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Supramolecular Hydrogels Made of End-Functionalized Low-Molecular-Weight PEG and α-Cyclodextrin and Their Hybridization with SiO_2 Nanoparticles through Host−Guest Interaction

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ABSTRACT: As quite generally stated in the literature, low-molecular-weight (MW) poly(ethylene glycol) (PEG) (M_n less than 2K) and α-cyclodextrin (α-CD) can lead to only crystalline precipitates (not hydrogels). However, in this study we found that: (1) adamantane monoend-functionalized low-MW PEG (Ada-PEG, M_n= 1.1 or 2K) and α-CD lead to hydrogels but not to crystalline precipitates and (2) β-cyclodextrin (β-CD) surface-functionalized silica nanoparticles (β-CD−SiO_2) can be well dispersed in low-MW Ada-PEG and α-CD aqueous mixtures, resulting in hybrid hydrogels. The hydrophobic aggregation of Ada-PEG in case 1 and the further functionalization of β-CD−SiO_2 with PEG chains due to the inclusion complexation between β-CD and the Ada group attached to PEG in case 2 were found to play a key role as a supra-crosslink that promoted the gelation of the inclusion complexes of α-CD and the low-MW Ada-PEG. The resultant native and hybrid hydrogels retained the basic characteristics of the supramolecular physical hydrogels, especially the shear-thinning property. The mechanical strength and the viscosity of the hybrid hydrogel were greatly improved in comparison with those of the corresponding native hydrogels.

Introduction

Cyclodextrins (CDs), mainly α-, β-, and γ-CDs, and their derivatives have been extensively studied as host molecules in supramolecular chemistry.[1,2] Either small molecules or linear polymers can serve as the guests interacting with CDs toward the formation of supramolecular complexes. Poly(ethylene glycol) (PEG) was found to be able to thread through a series of CD molecules forming linear supramolecular-nanostructured complexes, specifically named polypseudorotaxanes.[3−6] Since the first report on the formation of the necklacelike supramolecular structure of PEG and α-CD in 1990,[7] such polymer inclusion complexes have drawn increasing attention because of their great importance in basic studies as well as in applications.[3,8,9]

Li and coworkers first reported the sol−gel transition during complex formation between α-CD and high-MW PEG in aqueous solutions in 1994.[10] These hydrogels, which are based on the polyrotaxanes, can generally be classified as chemical and physical hydrogels. For the chemical hydrogel of α-CD and PEG, chemical cross-linking exists either between the α-CD molecules or between the high-MW PEG chains. The research groups of Yui,[11−14] Okumura, Ito,[15−18] Feng,[19−22] and Zhang[23] have made contributions to the studies of various chemical hydrogels. The physical hydrogel, which is always made of α-CD and high-MW PEG or PEG-containing copolymers without chemical cross-links, has drawn a broad interest in recent years. This is mainly because it shows unique rheological properties, which are required for injectable materials for drug delivery. Li et al. first reported the sol−gel transition and injectable and bioabsorbable properties of such hydrogels.[10,24] Here the inclusion complexes are thought to aggregate in microcrystals, acting as physical cross-links to induce the formation of a supramolecular polymer network. Kataoka et al. reported a thermoreversible polyrotaxane hydrogel based on high-MW PEG and methylated α-CD.[25] Yui et al. studied the gel−sol phase transition behavior of hydrogels of α-CD- and PEG-grafted (or poly(ε-lysine)-grafted) dextrans or chitosan.[26−28] Chen et al. investigated the gelation behavior between a densely PEG-grafted polymer brush and α-CD.[29] Several other such physical hydrogels have also been prepared from PEG-containing diblock and triblock copolymers, star, and hyperbranched polymers.[19−21,30−36]

As quite generally stated in the literature, for all of these physical gels based on linear homopolymer PEG, high-MW (M_n > 10K) PEG is necessary, because low-MW PEG (M_n less than 2K) and α-CD can only lead to crystals of stoichiometric complexes.[32] The reason for this seems to be simple: because the inclusion complexation between α-CD and PEG units occurs at both ends of PEG chains forming the cross-links, the remaining noncomplexed PEG segments are too short to form a network if the MW of PEG is low. However, it is known that water-soluble polymer chains with high MW (normally M_n > 10K) are not suitable for filtration through the human kidney membrane because of their large hydrodynamic radius.[37] We noticed that much work recently appeared that used PEG-containing block, grafted, star, or hyperbranched polymer instead of linear PEG homopolymer to construct the hydrogels based on the polyrotaxanes with α-CD. In these cases, the use of harsh or toxic chemicals, such as various initiators for radical polymerization or cross-linkers for the cross-linking reaction, also compromises the application safety of such hydrogels. Therefore, suitable preparation procedures based on low-MW PEG-yielding materials that are able to be used in pharmaceutical or medicinal applications are desirable for their exploitation as drug delivery and controlled release systems.

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In the present work, for the first time, we succeeded in constructing hydrogels based on the complexes of α-CD and low-MW PEG (MW 1.1 and 2K). The key point here is that we introduce a supra-crosslink to the polyrotaxanes of α-CD and PEG, which promotes the formation of the network. This idea is further used for constructing hybrid hydrogels from low-MW PEG by using β-CD-modified SiO_2 (β-CD−SiO_2) as a supra-cross-link, which not only aids the gel formation but also greatly improves the gel strength. It is noteworthy that the use of low-MW PEG is expected to produce hydrogels with better biocompatible properties. At the same time, both the native and the inorganic nanoparticle-containing hydrogels have very good shear-thinning properties, which are very important for hydrogels used in pharmaceutics.

