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Synthesis and characterization of biodegradable hydrogels based on photopolymerizable acrylate-terminated CL-PEG-CL macromers with supramolecular assemblies of α-cyclodextrins

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Abstract

A series of polypseudorotaxanes were synthesized from α-cyclodextrins (α-CDs) threaded onto photopolymerizable CL-PEG-CL oligomers bearing acrylate terminals. The corresponding supramolecular structured hydrogels were prepared from these polypseudorotaxanes in a mixed solvent of H_2O and DMSO via in situ photopolymerization under UV irradiation. The structure and properties of the gels were characterized by FTIR, TGA–DTG and WAXD. The results show that α-CDs are threaded and immobilized onto the network chains of the hydrogel with crosslinking junctions as stoppers topologically, and the feed molar ratio of α-CDs to the macromers affects the hydrogel structure and the water distribution in the hydrogel. These supramolecular structured hydrogels may be good candidates for biomaterial applications.

Keywords: Supramolecular structured hydrogel; Photopolymerization; Cyclodextrins

1. Introduction

Hydrogels are polymer networks that can absorb and retain large amount of water. Biodegradable hydrogels have been of particular interest in drug delivery as well as in tissue engineering. In the former, they are currently under investigation as matrices for the controlled release of bioactive molecules, e.g. proteins and oligonucleotides, and for the encapsulation of living cells. In the latter, as a new application of hydrogels, they are designed for use as scaffolds to engineer new tissue and organs [1,2]. A vast number of chemically crosslinking methods for synthesizing biodegradable hydrogels have been studied, including crosslinking by radical polymerization, by chemical reaction of complementary groups, by high energy irradiation, as well as using enzymes [3]. For hydrogels consisting of synthetic polymers, one of these most promising methods is the photoinitiated polymerization of poly(ethylene glycol)-based diacrylates (PEG-DA). In general, it proceeds at rapid polymerization rate under physicological conditions, and can significantly improve the adhesion of the hydrogel to surrounding tissue, due to close contact of the hydrogel with the tissue and the mechanical interlocking presumably resulted from surface roughness. Hubbell and colleagues first developed this kind of interesting biodegradable hydrogels through the photopolymerization of poly(ethylene glycol) bearing α-hydroxyl acid (lactic acid and glycolic acid) block copolymers end-capped with photocurable acrylate groups, and used these gels for the prevention of restenosis and post-surgical wound adhesions [4,5]. Pappas and coworkers have demonstrated the controlled release of proxyphylline and caffeine, low molecular mass compounds, from PEG-DA hydrogels [6]. Anseth and colleagues also studied the underlying hydrogel degradation kinetics and changes in the network structure during the drug release [7]. To render the resulting gels susceptible to enzymes existing in human body, a peptide sequence of Ala-Pro-Gly-Len has been incorporated into these gels to be used as tissue engineering scaffolds [8]. Except this kind of peptide-containing hydrogel, all these biodegradable hydrogels were generally lack of pendent

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functional groups along the main chains just as in hydrogels obtained from natural polymers, e.g. collagen and gelatin, hyaluronate, alginate, chitosan, etc.

In recent years, supramolecular polymer chemistry has emerged as a fascinating new field of macromolecular architecture, in which when the covalent bonds holding the monomeric units together in a macromolecule are replaced by highly directional noncovalent interactions, supramolecular polymers are yielded [9,10]. A number of inclusion complexes (ICs) consisting of polymer chains threading into macrocycles have been prepared as novel composite host/guest polymeric assemblies. This kind of the supramolecular polymer is called a polypseudorotaxane. In 1990, Harada and colleagues reported a first inclusion complexation of α-cyclodextrins (α-CDs) threaded onto PEG [11]. Yui et al. have designed and synthesized a family of biodegradable polyrotaxanes, in which α-CDs are threaded onto a PEG chain end-capped with an L-phenylalanine (L-Phe) blocker via a peptide linkage [12]. These biodegradable polyrotaxanes may be a promising new type of polymers suitable for drug delivery, tissue engineering and stimuli-responsible materials.

The intent of this study is to provide a modification of biodegradable hydrogels composed of CL-PEG-CL diacrylates by using α-CDs to thread onto their network chains to lead supramolecular assemblies. This type of biodegradable supramolecular structured hydrogels can be used as scaffolds to engineer human tissues and organs, in which α-CDs play a role of carbohydrates to promote the cell-matrix recognition, and mediate numerous physiological processes for cell growth.

2. Experimental

2.1. Materials

α-CD and stannous 2-ethyl hexanoate (Sigma, USA), and 2,2-dimethoxy-2-phenyl acetophenone (DMPA) (Fluka, Switzerland) were used as received. Various molecular masses of poly(ethylene glycol)s, PEG 4000 (4K), 6000 (6K) and 10,000 (10K), imported from Japan and distributed domestically, were purified by azeotropic distillation in toluene. ε-Caprolactone (ε-CL) (Aldric, USA), and both methylene chloride and triethylamine (Beijing Chemical Reagents Company, China), were purified by distillation under reduced pressure after being dehydrated by CaH_2. Acrylol chloride (Schuchardt, Germany) was purified by distillation just before use. All other reagents and solvents used were of analytical grade.

2.2. Preparation of oligomer (PECL) of PEG with ε-caprolactone

ε-Hydroxycaproate group was attached to both ends of PEG by a ring-opening addition reaction of ε-CL using stannous 2-ethyl hexanoate as a catalyst (Scheme 1). For synthesizing an oligomer of PEG 6K with ε-CL (a molar ratio of CL to PEG equal to 2), 16 g of distilled PEG, 0.86 g of ε-CL, and 17 mg of catalyst were added to a 100 ml round bottomed flask under a dried nitrogen atmosphere. The reaction mixture was stirred in an oil bath at 125 °C for 12 h. Then the mixture was cooled to room temperature and dissolved in $CHCl_3$. The product was precipitated in anhydrous diethyl ether, filtered, and dried under vacuum at 40 °C for 48 h.

