared to the FT-IR spectrum of PVA-SiO_2 (Figure 1(b)). This result is brought by the short wavenumber of O–H stretching absorption band of β-CD [22]. It shows that β-CD is modified chemically onto the PVA-SiO_2. Also, the absorption bands at 1160, 1115 and 1084 cm^{-1} representing the C–O–C bond are other indications to show the chemical modification of the β-CD onto the PVA-SiO_2 [23].

(2) TGA. The thermogravimetric analysis was performed to determine the amount of β-CD molecules immobilized on SiO_2 and PVA-SiO_2 by means of weight balance, and the results are listed in Figure 2. As seen here, there is about 10% of total weight loss on PVA-SiO_2 by calciantion from 250 to 485°C. The weight loss can be ascribed to the decomposition of PVA, and is similar to the results reported by other researcher [24,25]. As for samples of β-CD-SiO_2 and β-CD-PVA-SiO_2, the weight loss was determined to be about 13.5wt% and 53.1wt%, respectively. Based on the weight balance, the content of β-CD on PVA-SiO_2 is estimated to be about 43.1wt%, three times larger than that of pure SiO_2. Obviously, the high content of β-CD is attributed to the introduction of PVA long chains on silica gel, which provides more reaction sites to increase the amount of β-CD.

To more exactly elucidate the role of PVA long chain on the ligand density, the contents of β-CD on both PVA-grafted silica gel and pure silica gel were further measured according to the method described by Dubois [26], and

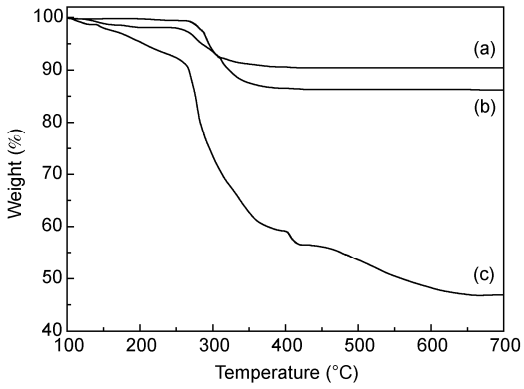


Figure 2 TGA spectrum of (a) PVA-SiO_2, (b) β-CD-SiO_2 and (c) β-CD-PVA-SiO_2.

the results were tabulated in Table 1. It was found that the experimental value of β-CD on PVA-SiO_2 reached 378 μmol g^{-1}, three times larger than pure SiO_2. The results matched well with the thermogravimetric analysis.

2.2 Adsorption studies

(1) Kinetic adsorption curves of two types of adsorbents. The adsorption kinetics of two types of adsorbents were investigated by using the R-MA and S-MA as model solutes, and shown in Figure 3. It is found that the introduction of PVA on silica gel has significant effect on the adsorption behavior of MA. In case of β-CD-PVA-SiO_2, the MA concentration in solution reduced to 0.68 mg mL^{-1} (R-MA) and 0.77 mg mL^{-1} (S-MA) after adsorption for 100 min, much lower than those of β-CD-SiO_2, indicating a higher adsorption rate. The high adsorption kinetics on β-CD-PVA-SiO_2 can be ascribed to the increasing amount of β-CD derived from the PVA on silica gel. Moreover, the curves of kinetic adsorption show that both types of β-CD adsorbents have better selectivity for R-form of MA instead of its counterpart. This can be explained by the fact that the β-CD has the chiral binding microenvironment, and can generate more stabile inclusion complex with R-MA than S-MA [27]. This phenomenon has been confirmed by Armstrong [28].

The adsorption of MA on both adsorbents occurred in two stages. For β-CD-SiO_2, the first stage underwent MA uptake immediately within 50 min, and then came to the second stage, i.e. the slow adsorption kinetics. Differently, for β-CD-PVA-SiO_2, the first stage of solute uptake continued for around 100 min, and then changed to its second stage. The variation in adsorption process is largely influenced by the polymer chains grafted on the adsorbent. Comparing to the non-grafted adsorbent, the β-CD-PVA-SiO_2 possesses more polymer chains anchoring the adsorption sites. It is well known that the film diffusion dominates the solute adsorption during the first adsorption stage. As for adsorbent of β-CD-PVA-SiO_2, the polymer long chains on support increase the film diffusion resistance; therefore, the inner adsorption sites on tentacle chains would need more time to contact the MA solutes. So, the first adsorption stage of β-CD-PVA-SiO_2 needs longer time period over the non-grafted ones.