Experimental Section

Materials. Polyethylene glycol monomethyl ether (mPEG, MW = 1.1 or 2K with polydispersity index (PDI) = 1.05) was purchased from Fluka. 1-adamantane carboxylic acid chloride and α-CD were purchased from Acros Organics. All other chemicals were obtained from Shanghai Chemicals.

Synthesis of Ada-PEG. Ada-PEG1.1K and Ada-PEG2K were synthesized by reacting the hydroxy end of mPEG1.1K and mPEG2K with 1-adamantane carboxylic acid chloride according to procedure described in ref 38. The degree of the end-functionalization reached 99%, as determined by ^{1}H NMR.

Preparation of β-CD−SiO_2 Nanoparticles. Bare SiO_2 nanoparticles were prepared using a method developed by Stöber et al.[39] Briefly, 15 mL of tetraethyl orthosilicate (TEOS) was added to a flask containing 37.5 mL of 25−28% ammonia and 500 mL of dry ethanol with stirring. The stirring was continued overnight at room temperature. This resulted in the formation of silica nanoparticles with a diameter of ∼200 nm, as measured by SEM. The bare silica particles were further modified with β-CD via a four-step procedure, as described in the literature, leading to β-CD−SiO_2.[40]

Formation of Hydrogels. The general protocol for the hydrogel formation is as follows: An aqueous solution of α-CD (145 mg/mL) was added to an aqueous solution of Ada-PEG1.1K or 2K. For the β-CD−SiO_2 hybridized hydrogels, an aqueous solution of β-CD−SiO_2 was added to an aqueous solution of Ada-PEG1.1K or 2K, and the mixed solution was stirred overnight at room temperature before the addition of α-CD. Various concentrations of Ada-PEG1.1K or 2K or β-CD−SiO_2 were used to formulate different hydrogels. For all samples, the solution was mixed thoroughly by sonication for 2 min followed by incubation at room temperature for 72 h before measurements.

Measurements. Turbidity measurements were carried out on a Perkin-Elmer Lambda 35 UV−vis spectrophotometer at a fixed wavelength of 500 nm at room temperature. The steady-state fluorescence measurements were recorded on a FLS 920 (Edinburg Instruments) spectrofluorophotometer. Pyrene was used as a fluorescence probe at a concentration of 6.0×10^{-7} g/mL using an excitation wavelength of 339 nm. The rheological behavior of the hydrogels was investigated by a TA-ARG2 rheometer using a 40 mm parallel-plate geometry at 25 °C. The gap distance between the two plates was fixed at 0.3 mm. Oscillating strain was fixed at 0.1 for all dynamic tests. X-ray diffraction (XRD) measurements were carried out on a PANalytical X′Pert Pro X-ray diffractometer with Cu Ka (1.542 Å) radiation (40 kV, 40 mA). For the SEM observations, the specimens were freeze dried under vacuum. The dried specimens were ground to fine powder and placed on conducting glue and were then coated with gold vapor and analyzed on a Philips XL30 electron microscope.

Results and Discussion

Native Hydrogels of α-CD and Low-Molecular-Weight PEG. When α-CD solutions in water were added to solutions of mPEG (MW 1.1 and 2K), which is commercially available and has a monoether end, as expected, precipitate (Figure 1A,B) rather than a homogeneous hydrogel was formed. This precipitate is actually comprised of crystalline complexes of the PEG/α-CD polypseudorotaxanes. To get a homogeneous hydrogel made of low-MW PEG and α-CD, one has to decrease the relative amount of the threaded CD to provide enough long uncovered part of PEG chains. However, this may reduce the degree of aggregation of the CD-complexed part of PEG chains as well, which, of course, is unfavorable to the gelation process. To solve this problem, we designed and utilized adamantane monoend-functionalized PEG (Ada-PEG1.1K and Ada-PEG2K) as the guest polymer instead of mPEG. The introduction of the hydrophobic Ada group is expected to function in two parallel ways: (a) in partially preventing the treading of CD and (b) in providing additional physical cross-links via its hydrophobic aggregation.

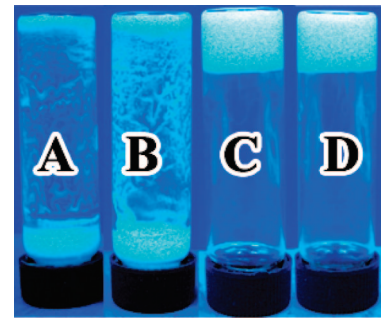


Figure 1. Optical photos of the crystal complexes of (A) mPEG1.1K and (B) mPEG2K with α-CD and invertible supramolecular hydrogels formed by (C) Ada-PEG1.1K and (D) Ada-PEG2K and α-CD. For all examples, the final concentration of PEG and α-CD is 30 and 96.7 mg/mL, respectively.

