

## Experimental Details

### Materials

Chemical grade  $\beta$ -CD (Guoyao Chemical Reagent Co., Ltd, Shanghai, China) was recrystallized twice from water and was dried under vacuum at 110 °C for 12 h prior to use. GMA of analytical reagent (Jinchao Chemical Reagent Co., Ltd, Shanghai, China) was distilled under reduced pressure and stored at 0°C. Dimethylformamide (DMF) of analytical reagent (Shanghai Chemical Reagent Co., Ltd, Shanghai, China) was dried by a molecular sieve (4A) for 12h. Other reagents were both analytical reagent and used without further purification.

### Preparation of PSI

PSI with molecular weight of  $1.8 \times 10^4$  synthesized from MA and  $(\text{NH}_4)_2\text{CO}_3$  was obtained by following method: 36.4 g of maleic anhydride and 21 ml of deionized water were mixed in a three-necked flask. Then the solution of 21.4 g of  $(\text{NH}_4)_2\text{CO}_3$  in 40 ml of deionized water was added dropwise into the three-necked flask and stirred for 30 min at 90 °C. After that, the flask was deoxygenated by degassing, back-filling with nitrogen under a vacuum of 0.013 MPa at 180 °C, with stirring for 4 h. Finally, the yellowish powder of PSI product was collected.

### Preparation of PSI-ethidene diamine-GMA (PSEG)

3.0 g of PSI was dissolved in a mixed solution of 10 ml of  $\text{H}_2\text{O}$  and 30 ml of DMF. To this mixture 4.2 ml of glycidyl methacrylate (GMA) was added. Subsequently, 2.1 ml of ethidene diamine was added dropwise into the solution. The solution was kept at 50 °C and stirred for 12 h. Once the reaction was completed, the solution was cooled to ambient temperature and poured into 250 ml of absolute alcohol. The precipitate obtained was recovered by filtration and dried at 40 °C under 0.01 MPa for 24 h.

### Preparation of PSI-hexamethyldiamine-GMA (PSHG)

3.0 g of PSI was dissolved in a mixed solution of 10 ml of  $\text{H}_2\text{O}$  and 30 ml of DMF. To this mixture 4.2 ml of glycidyl methacrylate (GMA) was added. Subsequently, the solution of 3.6 g of hexamethyldiamine in 10 ml of deionized water was added dropwise into the solution. The reaction conditions and precipitation of the product were similar with those for PSEG. The product was washed with ethanol in Soxhlet

extractor to remove impurity for further characterization.

#### Preparation of MACD

MACD was synthesized according to the procedures described elsewhere<sup>1</sup>. A known amount of  $\beta$ -CD (5.0 g, 4.4053 mmol) and maleic anhydride (MA) (6.0 g, 61.1870 mmol) was dissolved in 30 ml of DMF in a round-bottom flask. The mixture was allowed to react under stirring at 80 °C for 12 h. At the time of the reaction was finished, the solution was cooled to room temperature and subsequently slowly poured into 200 ml of ethyl acetate. The obtained precipitate was recovered by filtration and dried at 80 °C under 0.01 MPa for 24 h. The product was dissolved in methanol and precipitated with ethyl acetate twice to remove impurity for further characterization.

#### Radical copolymerization of MACD with PSEG or with PSHG

4.0g of PSEG (or 4.75 g of PSHG) and 3.6 g of MACD were dissolved in 30 ml of H<sub>2</sub>O. The mixture was bubbled by nitrogen for 40 min and the radical polymerization was carried out with 0.5%wt K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> as initiator at 90 °C for 12 h. Once the reaction was completed, the mixture was poured into 200 ml of methanol and the precipitate was filtered. The obtained product was dried at 40 °C under 0.01 MPa for 24 h. The product was washed with methanol in Soxhlet extractor to remove impurity for further characterization.