To further elucidate the adsorption behavior of tentacle-grafted adsorbent, a series of experiments were carried out to evaluate the influence of temperatures on adsorption kinetics, and the results were shown in Figure 4. It is evident from the results that the adsorption kinetics is dependant upon the temperature. The equilibrium adsorption time reduces with changing the temperature from 20 to 40°C. It is expected that the increased temperature can help the solutes improve the diffusion mass transfer from the solution to the interior chair ligands.

(2) Adsorption isotherms of the adsorbents. Adsorption isotherms were generated only for the R-MA on β-CD-SiO_2 and β-CD-PVA-SiO_2 as R-MA could provide better adsorption capacity compared to the S-MA. Effects of solution temperature on R-MA adsorption for the two types of adsorbents at the experimental temperature of 20, 30 and 40°C were investigated and presented in Figure 5. The figure shows that, the equilibrium adsorption amount decreases with increasing temperature, which indicates that the adsorption is an exothermic process. So the equilibrium adsorption amount for β-CD-PVA-SiO_2 containing more chiral ligands reveals more decrease with increasing temperature than β-CD-SiO_2. Langmuir model fitting the isotherm data to eq. (3) gave the static adsorption capacity (Q_m) and the dissociation constant (K_d) (Table 2). The results from Table 2 show that two types of adsorbents have similar dissociation constants at the experimental temperature. It reveals that the introduction of the polymer does not impact the adsorption mechanism. Moreover, the R-MA adsorption capacities based on β-CD-PVA-SiO_2 are higher than that of

Table 1 The supported quantity of β-CD in two types of adsorbents

Samples	β-CD-SiO_2	β-CD-PVA-SiO_2
β-CD (μmol g^{-1})	121±5	378±7

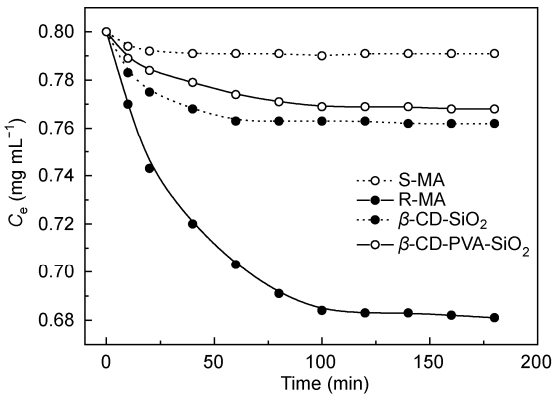


Figure 3 Kinetic adsorption curve for the enantiomers of MA. Temperature: 20°C; Initial concentration of R-MA and S-MA: 0.8 mg mL^{-1}.

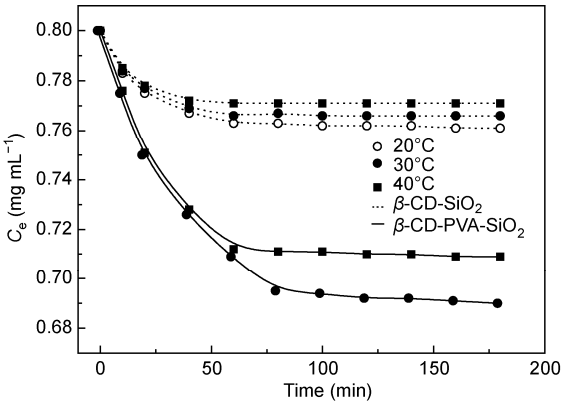


Figure 4 Kinetic adsorption curve for R-MA. Initial concentration of R-MA: 0.8 mg mL^{-1}.

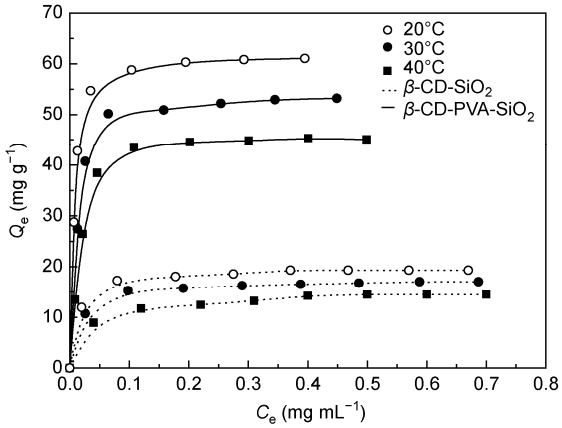


Figure 5 Adsorption isotherms of R-MA at different temperatures.