We succeeded in obtaining invertible hydrogels just by adding an α-CD solution to that of Ada-PEG1.1K or Ada-PEG2K under the same conditions as those for mPEG (Figure 1 C,D). This remarkable difference between mPEG and Ada-PEG can partially be attributed to the difference in their threading rate through CD molecules due to the presence of the bulky Ada group at one end of Ada-PEG. We measured the change in turbidity of the mixtures after adding an α-CD dilute solution to dilute mPEG and Ada-PEG solutions, respectively. The turbidity increase is associated with the threading and sliding of CD on PEG chains (Figure 2).[41] It was found that the turbidity increase of mPEG1.1K is much faster than that of Ada-PEG1.1K (Figure 2A), and a similar trend is observed for that of mPEG2K and Ada-PEG2K (Figure 2B). This fact may imply that the mPEG chains penetrate the α-CD cavities from two ends of the chains, whereas the Ada-PEG chains do it from only one end because the Ada group is larger than the α-CD cavities. The formation rate of the polypseudorotaxane further affects the speed of the microcrystals and the turbidity increase.

The adamantane-modified PEG is in fact an amphiphile because the Ada group is very hydrophobic. Here we measured the fluorescence spectra of pyrene in aqueous solutions of Ada-PEG. Curve A in Figure 3 shows the intensity ratio of the first to third peak (I_1/I_3) of the pyrene emission spectrum as a function of Ada-PEG concentration. I_1/I_3 remains constant at ∼1.85 at low concentrations of Ada-PEG2K and begins to decrease over the concentration range of 1−30 mg/mL and then reaches a constant value of 1.33. From the inflection point of the I_1/I_3 curve, we obtained the critical micellization concentration (CMC) of Ada-PEG2K, 8 mg/mL. Figure 4 displays typical fluorescence spectra of the pyrene probe in the solutions of Ada-PEG2K as well as in the hydrogel of Ada-PEG2K and α-CD, where the polymer concentration (30 mg/mL) is greater than the CMC. Both give an I_1/I_3 value of 1.33, which indicates the existence of the hydrophobic domains of adamantane in the

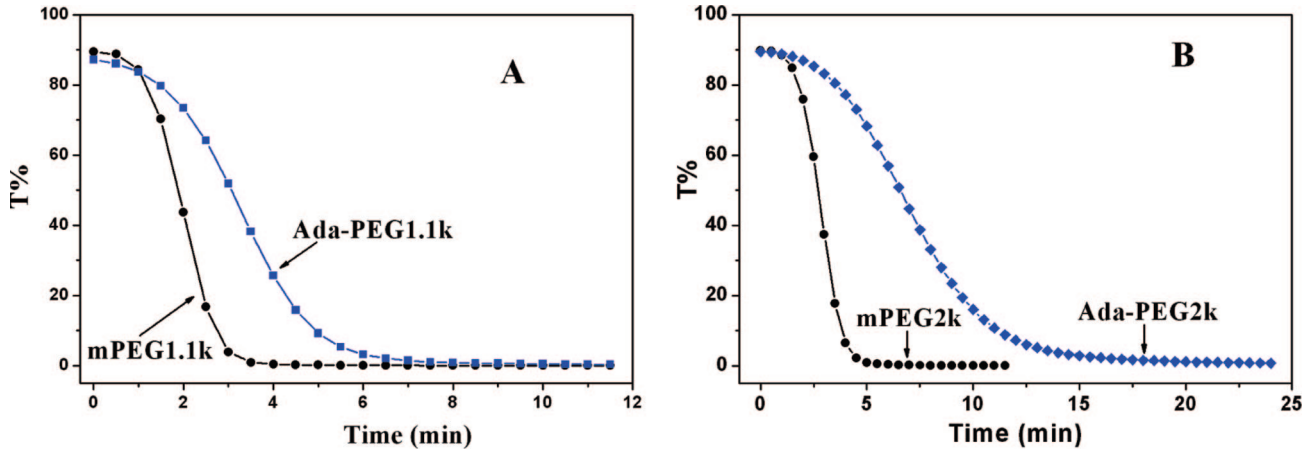


Figure 2. Evolution curves of optical transparency versus time after the addition of α-CD solution to (A) mPEG1.1K andAda-PEG1.1K and (B) mPEG2K and Ada-PEG2K solutions, without stirring at room temperature. For all samples, the concentration of the polymers is 5 mg/mL, and the ratio of the ethylene glycol units to α-CD is 2.

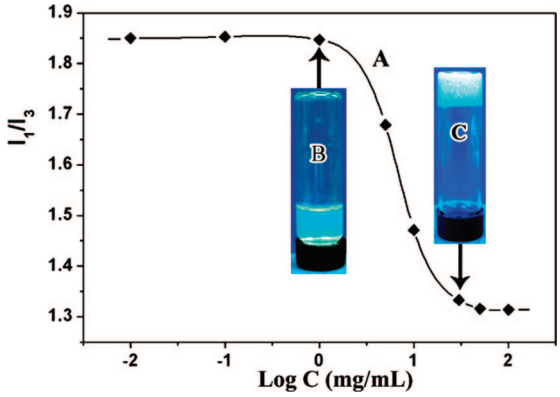


Figure 3. Plot of I_1/I_3 versus log C of Ada-PEG2K in aqueous solution using pyrene as a probe at room temperature (A). Optical photos of (B) and (C) of mixed solutions of α-CD (96.7 mg/mL) and Ada-PEG2K with concentrations of 1 and 30 mg/mL, respectively.