#### Characterization

Infrared spectroscopy was used to investigate the chemical structure of obtained copolymer. Fourier transform infrared spectra of obtained copolymer was recorded with KBr pellets at room temperature on a Nicolet 5700 spectrophotometer (Thermo Electron Corporation, America) in the range 4000-400 cm<sup>-1</sup>, with a resolution of 4 cm<sup>-1</sup> using 64 scans.

<sup>1</sup>H NMR spectra were taken at room temperature on an Avance 500 NMR spectrometer (Bruker, Germany) using deuterated water (D<sub>2</sub>O) as solvent. The D<sub>2</sub>O solution of PASP-CD was kept at room temperature for about 24 h prior to NMR characterization, in order to sufficiently solvate macromolecular chains of PASP-CD with D<sub>2</sub>O.

Thermal properties of the final copolymer were investigated by thermogravimetry. Thermal gravimetric analysis was carried out by SDT Q600 thermogravimetric analyzer from TA America, each sample was run from 50 to 800 °C at a scanning ramp of 10 °C min<sup>-1</sup> under a nitrogen atmosphere.

Elemental analysis of obtained copolymer was taken on Elementar Vario EL III from Germany.

#### Ibuprofen (IB) loading and releasing experiments

Solution immersing method is widely used for ibuprofen loading by immersing drug-free carriers in an organic solution of ibuprofen. In this study, ethanol was selected as loading solution, since ibuprofen has a good solubility in ethanol but the carrier (PASP-CD) has not. 4.0 g of PASP-CD was mixed with 25 ml solution of ibuprofen in ethanol (100mg/ml) at 25 °C. The mixer was stirred by magnetic stirrer for 24 h. At the end of loading period, the obtained PASP-CD-IB was washed with 10 ml ethanol quickly to remove unbound IB and dried for 12 h under 40 °C and 0.01 MPa.

IB dissolution was determined at 37 °C in static state. 0.5 g of dried IB loaded PASP-CD-IB was placed into a beaker with 10ml of water. The copolymer containing ibuprofen dissolves into water gradually. At certain time intervals, the aqueous solution was filtered and the concentration of IB was determined at 222 nm using a UV-7504 spectrophotometer from Xinmao China. PASP-CD did not interfere with the UV analysis. The dissolution profile of IB loaded CD and pure IB was also determined.