Table 2 Adsorption properties of the adsorbents for R-MA

Samples		Q_m(mg g^{-1})	K_d(mg mL^{-1})
β-CD-SiO$_2$	20°C	19.92 ± 0.81	0.014± 0.002
	30°C	17.54 ± 0.73	0.017± 0.003
	40°C	14.93 ± 0.62	0.025± 0.003
β-CD-PVA-SiO$_2$	20°C	68.97 ± 2.13	0.014± 0.003
	30°C	57.47 ± 2.01	0.017± 0.002
	40°C	52.36 ± 1.95	0.026± 0.005

the β-CD-SiO$_2$ at the experimental temperature. As expected, the tentacle-type structure could provide more adsorption sites accessible for chiral molecule approach, thus leading to high static adsorption capacity.

(3) Dynamic adsorption curve. To elucidate clearly the adsorption performance of the adsorbents under actual conditions, breakthrough analysis were performed by using the adsorbents-packed column at 20°C, and the results were illustrated in Figure 6 and Table 3. It is found that the dynamic binding capacity of R-MA on β-CD-PVA-SiO$_2$ reaches around 46.51 mg g^{-1}, more than three times that on β-CD-SiO$_2$ (15.04 mg g^{-1}). At the same time, the selectivity of adsorption in the dynamic experiment is also rather obvious. For example, the adsorption amount of R-MA(39.43 mg g^{-1}) on β-CD-PVA-SiO$_2$ is far more than that of S-MA (10.53 mg g^{-1}) in the racemic MA solution. These results suggest that the tentacle-type polymer chains have enhanced the multipoint adsorption of the MA and the resolution ability of β-CD-PVA-SiO$_2$ for racemic MA is affirmed. In addition, for these two adsorbents, the dynamic binding capacities of R-MA are lower slightly than their corresponding static adsorption capacities. Analogous phenomenon can be seen for S-MA and racemic MA. It can be explained by the fact that the adsorbent can get full access to the adsorbate in the static adsorption process; differently, in the dynamic tests, the adsorption sites on tentacle-type adsorbent were not sufficiently utilized due to short adsorption time during the breakthrough adsorption [29]. Elution experiment data were tabulated in the Table 3. The results reveal that β-CD-PVA-SiO$_2$ has the same outstanding elution properties with β-CD-SiO$_2$. It is expected that the excellent retention and elution properties would make the novel tentacle-type adsorbent produce better resolution capacity for chiral drugs.

2.3 Selectivity of adsorption

To evaluate the chiral resolution capacity of the adsorbents, the selectivity of adsorption to the enantiomers of MA was carried out on two types of adsorbents and the results were

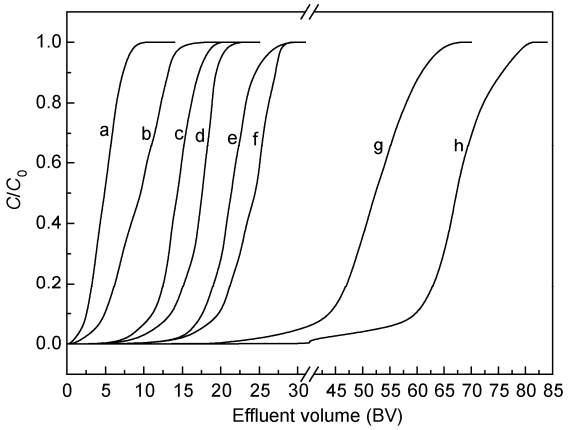


Figure 6 Breakthrough curves of R-MA, S-MA and racemic MA on the column. a, S-MA on β-CD-SiO$_2$; b, S-MA on β-CD-SiO$_2$ in racemic MA solution; c, S-MA on β-CD-PVA-SiO$_2$; d, R-MA on β-CD-SiO$_2$; e, S-MA on β-CD-PVA-SiO$_2$ in racemic MA solution; f, R-MA on β-CD-SiO$_2$ in racemic MA solution; g, R-MA on β-CD-PVA-SiO$_2$; h, R-MA on β-CD-PVA-SiO$_2$ in racemic MA solution.