2.3. Preparation of photocurable macromer (APECL)

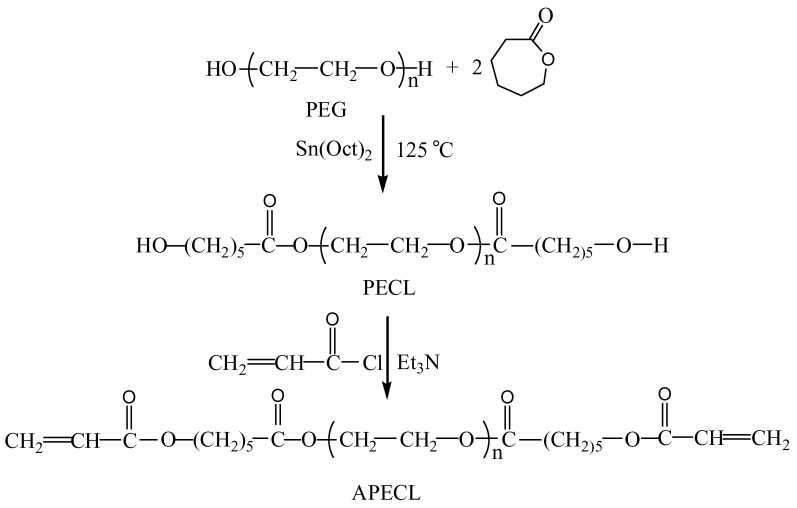
To obtain a photocurable macromer, acrylol chloride was used. For a typical reaction, 10 g of above-mentioned PECL was dissolved in 100 ml dry CH_2Cl_2 in a 250 ml round bottomed flask and cooled to 0 °C in an ice bath. A total amount of 11.2 ml triethylamine and 0.7 ml acrylol chloride were added dropwise, respectively. The resulting mixture was stirred at 0 °C for 12 h, and then at room temperature for 12 h. The reaction mixture was filtered to remove triethylamine hydrochloride, and precipitated in a large excess of dry diethyl ether. The product was filtered, and dried at 40 °C under vacuum for 48 h.

2.4. Preparation of saturated polypseudorotaxane of macromer with α-CDs (APECL-CD)

A photocurable macromer APECL was dissolved in water at room temperature. A saturated aqueous solution of α-CD containing stoichiometric α-CDs (one CD matching two ethylene glycol units of the macromer) was added, and the solution became turbid. The mixture was stirred for 2 h and the precipitate was collected by centrifugation. The product was washed several times with acetone and water, respectively, and dried at 60 °C under vacuum to constant weight.

2.5. Preparation of supramolecular structured hydrogel by photopolymerization

A photocurable macromers APECL was dissolved in phosphate buffered saline (PBS, pH 7.4) at room temperature. A saturated aqueous solution of α-CD was added according to a predetermined feed molar ratio of CD to the macromer. The solution became turbid, and continued to stir for 2 h. DMSO was added until the reaction mixture turned transparent. To 1 ml of the resulting clear solution was added 3 μl of photoinitiator solution (100 mg of DMPA dissolved in 1 ml of N-vinylpyrrolidone). About 0.5 ml of the solution was poured onto a 2 cm × 8 cm glass coverslip and exposed to 365 nm LWUV lamp (UV-III type, Beijing Institute of Kaixing Electronic Equipment) to lead the solution to fast polymerize in several seconds. The fabricated hydrogel was transparent and colorless when swollen in DMSO. To remove unthreaded α-CDs



Scheme 1. Synthesis of photocurable macromers.

presumably entrapped in the hydrogel matrix and unreacted macromers, the gels were completely immersed in DMSO at room temperature for 7 days. The solvent was changed every day. After drying under vacuum for 24 h, the gels were again swollen in water at 40 °C for two weeks so as to further remove entrapped α-CDs, unreacted macromers, and DMSO in the hydrogel network. Water was also changed every day during the process. Finally, the hydrogels were dried at 60 °C under vacuum to constant weight.

2.6. FTIR and NMR spectroscopy

FTIR spectra were measured using Nicolet Magam 560 FTIR spectrometer. ^{1}H- and ^{13}C-NMR measurements were carried out at room temperature on a Bruker DMX-300 NMR instrument with DMSO-d_6 as solvent and TMS as external standard.

2.7. Wide angle X-ray diffraction

Wide angle X-ray diffraction (WAXD) was recorded on powdered and film samples using Rigaku D/max-2500 type X-ray diffractometer. The radiation source used was Ni-filtered, Cu Kα radiation with a wavelength of 0.154 nm. The voltage was set to be 30 kV and the current 20 mA. Samples were mounted on a circular sample holder, and the proportional counter detector collected data at a rate of $2\theta = 5^{\circ}\ \mathrm{min}^{-1}$ over the $2\theta = 3$–60° range.

2.8. Thermal property analysis

Thermogravimetric analysis (TGA) of samples were made using TA Instrument 2050 thermogravimetric analyzer at a heating rate of 10 °C min^{-1} with nitrogen used as purge gas. Differential scanning calorimetry (DSC) measurements were conducted on TA Instrument 2910 differential scanning calorimeter. For melting point measurements, a heating rate of 5 °C min^{-1} was used with nitrogen used as purge gas. To characterize water in hydrogel, samples of 8–10 mg were sealed in cells and scanned at a heating rate of 5 °C min^{-1} from the temperature range of −70–50 °C. The free water and frozen bound water in gels can be calculated, respectively, by comparing the endotherms measured while warming the frozen gels with standard melting enthalpy of pure water (334 J g^{-1}). The amount of unfrozen bound water is obtained by difference of the measured total water content of hydrogel, and the calculated free water and frozen bound water content.

3. Results and discussion

3.1. Synthesis of photocurable macromers and polypseudorotaxanes

Preparation of oligomers consisting of PEG with ε-caprolactone and their diacrylates was shown in Scheme 1. The reaction results were summarized in Table 1. In order to incorporate biodegradably labile unit into the polymeric backbone, ε-CL was used as a comonomer. The term ring-opening addition instead of polymerization was employed to describe the addition reaction of ε-CL with PEG catalyzed by stannous 2-ethyl hexanoate, because a molar ratio of ε-CL to PEG was controlled to be 2 here.