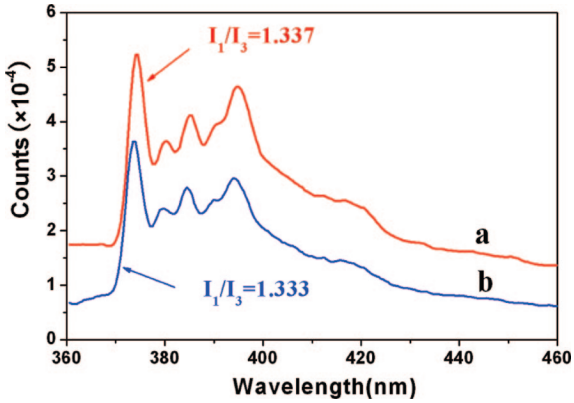


Figure 4. Emission spectra of pyrene in (a) supramolecular hydrogels made of Ada-PEG2K (30 mg/mL) and α-CD (96.7 mg/mL) and (b) aqueous solution of Ada-PEG2K (30 mg/mL).

systems. In fact, no stable bulky hydrogel forms when the concentration of Ada-PEG2K is ~10 mg/mL, which is close to the CMC. It was reported that for hydrogels composed of an amphiphilic triblock copolymer and α-CD the driving force for gelation is a combination of the inclusion complexation between α-CD and PEG blocks as well as the aggregation of the hydrophobic blocks.[30−32] Therefore, we have reason to believe that in the present case, the hydrophobic aggregation of the Ada groups promotes the hydrogel formation as well. This conclusion was also supported by simple experiments in which no hydrogel

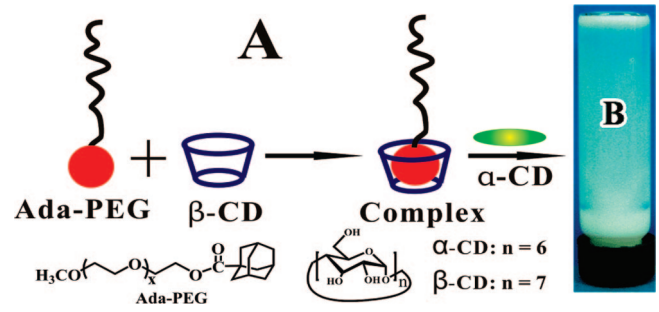
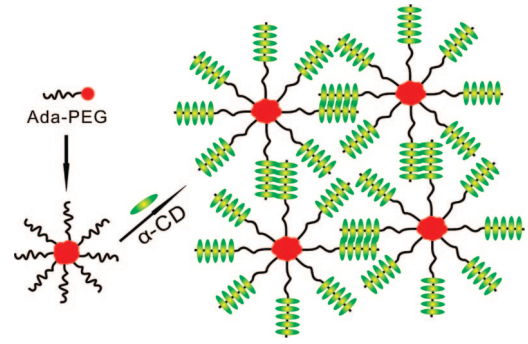


Figure 5. (A) Schematic representation of the complex between Ada-PEG and β-CD and (B) optical photo of the sol made of Ada-PEG2K (30 mg/mL), β-CD, and α-CD (96.7 mg/mL). The molar ratio of β-CD to Ada is 1.

Scheme 1. Schematic Representation of the Supramolecular Hydrogels Made of Ada-PEG and α-CD



was observed when aqueous solutions of α-CD and Ada-PEG2K with concentrations lower than its CMC (as shown in Figure 3B) were mixed.

To further confirm the effect of the hydrophobic aggregation of the Ada groups on gelation, we carried out experiments as follows: an equivalent molar amount of β-CD, which can form a very stable complex with Ada but not with PEG, was added to the Ada-PEG2K aqueous solution to convert its hydrophobic end to a hydrophilic end (Figure 5A). Then, when α-CD was added to the mixture, only sol (no gel) was obtained (Figure 5B).

On the basis of the results in Figures 3, 4, and 5, we may conclude that the gelation of the present Ada monoend-functionalized low-MW PEG and α-CD is caused by both the microcrystalline domains of the included PEG chain end and

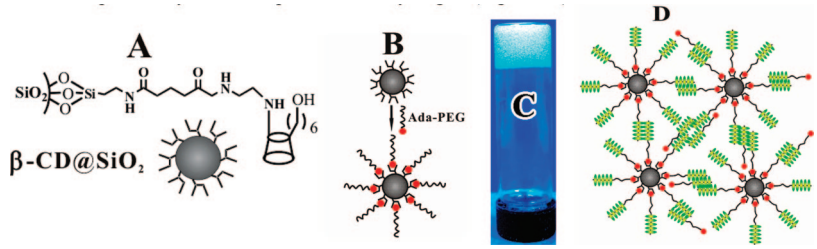


Figure 6. (A) Chemical structure and (B) schematic representation of β-CD−SiO_2 and its inclusion complex with Ada-PEG. (C) Optical photo and (D) schematic representation of the supramolecular hydrogels made of Ada-PEG2K (10 mg/mL), α-CD (96.7 mg/mL), and β-CD−SiO_2 (10 mg/mL).