Table 3 The results of the dynamic tests

Samples	β-CD-SiO$_2$		β-CD-PVA-SiO$_2$	
	R-MA	S-MA	R-MA	S-MA
Breakthrough capacity (mg g^{-1})	15.04 ± 0.65	4.52 ± 0.34	46.51 ± 1.65	13.53 ± 0.60
Desorption ratio (%)	97.36 ± 0.81	98.14 ± 0.78	96.17 ± 0.85	96.68 ± 0.65
Samples	β-CD-SiO$_2$ (racemic MA)		β-CD-PVA-SiO$_2$ (racemic MA)	
	R-MA	S-MA	R-MA	S-MA
Breakthrough capacity (mg g^{-1})	12.34 ± 0.45	3.63 ± 0.46	39.43 ± 0.77	10.53 ± 0.60
Desorption ratio (%)	97.22 ± 0.31	99.01 ± 0.45	96.37 ± 0.98	96.54 ± 0.71

plotted in Figure 7. The figure shows that, with the increase of adsorption time, the change value of ee% on β-CD-PVA-SiO_2 is significantly higher than that on β-CD-SiO_2. And ee% based on β-CD-PVA-SiO_2 reaches about 18.28, 3.02 times than that of β-CD-SiO_2 (6.04) after adsorption equilibrium. In addition, Figure 8 shows the ee% value of racemic MA separated in dynamic condition. It could be found that the time with an ee% value of 100% based on β-CD-PVA-SiO_2 (7 h) were much longer than that of β-CD-SiO_2 (2 h). What's more, the ee% value based on β-CD-SiO_2 dropped faster than that of β-CD-PVA-SiO_2. These certify that the tentacle-type adsorbent is possessed of better selectivity to the enantiomers in racemic solution and more outstanding chiral resolution property over the conventional one. As expected, the novel tentacle-type adsorbent could be as potential CSPs to achieve preparative scale resolution of chiral pharmaceuticals.

3 Conclusions

Novel tentacle-type chiral adsorbent and the conventional chiral adsorbent based on β-CD immobilized on silica were synthesized. The results revealed that, owing to the introduction of the PVA, the density of ligands on the novel chiral adsorbent was increased by over 200% comparing to the conventional one. And then the resolution properties to MA on these two chiral adsorbents were investigated in terms of static, dynamic and selective adsorption. It was found that, the presence of the polymer had no effect on the adsorption mechanism. However, equilibrium adsorption amount to model solute on the tentacle-type chiral adsorbent was increased significantly, over threefold to its un-grafted counterpart; the same outstanding elution property with the conventional chiral adsorbent was exhibited by the novel chiral adsorbent; and the e.e% value of racemic solution was raised from 6.04 to 18.28 in the static adsorption because of the introdunction of polymer. What's more, the selectivity is still outstanding in dynamic condition. As been seen that, the excellent elution property, lager retention capacity and better selectivity to the enantiomers made the novel tentacle-type chiral adsorbent possess a bright prospects as potential application in preparative scale resolution of chiral pharmaceuticals.

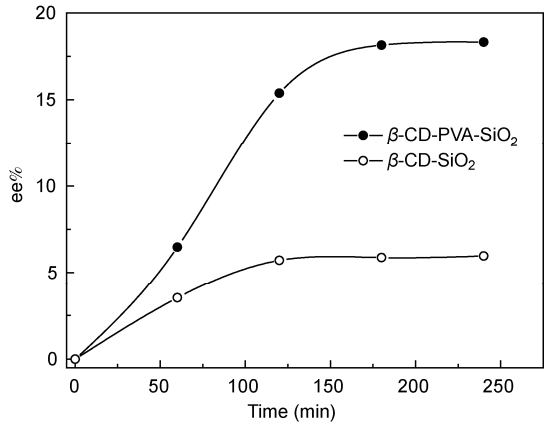


Figure 7 The change of ee% of racemic MA solution resolution on the presence of the CSPs.

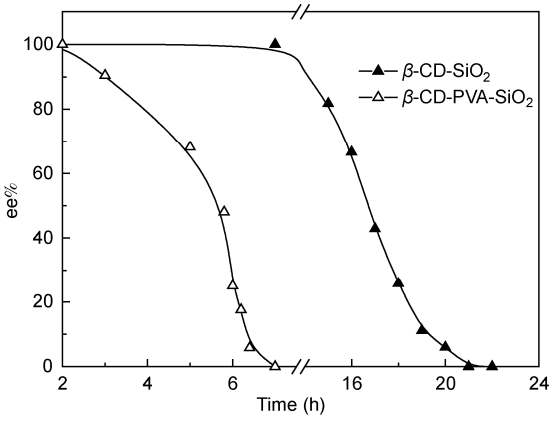


Figure 8 The change of ee% of racemic MA solution resolution in dynamic condition.

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