As known, a number of inclusion complexes of cyclodextrins (α-, β- and γ-CDs) noncovalently threaded onto PEG as polypseudorotaxanes have been synthesized from non-degradable polymers such as PPO-PEG-PPO

Table 1
Diacrylate composition of oligomer consisting of PEG with ε-CL

Mame	APECL-4K	APECL-6K	APECL-10K
M_n of PEG	4000	6000	10000
Unit number of ε-CL	2	2	2

copolymers, and degradable polymers, e.g. poly(ε-caprolactone) (PCL) and PCL–PEG–PCL [13], respectively. A widely used synthesis of biodegradable polyrotaxanes consisting of α-CD and PEG was carried out by (1) modifying end groups of PEG and changing them into more reactive amine groups, (2) preparing polypseudorotaxanes using α-CDs to thread onto amine-terminated PEG, and (3) capping both terminals of amine groups in the polypseudorotaxanes with bulky components, e.g. adamantane [14] as well as protected L-Phe as stoppers [12]. In a previous study, we reported a synthesis and characterization of bioerodable hydrogels formed from photopolymerized PCL–PEG–PCL diacrylate macromers [15]. In the present paper, it is found that the acrylate-terminated macromers consisting of one mole of PEG with two moles of ε-CL are able to thread through α-CDs to give polypseudorotaxanes as outlined in Scheme 2.

3.1.1. FTIR spectroscopy

The FTIR spectra of photopolymerizable macromer APECL-4K (a), inclusion complex of APECL-4K-CD (b), and α-CD (c) in the region from 400 to 4000 cm^{-1} were presented in Fig. 1. The peaks between 3000 and 4000 cm^{-1} are normally assigned to symmetric and asymmetric stretching vibration modes of O–H bonds. This band for pure α-CD is located at 3370 cm^{-1}, and is shifted to higher frequency of 3401 cm^{-1} upon forming an inclusion complex with macromer APECL. The shift is maybe ascribed to the non-covalent interaction between the hydroxyl groups of α-CDs and the included macromer backbone. The bands in the range of 2700 to 3000 cm^{-1} are also observed to be different from that of pure α-CD. There appears a new band at 2923 cm^{-1} with a shoulder at 2868 cm^{-1}, which is slightly shifted to low frequency, and

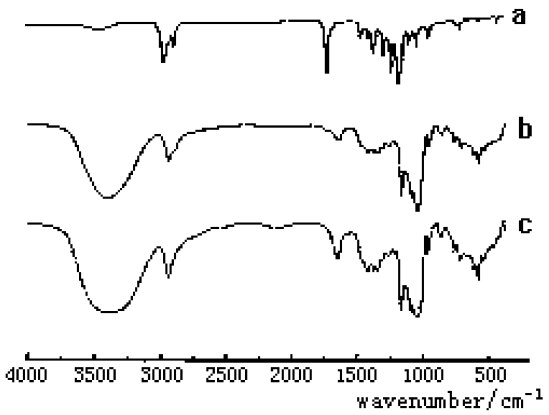


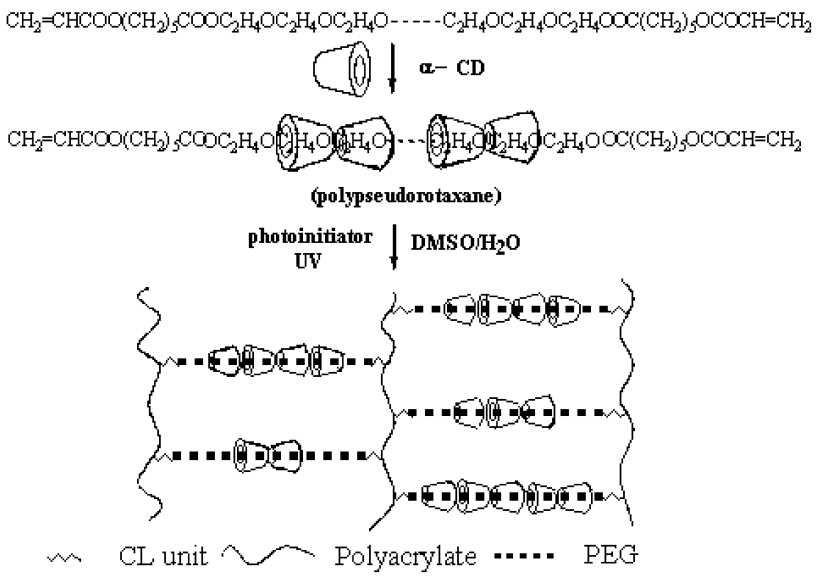
Fig. 1. FTIR spectra of APECL-4K (a), and inclusion complex of APECL-4K-CD (b) and α-CD (c).

most probably attributed to the included macromer chain in the complexes.

Fig. 1 further shows a new band appearing at 1732 cm^{-1} likely stemmed from the C=O stretching modes of ε-hydroxyl caproate units as well as acrylate groups in the sample of APECL-4K-CD. Since a low feed molar ratio of ε-CL to PEG, this new band intensity is not so strong. The positions of the skeleton vibration peaks of α-CD appeared at 575, 709 and 759 cm^{-1} in the inclusion complex of APECL-4K-CD are very similar to that of pure α-CD.

3.1.2. X-ray diffraction

The X-ray diffraction pattern of the inclusion complex of APECL-4K-CD was presented in Fig. 2. Compared with pure α-CD and oligomer PCL–PEG–PCL reported by Lu et al. [14], it clearly reveals that the inclusion complex of APECL-4K with saturated α-CDs is never a mixture of two components, but a supramolecular assembly formed by α-CDs threading onto the macromer chain. Furthermore, this



Scheme 2. Synthesis of supramolecular structured hydrogel with α-CD assemblies.