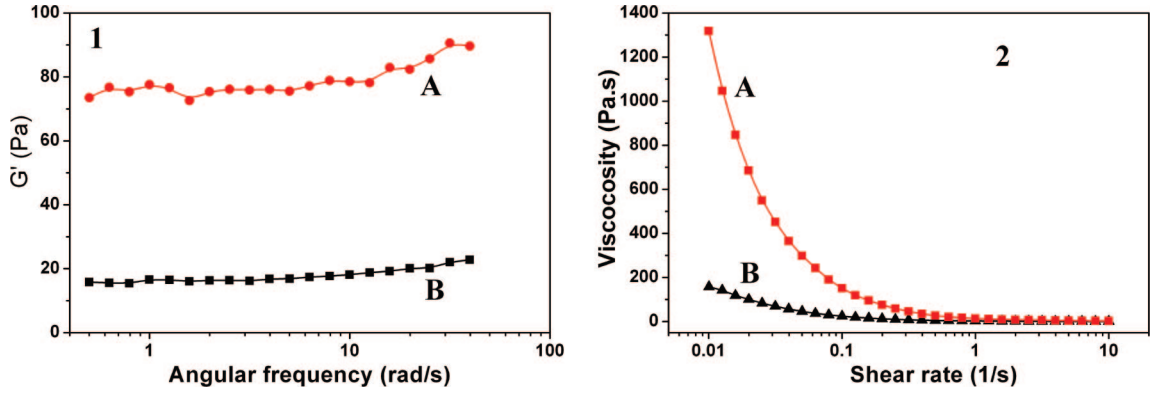


Figure 7. (1) Dynamic and (2) steady rheological behaviors of the hydrogels made of (A) Ada-PEG2K (30 mg/mL), α-CD, and β-CD−SiO_2 (10 mg/mL) and (B) Ada-PEO2K (30 mg/mL) and α-CD. For all samples, [α-CD] = 96.7 mg/mL.

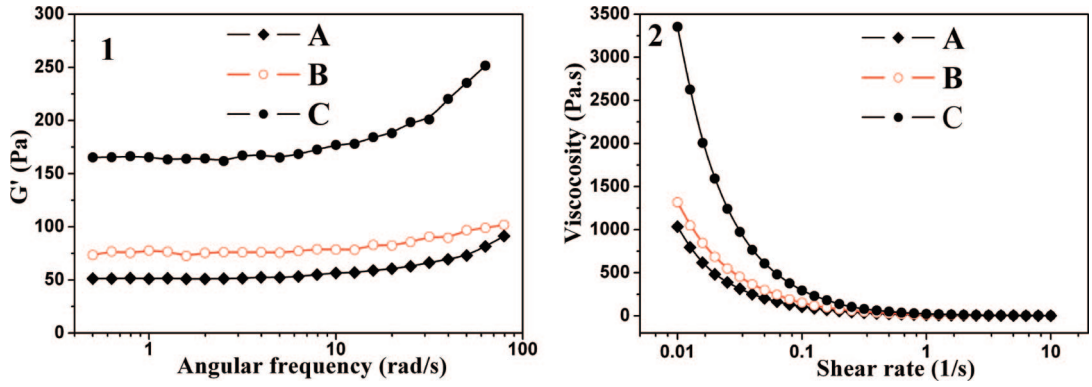


Figure 8. (1) Dynamic and (2) steady rheological behaviors of the hybrid hydrogels made of Ada-PEG2K, α-CD, and β-CD−SiO_2 with various concentrations: (A) 5, (B) 10, and (C) 15 mg/mL. For all samples: [Ada-PEG2K] = 10 mg/mL, [α-CD] = 96.7 mg/mL.

the hydrophobic aggregation domains of Ada groups (as shown in Scheme 1). Because each of such hydrophobic domains connects many PEG chains, we may call it a supra-crosslink. The role of such supra-cross-link is quite similar to that of the hydrophobic domains of the PEG-containing block copolymers when forming hydrogels.[30−32] However, our present strategy of using a modified low-MW PEG seems to be more clean and simple because there is no need for complex and time-consuming preparation of amphiphilic block copolymers.

Hybrid Hydrogels. We extended the idea of using supra-cross-links to produce hybrid organic−inorganic hydrogels based on low-MW PEG. For this purpose, we synthesized β-CD modified silica nanoparticles (β-CD−SiO_2) (Figure 6A) with β-CD groups on the surface. Because β-CD and Ada can form inclusion complexes (with a stable constant as high as 5×10^5 M^{-1}),[42] mixing Ada-PEG2K and β-CD−SiO_2 leads to the formation of a supra-cross-link that contains numerous PEG chains on the surface (Figure 6B). Upon the addition of an α-CD solution to the supra-cross-link solution, invertible hybrid hydrogels were obtained in several minutes (Figure 6C). Note

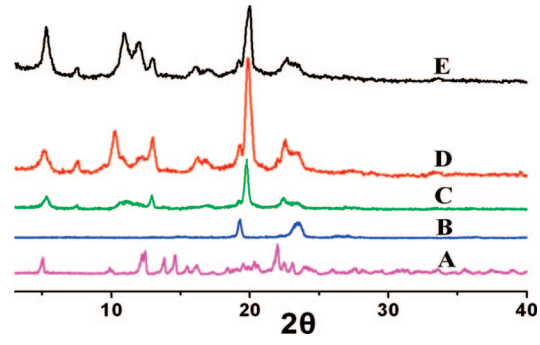


Figure 9. X-ray diffraction power patterns for dried (A) pure α-CD, (B) pure Ada-PEG2K, (C) α-CD/Ada-PEG1.1K gel, (D) α-CD/Ada-PEG2K gel, and (E) α-CD/Ada-PEG2K/β-CD−SiO_2 gel. For all gel samples, the concentrations of Ada-PEG and α-CD are 30 and 96.7 mg/mL, respectively, and for E, the concentration of β-CD−SiO_2 is 10 mg/mL.