## FT-IR characterization

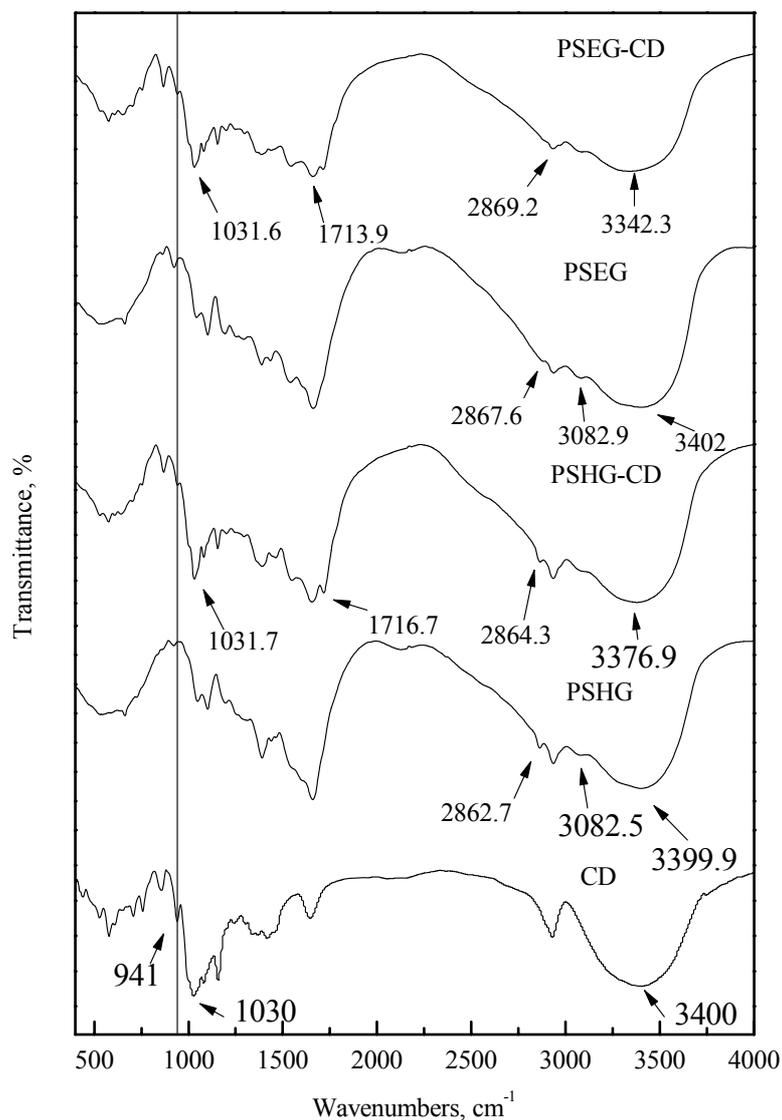


Figure 1 FT-IR characterization of  $\beta$ -CD, PSEG, PSEG-CD, PSHG and PSHG-CD. Figure 1 shows the FT-IR characterization of  $\beta$ -CD, PSEG, PSEG-CD, PSHG and PSHG-CD. The peaks of PSEG and PSHG at 2867.6 and 2862.7  $\text{cm}^{-1}$  belonging to the  $\text{CH}_3$  group originate from GMA reveals that GMA has been immobilized on PASP chain. Simultaneously, the C=C groups of GMA in PSEG and PSHG are observed at 3082.9 and 3082.5  $\text{cm}^{-1}$ , respectively. In comparison with FTIR characteristic absorptions of PSEG- $\beta$ -CD, PSEG and  $\beta$ -CD, it is clearly observed from FTIR absorption curve of PSEG- $\beta$ -CD that there are a strong C-O-C characteristic stretching vibration at 1031.6  $\text{cm}^{-1}$  from  $\beta$ -CD units, and a characteristic peak of  $\alpha$ -pyranil vibration of  $\beta$ -CD at 942.1  $\text{cm}^{-1}$ . Meanwhile, those characteristic signals of

C-O-C stretching vibration at  $1031.7\text{ cm}^{-1}$  and  $\alpha$ -pyranyl vibration at  $942.7\text{ cm}^{-1}$  from  $\beta$ -CD units are also observed from FTIR absorption curve of PSEG-CD. All of those signals are also found in PSHG-CD. It can be concluded that  $\beta$ -CD was conjugated into PASP backbone of PSEG-CD and PSHG-CD. Those signals at  $1713.9\text{ cm}^{-1}$  of PSEG-CD and  $1716.7\text{ cm}^{-1}$  of PSHG-CD are both from the C=O group of MACD. The FTIR spectrum of PSEG-CD and PSHG-CD show a broad absorption band between  $3100$  and  $3750\text{ cm}^{-1}$ . This is result from the overlapping of N-H stretching band located around  $3300\text{ cm}^{-1}$  with the -OH band of  $\beta$ -CD hydroxyl groups.