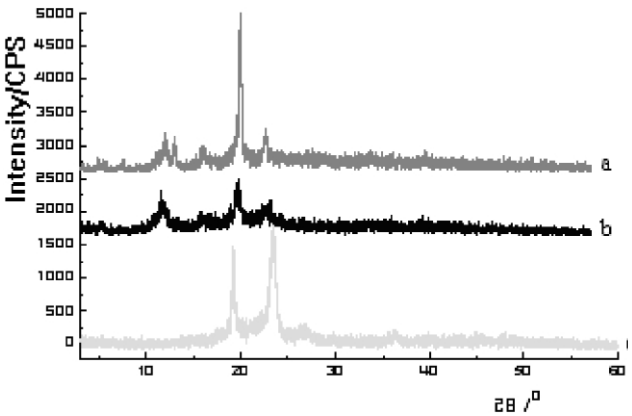


Fig. 2. X-Ray diffraction results of APECL-4K-CD (a), $CD6K_{20}$ (b) and $CD6K_5$ (c).

pattern is very similar to those of the complex of valeric acid or octanol, which have been reported to have a channel type structure, and is sharply different from that of the complex with propionic acid, which has a cage type structure. Therefore, the strongest peak appeared at $2\theta = 20°$ is characteristic for the formation of this channel type structure of the macromer included in the α-CD cavity. All results indicate that the inclusion complexes of APECL with α-CDs are featured with a strong trend to form the channel type structure rather than the 'cage' type structure.

3.1.3. NMR spectroscopy

Fig. 3 showed the ^{1}H NMR spectrum of the inclusion complex of APECL-4K with saturated α-CD. It is observed that there exist α-CD and PEG component in the inclusion complex. The peaks are assigned as OH_2 at δ 5.54, OH_3 5.51, H_1 4.80, and OH_6 4.50 ppm, respectively. Multiple resonances at δ 3.51–3.80 ppm show chemical shifts of $H_{3,5,6}$ protons, and at 3.25–3.42 are those of H_2O and $H_{2,4}$ protons. By comparing with linear PCL–PEG–PCL triblock copolymers (δ 3.60 ppm) [15], methylene protons of the PEG block appeared at δ 3.52 ppm in the inclusion complex shift to high field, which is a direct proof of the inclusion complex between macromer APECL and α-CDs.

The ^{13}C NMR spectrum of the inclusion complex of APECL-4K with saturated α-CD was illustrated in Fig. 4. The resonances assigned to α-CD are C(1) at 102, C(2) 73, C(3) 74,C (4) 83, C(5) 73, and C(6) 60 ppm, respectively. The carbons in PEG block give a signal at 70 ppm. All these carbon resonances are good in accordance with values reported in Ref. [14].

3.1.4. TGA–DTG thermal analysis

The TGA–DTG thermograms of free α-CD and its inclusion complex with the macromer APECL-4K recorded at a heating rate of 10 °C min^{-1} under nitrogen as purge gas from 0 to 500 °C were presented in Fig. 5. It is observed that the inclusion complex APECL-4K-CD starts to decompose at 294 °C, while the initial decomposition temperature of pure α-CD is 272 °C. In addition, the corresponding temperature at the maximum decomposition rate of the inclusion complex (the peak temperature of DTG) is 322 °C, which is still higher than that of pure α-CD (293 °C). These results suggest the supramolecular interactions originated from the macromer chain threading into the α-CD channel can increase the α-CD thermal stability. A peak appeared before 100 °C is observed in Fig. 5(a), which may be resulted from the dehydration of pure α-CD. At the same time, a small peak appeared at about 390 °C in Fig. 5(b) can be attributed to the thermal decomposition of the PEG blocks. However, the decomposition temperature of pure poly(ethylene glycol)s is about 360 °C. This fact may imply that thermal stability of individual component can substantially improve as long as an inclusion complex is formed between them.

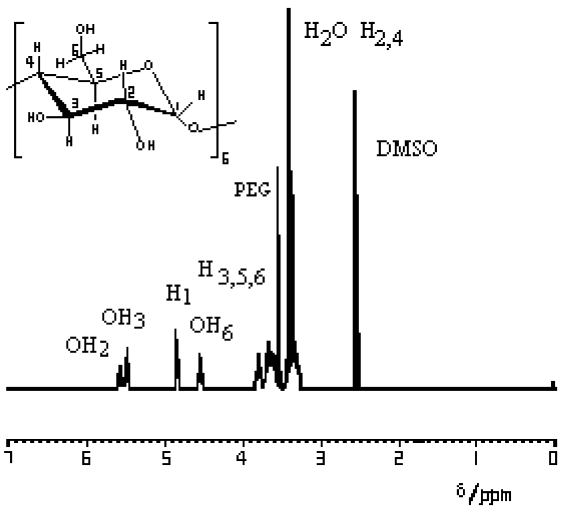


Fig. 3. ^{1}H NMR spectrum of the inclusion complex of APECL-4K-CD in DMSO-d_6.

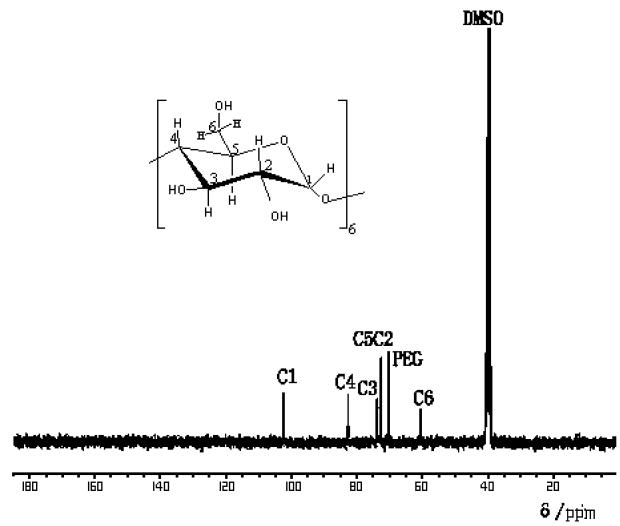


Fig. 4. ^{13}C NMR spectrum of the inclusion complex of APECL-4K-CD in DMSO-d_6.