that this hydrogel formation was realized over a broad range of Ada-PEG2K concentrations, even as low as 10 mg/mL (Figure

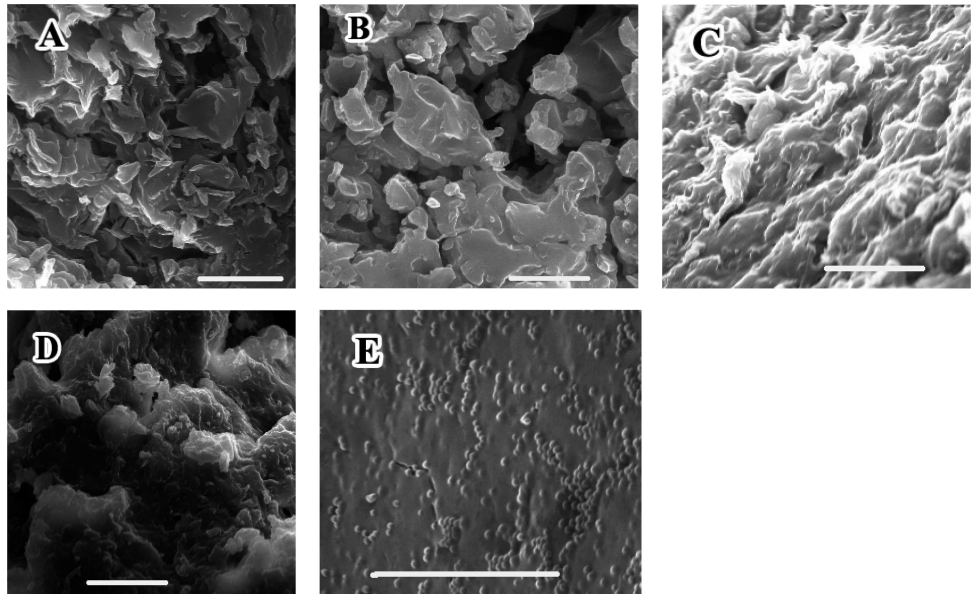


Figure 10. SEM images of the crystal complexes made of (A) α-CD-mPEG1.1K and (B) α-CD-mPEG2K and hydrogels made of (C) α-CD-Ada-PEG1.1K, (D) α-CD-Ada-PEG2K, and (E) α-CD-Ada-PEG2K-β-CD−SiO_2. The bar is 5 μm in all images.

6C). Thus, the β-CD−SiO_2 nanoparticles did facilitate the formation of the hydrogel. In other words, the partial one-end inclusion complexation of the low-MW PEG chains and α-CD, together with the β-CD−SiO_2 nanoparticles, cooperatively results in a strong network structure and gives rise to novel nanoparticle-hybridized supramolecular hydrogels (Figure 6D).

Sabadini et al. reported hydrogels based on similar ternary systems in which the PEG chains were only physically adsorbed on the surface of SiO_2 nanoparticles,[43] and the gels were formed only when the MW of PEG was greater than 2K. When the MW is less than 2K, the adsorbed PEG chains are completely desorbed from the surface of SiO_2 nanoparticles as a result of most of the ethylene oxide units being covered by α-CD. Chen et al. reported hydrogels from PEO−PPO−PEO triblock copolymers, α-CD, and inorganic nanotube.[44] The addition of the nanotube resulted in a decrease in the hydrophobic aggregation of the middle PPO block and hence weakened the strength of the final organic−inorganic hydrogels. Differing from these reports, in our present ternary systems, the inorganic nanoparticles are fixed within the network through the inclusion complexation interaction between the β-CD groups and the Ada groups, which not only promote gelation but also strengthen the hydrogels.

Physical Properties of the Native and Hybrid Hydrogels. The introduction of β-CD−SiO_2 nanoparticles shows remarkable positive effects on the strength and viscosity of the hydrogels. The hydrogel samples were measured after 72 h of standing at room temperature. As shown in Figure 7-1, the storage modulus (G') of the hybrid hydrogel containing ∼8.8 wt % of the modified nanoparticles is ∼4 times higher than that of the native hydrogel over a broad frequency range. Meanwhile, the viscosity at a low shear rate of the hybrid hydrogels reaches ∼1300 Pa·s, whereas that of the native hydrogel is only 157 Pa·s. More importantly, the hybrid hydrogel shows a large shear thinning effect: the viscosity is reduced to 10 Pa·s, close to that of the native gel, when a shear rate of 1/s was applied (Figure 7-2).