## TG and DSC characterization

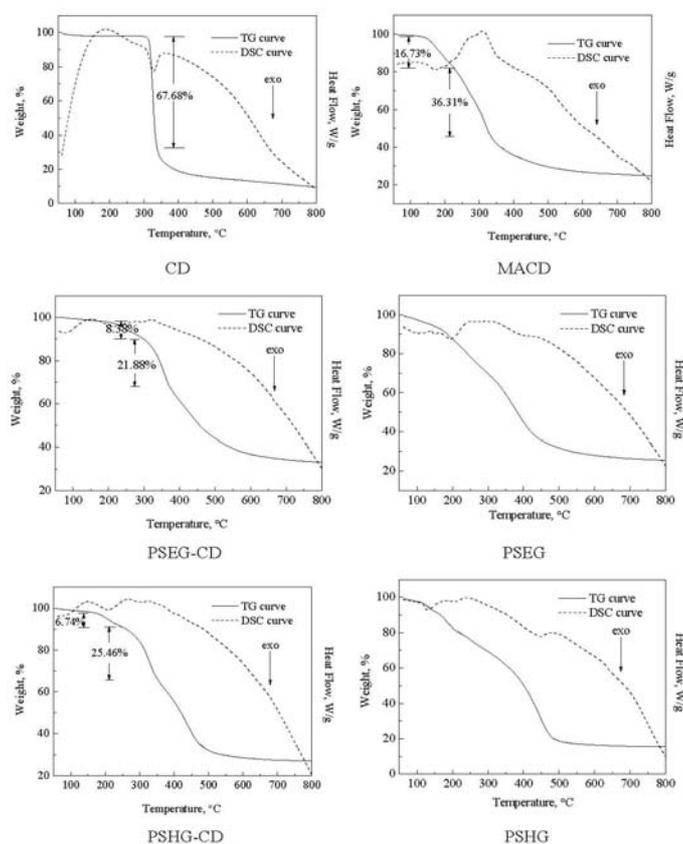


Figure 2 TG and DSC characterization of  $\beta$ -CD, MACD, PSEG, PSEG-CD, PSHG and PSHG-CD.

The thermal stability of MACD, PSEG, PSEG-CD, PSHG and PSHG-CD has been investigated by thermogravimetric analysis. The results of those copolymers were shown in Figure 2. Meanwhile, the DSC characterization of  $\beta$ -CD, MACD, PSEG, PSEG-CD, PSHG and PSHG-CD were also listed. The first thermal event of PSEG-CD and PSHG-CD occurred at 160 °C. Comparing with the curve of MACD, the first weight loss of 5% on PSEG-CD and PSHG-CD should be attributed to the decomposition of MACD. Comparing with the curve of  $\beta$ -CD, the second weight loss of 15% on PSEG-CD and PSHG-CD at about 300 °C could be considered as degradation of the  $\beta$ -CD molecule. PSEG and PSHG decomposed at a wide temperature range from 100 °C to 500 °C. For this reason, the third weight loss at 350 °C on PSEG-CD and PSHG-CD were attributed to the thermal degradation of PSEG and PSHG. Meanwhile, the polymer containing  $\beta$ -cyclodextrin is more thermally stable than PSEG and PSHG. This can be interpreted that the copolymerization of

MACD with PSEG and PSHG improves the molecular weight and crosslinking of the polymer.

In DSC characterization, the absence of melting peak of PSEG-CD and PSHG-CD may be due to amorphous pattern of the CD copolymer. In MACD, there were more than one vinyl groups on a  $\beta$ -cyclodextrin molecule. When MACD copolymerized with PSHG or PSEG, there will be more than one branched chain on a  $\beta$ -cyclodextrin molecule, that means the whole structure of obtained  $\beta$ -cyclodextrin copolymer is high crosslinked structure. Related with TG curve, it can be concluded that the exothermic peaks of PSEG-CD and PSHG-CD around 200 °C were caused by the decomposition of these materials.

## Elemental analysis

Table 1 Elemental analysis results of MACD, PSEG, PSEG-CD, PSHG and PSHG-CD.

	N	C	H
MACD	0	42.52	4.50
PSEG	15.02	44.26	6.56
PSHG	12.82	48.48	7.62
PSEGCD	10.51	43.68	5.92
PSHGCD	9.02	46.54	6.54

The elemental analysis results of MACD, PSEG, PSEG-CD, PSHG and PSHG-CD are listed in Table 1. With the obtained elemental content value, the CD content in MACD, PSEG-CD, and PSHG-CD is 0.555mmol/g, 0.16mmol/g, and 0.195mmol/g, respectively.

## Reference

1. F. Trotta, P. Ferruti, E. Ranucci, M. Veglia, C. Baggiani and C. Giovannoli, *J. Incl. Phenom. Macro.*, 2001, **1**, 139-143.