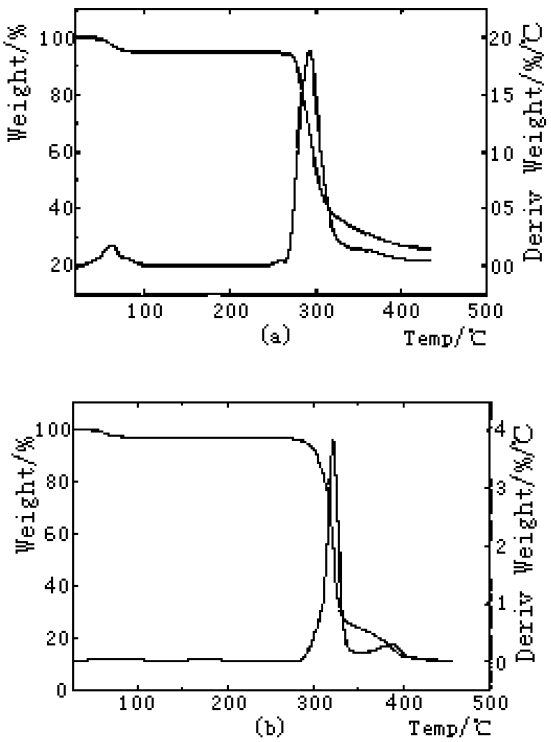


Fig. 5. TGA–DTG thermograms of free α-CD (a) and the inclusion complex of APECL-4K-CD (b), at a heating rate of 10 °C min^{-1}.

3.2. Synthesis of supramolecular structured hydrogel with α-CD assemblies

Depending on different feed molar ratio of α-CDs to the macromer, a series of inclusion complexes as a form of polypseudorotaxanes are available with the same macromer. These complexes are generally insoluble in water, but soluble in a mixed solvent of DMSO and H_2O. When DMPA as a photoinitiator was added to the resulting solution, supramolecular structured hydrogels were formed by photopolymerization under UV irradiation, in which α-CDs are threaded onto network chains and stopped by crosslinking junctions topologically. Synthesis of photopolymerized hydrogels with α-CD assemblies was illustrated in Scheme 2 and their compositions were summarized in Table 2. Briefly, CD in the composition means α-CD incorporated, 6K or 10K is a molecular mass of PEG in the macromer, and a subscription denotes a feed molar ratio of α-CD to a macromer.

As known, water plays a significant role in the hydrogel preparation. It has shown that a small amount of the crosslinked gel is formed when dried polypseudorotaxane consisting of APECL and α-CDs is dissolved only in DMSO with DMPA as a photoinitiator added, and exposed to UV light even for 30 min. However, to a suspension of this polypseudorotaxane in water is added DMSO to give a clear solution, and a supramolecular structured hydrogel is rapidly formed within a very short time (about 10 s) under UV irradiation. DMSO is a polar aprotic solvent, and facilitates the polypseudorotaxane dissolving into water to form a micellar structure. Although DMSO dissolves this type of the inclusion complexes under study very easily, the resultant solution probably do not possess such a micellar structure just as in the mixed solvent of DMSO and water. The formation of the micellar structure of amphiphilic macromers in water was supposed to highlight the fact that the free radical polymerization rate of the macromers in water is substantially higher than in organic media [16]. Similarly, the increase of the photopolymerization rate of polypseudorotaxanes formed from α-CDs threaded onto the photocurable macromers is attributed to the formation of such micellar structure in the mixed solvent.

Table 2
The composition of supramolecular structured hydrogel

Macromer	Name of hydrogel			
APECL-6K	$6K_0$	$CD6K_5$	$CD6K_{10}$	$CD6K_{20}$
APECL-10K	$10K_0$	$CD10K_8$	$CD10K_{20}$	

3.2.1. FTIR spectroscopy

The FTIR spectra of dried supramolecular structured hydrogels composed of APECL-6K and − 10K with α-CDs, their precursor hydrogels without α-CD, as well as free α-CD in the range of 400–4000 cm^{-1}, were shown in Figs. 6 and 7, respectively. The broad peaks appeared between 3000 and 4000 cm^{-1} are assigned to symmetric and asymmetric stretching vibration modes of O-H bonds. The bands are observed at 3370 cm^{-1} in pure α-CD, and shifted to high frequency of 3402 cm^{-1} when a supramolecular structured hydrogel is formed upon exposing a solution of macromer APECL-6K- or 10K-CD in a mixture of DMSO and water to UV light. These shifts are most likely resulted from the bridging association of O–H bonds of the neighboring α-CDs threaded onto the polymer chains, and the hydrogen bond interaction between hydroxyl groups of α-CDs and the included macromer chains. The center of the bands is located at the same position as in the polypseudorotaxanes as described in Section 2.4. In addition, it is observed in these two types of hydrogels that the peaks in the region from 2700 to 3000 cm^{-1} are different from that of

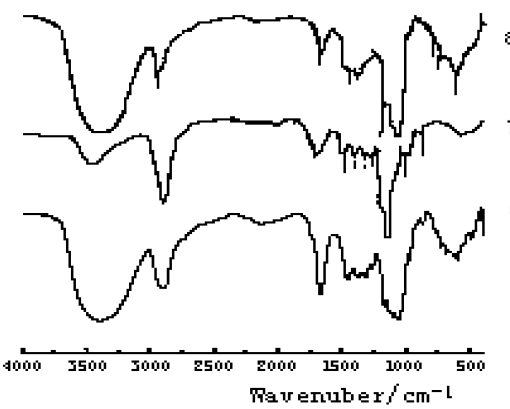


Fig. 6. FTIR spectra of α-CD (a), $6K_0$ (b) and $CD6K_{20}$ (c) dried samples.

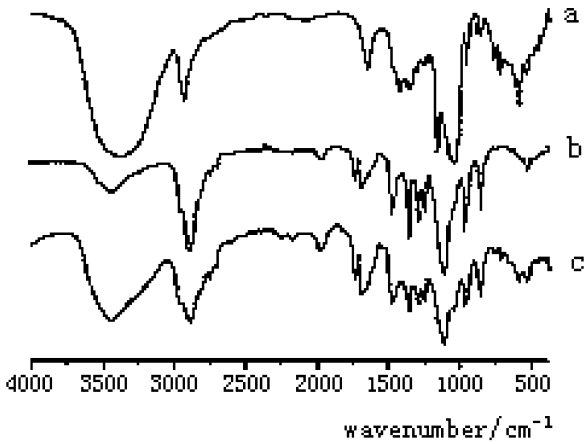


Fig. 7. FTIR spectra of α-CD (a), $10K_0$ (b) and $CD10K_8$ (c) dried samples.