Three samples with different contents of β-CD−SiO_2 nanoparticles were examined to explore the effect of the nanoparticle concentration on the rheological properties. As shown in Figure 8, both G' and the viscosity of the hybrid hydrogels increase with an increase in β-CD−SiO_2 nanoparticle content. For sample C, which has 12 wt % nanoparticles, the G' reaches 160−250 Pa depending on the frequency, and the viscosity is as high as 3350 Pa·s. The viscosity shows a remarkable shear-thinning effect. When a shear rate of 0.5/s is exerted, the viscosity dramatically drops to 50 Pa·s. In short, on the basis of the results in Figures 3B, 6, 7, and 8, we may conclude that the introduction of β-CD−SiO_2 not only aids the formation of the hydrogel but also greatly improves the strength of the hydrogels. In addition, both the native and the hybridized hydrogels exhibit good shear-thinning behavior, a basic and valuable property for injectable hydrogels.[32] This shear-thinning effect can be attributed to the supramolecular chemistry nature of the supra-cross-links. Under shearing, partial dissociation of both the micelles of Ada-PEG in the native hydrogels and the inclusion complex between the adamentane and β-CD takes place, which of course leads to a substantial decrease in the degree of cross-links.

Complementary XRD studies indicate the formation of the complexes of α-CD and PEG chains in the hydrogels and give additional information on their nanoscale structure (Figure 9). For comparison, pure α-CD and pure Ada-PEG2K were also measured. The sharp diffraction peak at $2\theta = 19.8°$ (in Figure 9C−E) is identical with the extended channel structure of α-CD, which corresponds to the crystalline α-CD-PEG inclusion complexes.[31,32] Two weak and broad peaks (15.5−17.5 and 21.5−24°) associated with the random structure of α-CD exist in Figure 9C−E, and the peak intensity increases with an increase in the MW of Ada-PEG. This indicates that there is both complexed and uncomplexed α-CD in the gel systems.[10] At the same time, the two characteristic peaks of PEG (19.2 and 23.4°, Figure 9B) can also be observed in Figure 9 C−E. This fact implies that the Ada-PEG chains in the network are only partially covered with CD molecules because they can penetrate the α-CD cavities from only one end. At the same time, the micellation of Ada-PEG and its promotion of the gel formation will also reduce the threading ratio of α-CD.

The morphology of the hydrogels was also observed by SEM. For a comparison, the crystalline complexes formed by α-CD and mPEG were also examined. As shown in Figure 10, the complexes made of α-CD and mPEG1.1K (Figure 10A) and mPEG2K (Figure 10B) show a disklike crystalline structure. Those made of α-CD and Ada-PEG1.1K (Figure 10C) and Ada-PEG2K (Figure 10D) display a relatively homogeneous 3D gel structure. For the hybrid hydrogels (Figure 10E), well-dispersed,

individual, or slightly aggregated β-CD−SiO_2 nanoparticles could be clearly identified. By comparing Figure 10C,D with Figure 10E, one can observe that the surface of the hybrid hydrogels is smooth and compact, whereas the native hydrogels look a bit coarse with plentiful undulant pimples. This difference may be caused by the inclusion interaction between Ada-PEG chains and the surface of the β-CD−SiO_2 nanoparticles, which limits the mobility of the PEG chains.

Conclusions

The present work demonstrates a simple and effective method for preparing supramolecular hydrogels by using Ada monoend-functionalized low-MW PEG and α-CD. The driving force for gelation is a combination of the partial inclusion complexation between one end of the PEG blocks and α-CD and the hydrophobic aggregation of the Ada groups. The addition of β-CD−SiO_2 nanoparticles, which contain host β-CD molecules on the surface that are capable of forming a complex with Ada groups, not only promotes the gelation of the system but also improves the strength of the gels. Both the native and hybrid hydrogels retained the basic characteristics of supramolecular hydrogels, especially the shear-thinning property, which is very important in drug delivery and controlled release systems. To the best of our knowledge, this is the first report on hydrogels and hybrid organic−inorganic hydrogels based on α-CD and low-MW PEG (MW ≤ 2K). This finding may open a new, simple, and mild avenue for the development of injectable hydrogels as new materials in nanomedicine.