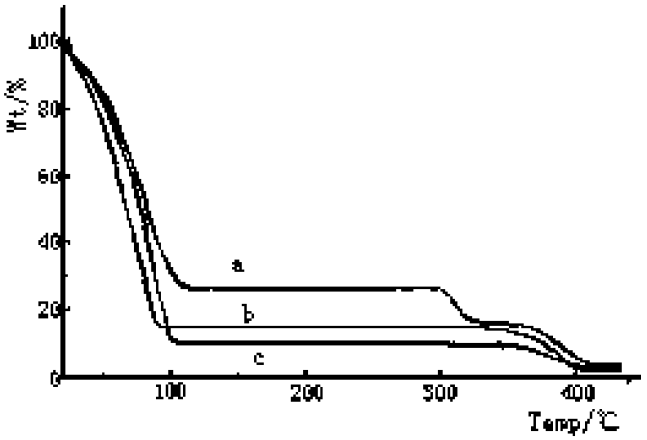


Fig. 8. TGA scans of $CD6K_{20}$ (a), $6K_0$ (b) and $CD6K_5$ (c) hydrogel in the equilibrium swelling state, at a heating rate of 10 °C min^{-1}.

pure α-CD. Due to a overlap between C–H stretching vibration modes of α-CD at 2929 cm^{-1} and $6K_0$ with a wider shoulder at 2942 cm^{-1} and a sharp peak at 2888 cm^{-1}, a new multiple band at about 2916 cm^{-1} with a sharp shoulder at 2886 cm^{-1} can be confirmed both in Figs. 6 and 7, which is presumably ascribed to the formation of polyrotaxanes with the crosslinking junctions as stoppers topologically.

In Figs. 6 and 7, a new band appeared at 1732 cm^{-1} is ascribed to C=O stretching modes of ε-hydroxyl caproate units and acrylate groups in the samples of $6K_0$ and $CD6K_{20}$, as well as in $10K_0$ and $CD10K_8$. Since a low molar ratio of CL to PEG incorporated into the backbone, the intensity of this characteristic band for the C=O groups is lower. The peaks appeared at 575, 709, and 759 cm^{-1} in supramolecular structured hydrogels $CD6K_{20}$ and $CD10K_8$ are assigned to the corresponding α-CD framework vibration, which is in line with the characteristic bands of pure α-CD in this region.

3.2.2. TGA–DTG thermal analysis

The TGA thermograms of two types of supramolecular structured hydrogels, $CD6K_{0-20}$ and $CD10_{0-20}$ in the equilibrium swelling state, recorded at a heating rate of 10 °C min^{-1} in the range of the temperature of 0–500 °C were shown in Figs. 8 and 9, respectively. It can be seen that a hydrogel without α-CD assemblies has nearly lost its retaining water in the crosslinked matrix before 100 °C, and the corresponding temperature for a hydrogel with α-CD assemblies gradually rises. For example, this temperature for $6K_0$, $CD6K_5$, and $CD6K_{20}$ is 96, 104, and 108 °C, respectively. The fact suggests that α-CDs threaded onto polymer chains affect not only the water distribution, but also improve the water thermal stability in the matrix. Since the macromers are included in the channels of α-CDs, these α-CDs can freely move forward and backward as well as rotate around the polymer chains when the amount of α-CDs threaded is well below the stoichiometric ratio required to form a saturated polypseudorotaxane. Thus, water molecules entering the matrix interact with the polar groups in the amorphous α-CDs and in the polymer backbone to exist as bound water, besides the additional swelling water called free water which is imbibed after the polar hydroxyl groups become saturated with bound water. As a consequence, the threading of α-CD onto the macromer chains increase the content of bound water, as well as the content of water in the equilibrium swelling state, i.e. the total water content. For instance, the total water content of $6K_0$ and $CD6K_5$ is 85.8 and 90.7 %, respectively.

Both figures further show that the temperature at which the hydrogel has lost its total water rises significantly, while water content in the equilibrium swelling state descends evidently as the feed molar ratio of α-CDs ascends steadily, e.g. in $CD6K_{20}$ and $CD10K_{20}$, respectively. This gives a strong evidence that α-CDs in the hydrogel exhibit a different packing pattern with the change of the CD content. It had proved that the inclusion complex as a saturated polypseudorotaxane has a channel structure, which is formed by adding a solution of stoichiometric α-CDs to the macromer solution in water. It is reasonable that the hydrogel obtained from the increasing content of α-CDs

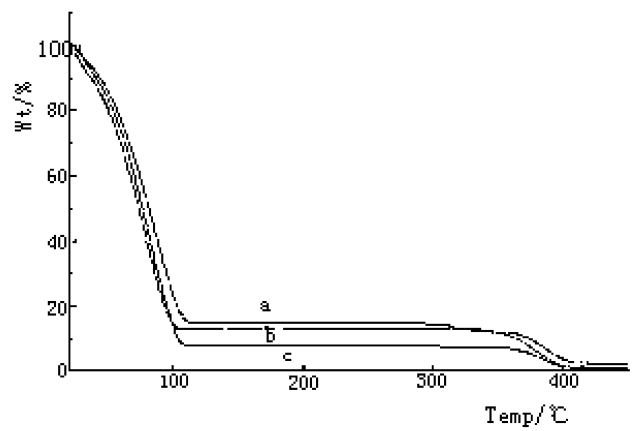


Fig. 9. TGA scans of $CD10K_{20}$ (a), $10K_0$ (b) and $CD10K_8$ (c) hydrogel in the equilibrium swelling state, at a heating rate of 10 °C min^{-1}.

assumes also a channel structure like that of the APECL-CD inclusion complexes. In the X-ray diffractograms as shown in Fig. 2, it is observed that the diffraction result of $CD6K_{20}$ is very similar to APECK-4K-CD, but quite different from the $CD6K_5$, in which the α-CD concentration is too low to form such a channel structure of the α-CDs threaded onto the macromer backbone. Although the number of the α-CDs threaded is not sufficient to assume a perfect channel structure, they show a strong trend to form this structure, which consequently increases the rigidity of the network chain of the hydrogel. When water molecules enter this hydrogel matrix, the rigid network has a poor elasticity to extend to absorb water. In addition, once a channel structure formed, it can only facilitate water molecules to hydrate polar hydrophilic groups on the external wall of the channel. These two effects synergistically result in decreasing the water content in the equilibrium swelling state, while increasing the thermal stability of the bound water to cause the final temperature of water loss to rise.

As presented in Figs. 8 and 9, the TGA scans of two types of swollen hydrogels reveal that both of them having α-CD assemblies start to decompose at about 300 °C after they have lost the total water to become dried gels. In order to further study the relationship between the α-CDs threaded and the hydrogel network, the TGA thermograms of pure α-CD, dried $CD6K_5$, and $CD6K_{20}$ scanned at a heating rate of 10 °C min^{-1} between 0 and 500 °C were shown in Fig. 10. Two weight loss processes are observed in the TGA curves of both $CD6K_5$ and $CD6K_{20}$. The first attributes to the decomposition of α-CD with an onset of the thermal decomposition at 294s °C, which is higher than that of pure α-CD (272 °C), and the second to the decomposition of the matrix framework and α-CD residue with an onset at 338 °C. It shows that an initial residue of pure α-CD is 33.4%, then this value for $CD6K_5$ and $CD6K_{20}$ remains 85.6 and 58.4%, respectively. These results indicate that when pure α-CD is about to finish the decomposition, the network of hydrogels with α-CD assemblies is still in the melting state to continue to decompose. It can be seen that the onset of thermal decomposition of the framework of supramolecular structured hydrogel is higher than that of the hydrogel without α-CD assemblies. Therefore, the PEG blocks of the hydrogel network chains and the α-CDs threaded onto the blocks can stabilize each other.

The TGA scans of pure α-CD and dried $CD10K_{20}$ were presented in Fig. 11. It shows likewise that the α-CD threaded onto the macromer chains starts to decompose at the temperature higher than the pure α-CD. As documented in Refs. [17,18], when an inclusion complex of α-CD is formed by threading onto the polymer PEG blocks, its onset of thermal decomposition is about 20 °C higher than itself. Alternatively, if the α-CD mixes with the PEG directly, its decomposition behavior remains the same as the pure α-CD. This observation further confirms that the inclusion complex of α-CDs is proceeded by threading onto the macromer chains, and the supramolecular structured hydrogel is formed with the crosslinking junctions acted as stoppers simultaneously.

3.2.3. DSC thermal analysis

Based on the assumption that free water and part of the bound water may be frozen, DSC was used to characterize water in hydrogels at a low heating rate of 5 °C min^{-1} in the low temperature region from − 70 to 50 °C. The DSC curves for $6K_0$ and $CD6K_5$ in the equilibrium swelling state were presented in Fig. 12. Three types of water, namely frozen bound water, free water, and unfrozen bound water can be obtained from the curves. A small endothermic peak (1) appeared at relatively low temperature (about − 14 °C) corresponds to the melting of crystalline of frozen bound water in the hydrogel. The endotherm at about 0 °C, which is similar to pure water, is ascribed to the melting process of the crystalline formed by free water. By comparing with melting enthalpy of pure water (334 J g^{-1}), the two corresponding endotherm values (1) and (2) measured when warming the frozen hydrogel can give the amounts of frozen bound water and free water in the hydrogel sample being tested. The amount of unfrozen bound water can be obtained by difference of the measured total water content

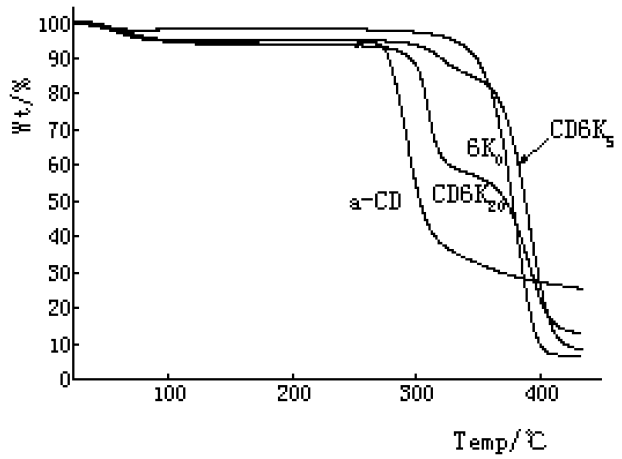


Fig. 10. TGA scans of pure α-CD, and dried $6K_0$, $CD6K_5$ and $CD6K_{20}$.

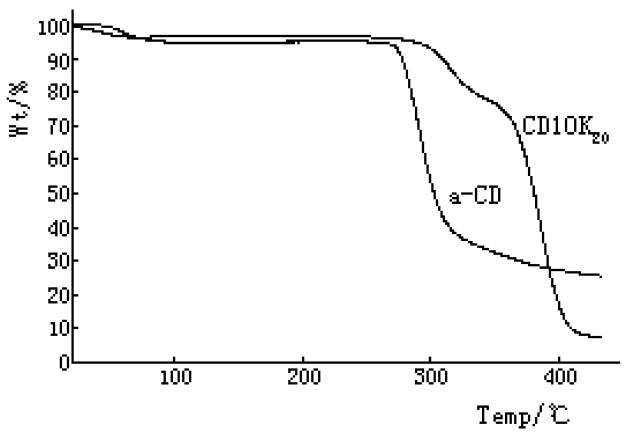


Fig. 11. TGA scans of pure α-CD and dried $CD10K_{20}$.