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References and Notes

(1) Hapiot, F.; Tilloy, S.; Monflier, E. *Chem. Rev.* **2006**, *106*, 767–781.
(2) Villalonga, R.; Cao, R.; Fragoso, A. *Chem. Rev.* **2007**, *107*, 3088–3116.
(3) Wenz, G.; Han, B. H.; Müller, A. *Chem. Rev.* **2006**, *106*, 782–817.
(4) Huang, F. H.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982–1018.
(5) Harada, A. *Coord. Chem. Rev.* **1996**, *148*, 115–133.
(6) Harada, A. *Adv. Polym. Sci.* **1997**, *133*, 141–191.
(7) Harada, A.; Kamachi, M. *Macromolecules* **1990**, *23*, 2821–2824.
(8) Harada, A. *Acc. Chem. Res.* **2001**, *34*, 456–464.
(9) Loethen, S.; Kim, J.-M.; Thompson, D. H. *Polym. Rev.* **2007**, *47*, 383–418.
(10) Li, J.; Harada, A.; Kamachi, M. *Polym. J.* **1994**, *26*, 1019–1026.
(11) Watanabe, J.; Ooya, T.; Yui, N. *Chem. Lett.* **1998**, 1031–1032.
(12) Watanabe, J.; Ooya, T.; Yui, N. *J. Biomater. Sci., Polym. Ed.* **1999**, *10*, 1275–1288.
(13) Ichi, T.; Watanabe, J.; Ooya, T.; Yui, N. *Biomacromolecules* **2001**, *2*, 204–210.
(14) Ichi, T.; Ooya, T.; Yui, N. *Macromol. Biosci.* **2003**, *3*, 373–380.
(15) Okumura, Y.; Ito, K. *Adv. Mater.* **2001**, *13*, 485–487.
(16) Zhao, C. M.; Domon, Y.; Okumura, Y.; Okabe, S.; Shibayama, M.; Ito, K. *J. Phys.: Condens. Matter* **2005**, *17*, S2841−S2846.
(17) Karino, T.; Okumura, Y.; Zhao, C. M.; Kataoka, T.; Ito, K.; Hibayama, M. *Macromolecules* **2005**, *38*, 6161–6167.
(18) Karino, T.; Okumura, Y.; Ito, K.; Shibayama, M. *Macromolecules* **2004**, *37*, 6177–6182.
(19) Wei, H.; He, J.; Sun, L.; Zhu, K.; Feng, Z. *Eur. Polym. J.* **2005**, *41*, 948–957.
(20) Wei, H.; Yu, H.; Zhang, A.; Sun, L.; Hou, D.; Feng, Z. *Macromolecules* **2005**, *38*, 8833–8839.
(21) Wei, H.; Zhang, A.; Qian, L.; Yu, H.; Hou, D.; Qiu, R.; Feng, Z. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 2941–2949.
(22) Yu, H.; Feng, Z.; Zhang, A.; Sun, L.; Qian, L. *Soft Matter* **2006**, *2*, 343–349.
(23) Zhao, S. P.; Zhang, L. M.; Ma, D.; Yang, C.; Yan, L. *J. Phys. Chem. B* **2006**, *110*, 16503–6507.
(24) Li, J.; Ni, X.; Leong, K. W. *J. Biomed. Mater. Res.* **2003**, *65A*, 196–202.
(25) Kataoka, T.; Kidowaki, M.; Zhao, C.; Minamikawa, H.; Shimizu, T.; Ito, K. *J. Phys. Chem. B* **2006**, *110*, 24377–24383.
(26) Huh, K. M.; Cho, Y. W.; Chung, H.; Kwon, I. C.; Jeong, S. Y.; Ooya, T.; Lee, W. K.; Sasaki, S.; Yui, N. *Macromol. Biosci.* **2004**, *4*, 92–99.
(27) Huh, K. M.; Ooya, T.; Lee, W. K.; Sasaki, S.; Kwon, I. C.; Jeong, S. Y.; Yui, N. *Macromolecules* **2001**, *34*, 8657–8662.
(28) Choi, H. S.; Yamamoto, K.; Ooya, T.; Yui, N. *ChemPhysChem* **2005**, *6*, 1081–1086.
(29) He, L.; Huang, J.; Chen, Y.; Xu, X.; Liu, L. *Macromolecules* **2005**, *38*, 3845–3851.
(30) Zhao, S. P.; Zhang, L. M.; Ma, D. *J. Phys. Chem. B* **2006**, *110*, 12225–12229.
(31) Li, J.; Li, X.; Zhou, Z.; Ni, X.; Leong, K. W. *Macromolecules* **2001**, *34*, 7236–7237.
(32) Li, J.; Li, X.; Ni, X.; Wang, X.; Li, H.; Leong, K. W. *Biomaterials* **2006**, *27*, 4132–4140.
(33) Yuan, R. X.; Shuai, X. T. *J. Polym. Sci., Part B: Polym. Phys.* **2008**, *46*, 782–790.
(34) Sabadini, E.; Cosgrove, T. *Langmuir* **2003**, *19*, 9680–9683.
(35) Zhu, X. Y.; Chen, L.; Yan, D. Y.; Chen, Q.; Yao, Y. F.; Xiao, Y.; Hou, J.; Li, J. Y. *Langmuir* **2004**, *20*, 484–490.
(36) Zhang, Z. X.; Liu, X.; Xu, F. J.; Loh, X. J.; Kang, E. T.; Neoh, K. G.; Li, J. *Macromolecules* **2008**, *41*, 5967–5970.
(37) Jeong, B.; Bae, Y. H.; Lee, D. S.; Kim, S. W. *Nature* **1997**, *388*, 860–862.
(38) Liu, S. Y.; Weaver, J. V. M.; Save, M.; Armes, S. P. *Langmuir* **2002**, *18*, 8350–8357.
(39) Stoeber, W.; Fink, A.; Bohn, E. *J. Colloid Interface Sci.* **1968**, *26*, 62–69.
(40) Mahalingam, V.; Onclin, S.; Péter, M.; Ravoo, B. J.; Huskens, J.; Reinhoudt, D. N. *Langmuir* **2004**, *20*, 11756–11762.
(41) Xue, J.; Jia, Z. F.; Jiang, X. L.; Wang, Y. P.; Chen, L.; Zhou, L.; He, P.; Zhu, X. Y.; Yan, D. Y. *Macromolecules* **2006**, *39*, 8905–8907.
(42) Harries, D.; Rau, D. C.; Parsegian, V. A. *J. Am. Chem. Soc.* **2005**, *127*, 2184–2190.
(43) Sabadini, E.; Cosgrove, T.; Taweepreda, W. *Langmuir* **2003**, *19*, 4812–4816.
(44) Wang, Z.; Chen, Y. *Macromolecules* **2007**, *40*, 3402–3407.

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