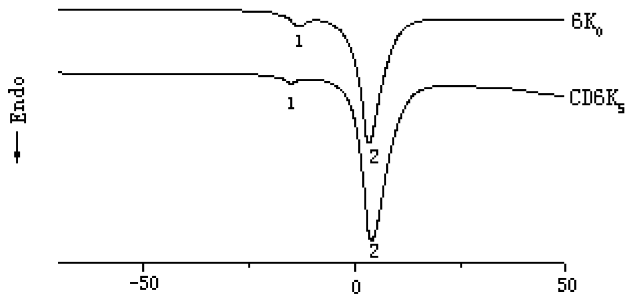


Fig. 12. DSC curves of hydrogel $6K_0$ and $CD6K_5$ in the equilibrium swelling state, at a heating rate of 5 °C min^{-1}.

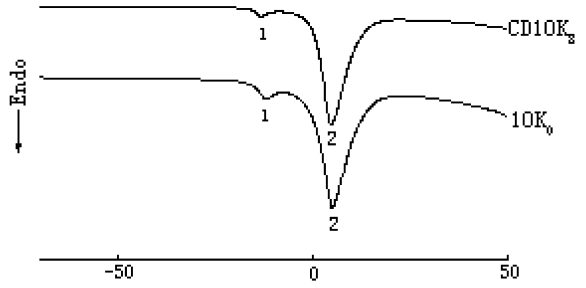


Fig. 13. DSC curves of hydrogel $10K_0$ and $CD10K_8$ in the equilibrium swelling state, at a heating rate of 5 °C min^{-1}.

of the hydrogel test specimen, and the calculated content of both frozen bound water and free water. The contents of three types of water in the hydrogel in the equilibrium swelling state were listed in Table 3. The data show that the content of unfrozen bound water in the hydrogel with α-CD assemblies is higher than that without this supramolecular packing. The phenomenon implies that the threaded α-CDs indeed affect the water distribution in the hydrogel matrix.

As shown in Fig. 13, water in the hydrogel of $10K_0$ and $CD10K_8$ behaves as in $6K_0$ and $CD6K_5$. The different distributions of water were summarized also in Table 3.

3.2.4. Equilibrium swelling test

The relationship of the swelling ratio of supramolecular structured hydrogels with α-CD assemblies against time measured at 25 °C in water was presented in Fig. 14. As can be seen from the figure, all samples absorb water rapidly and reach an equilibrium swelling level. A small amount of α-CDs threaded onto the network chains can improve the swelling characteristics of a hydrogel specimen. The increase of the swelling ratio of $CD6K_5$ and $CD10K_8$ compared with $6K_0$ and $10K_0$, respectively, is mainly caused by α-CDs threaded onto and localized randomly over the hydrogel chains. As presented in Figs. 8 and 9, a further increase of the feed molar ratio of α-CDs to the macromer, e.g. in $CD6K_{20}$ and $CD10K_{20}$, can lower the water content of the hydrogel samples. This result indicates that when a channel structure is formed between α-CDs and the macromer, it is difficult for water molecules to enter the matrix due to the rigidity of the network chains caused by the self-assembly of α-CDs.

3.2.5. X-ray diffraction

As outlined in Fig. 2, the X-ray diffraction pattern of the supramolecular structured hydrogel $CD6K_5$ (c) with a small amount of α-CDs assemblies presents only a characteristic reflection with two prominent peaks of the PEG blocks appeared at $2\theta = 19.3$ and 23.5°. It had been reported that major diffraction peaks at $2\theta = 10.2$, 12.8, 14.7, 20.4; and 22.5° are observed in the pure α-CD [13]. As the content of α-CDs threaded increases, the X-ray diffractogram of the hydrogel sample under study never shows a simple mixture of pure α-CD and the PEG blocks of the macromer chains. Instead, a number of new diffraction peaks in the hydrogel $CD6K_{20}$ (b) appear at $2\theta = 12.2$, 16.2, 20.0, and 22.6°, which is very similar to the characteristic diffraction pattern of the channel structure of the saturated polypseudorotaxane APECL-4K-CD (a). This observation indicates that the α-CDs threaded onto the hydrogel network chains exhibits a strong tendency to form a channel structure.

In summary, we have synthesized a series of polypseudorotaxanes from α-cyclodextrins (α-CDs) threaded onto CL-PEG-CL oligomers terminated with acrylate groups, from which supramolecular structured hydrogels are prepared in a mixed solvent of H_2O and DMSO via in situ photopolymerization under UV irradiation. The results show that α-CDs are threaded and immobilized onto the network chains of the hydrogel with crosslinking junctions as stoppers topologically, and the feed molar ratio of α-CDs affects the hydrogel structure and the water distribution in

Table 3
Water distribution in hydrogel

No. of hydrogel	Total water (wt%)[a]	Free water (wt%)[b]	Frozen bound water (wt%)[b]	Unfrozen bound water (wt%)[c]
$6K_0$	85.8	72.3	3.7	9.8
$CD6K_5$	90.7	69.8	5.3	15.6
$10K_0$	88.2	71.9	4.8	11.5
$CD10K_8$	92.8	69.3	6.1	17.4

[a] Determined by TGA.
[b] Determined by DSC.
[c] Obtained by difference of the total water and the calculated free water and frozen water content.

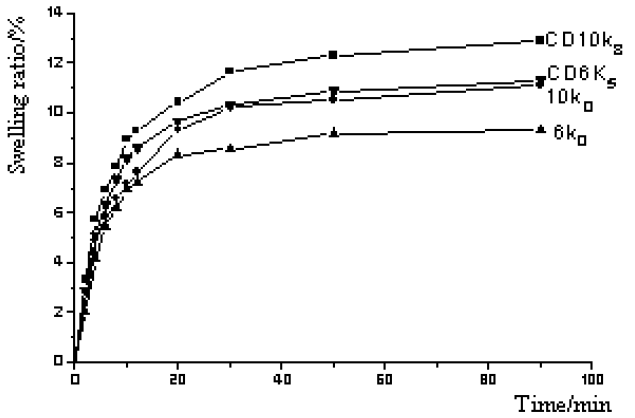


Fig. 14. The relationship of the swelling ratio of dried hydrogel against time at 25 °C in water.

the hydrogel. Further studies on these supramolecular structured hydrogels used in the field of biomaterials are now in progress.

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