Highly stretchable and resilient hydrogels from the copolymerization of acrylamide and a polymerizable macromolecular surfactant†

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In order to overcome the poor mechanical property of classic hydrogels, many methods have been explored to prepare hydrogels with excellent performance during the last few decades. In this paper, we developed a novel micellar cross-linking copolymerization method without small molecular surfactants to prepare highly stretchable and resilient hydrogels. The polymerization is based on free-radical copolymerization of water soluble acrylamide and a polymerizable macromolecular surfactant (i.e., amphiphilic polyurethane (PU) macromonomer) which can self-assemble into micelles acting as multifunctional cross-linkers. The mechanical properties, such as breaking elongation ratio, modulus and fracture toughness can be easily adjusted by varying the concentration of the polymerizable macromolecular surfactants. In addition, the mechanical energy storage efficiency (also known as resilience) is more than 96% at a strain up to 400%. The high resilience of the obtained hydrogels is due to the reversible assembly of the hydrogen-bonded hydrophobe, which contributes to the dissipation of the crack energy along the hydrogel sample, inside the micelles within the gel network.

Introduction

Hydrogels are chemically or physically cross-linked three-dimensional networks that are water insoluble but can absorb a large amount of water or biological fluids and maintain their semisolid morphology. Besides their various applications in superabsorbents, cosmetics and food, contact lenses, actuators and sensors in the materials science domain, hydrogels have become more and more attractive in artificial implants, biomedical devices, tissue engineering and regenerative medicine, etc., due to their unique properties such as similar flexibility, high water content, and molecule diffusion to natural tissues.1–7 However, unlike natural hydrogel-like bio-tissues, such as skin, muscle, cartilage, tendon, and blood-vessel which are generally strong and resilient, classic hydrogels are often brittle and have very poor mechanical performance, including low strain to break, low toughness and high strain–stress hysteresis, especially in the high strain region.1,8–11 It is these disadvantages that severely limit their potential applications as biomaterials in biological studies. Thus, design of hydrogels with good mechanical properties, such as high toughness, high stretchability and resilience, is crucially important and has drawn extensive interest of many scientists.

During the last few decades, several types of hydrogels with excellent mechanical performances have been successfully developed. For example, highly extensible hydrogels with a topological interlock by figure-of-eight that can slide along the polymer chains were produced (sliding ring, SR, gel) in 2001.12 Hydrogels with a high modulus and toughness and with composite structures were developed by combining clay with polymers (nanocomposite, NC, gel) in 2002.13 High-water-content clay hybrid hydrogels with rapid and complete self-healing ability and exceptionally great mechanical strength were also obtained recently.14 A ‘double network gel (DN gel)’ with high mechanical strength via the interpenetrating polymer network (IPN) method was reported in 2003.14 A similar method was used to construct tough and notch-insensitive DN hydrogels which were ionically and covalently cross-linked in 2012.15 In 2007, a macromolecular microsphere composite hydrogel (MMC gel) with high mechanical performance was prepared by Wang and co-workers.15 The ideally homogeneous gel network with high mechanical properties including modulus and breaking strength from a tetrahedron-like macromonomer was fabricated in 2008.16 At the same time, more and more reported results showed that the weakness, especially the brittleness, of classic hydrogels is due to their lack of efficient energy dissipation in the gel network, giving rise to low resistance to crack propagation.10,17,17 Introducing a multifunctional cross-linking agent, for example, the above-mentioned...
clay, macromolecular monomer spheres, graphene oxide and SiO₂ nanoparticles, 13,15,18-20 can efficiently improve the extensibility of the prepared hydrogels.

The micellar copolymerization technique, first developed by Candau and co-workers, 21 is another simple and straightforward method to greatly improve the stretchable property of hydrogels, and has been used to prepare high-toughness hydrogels by Liu and Okay’s groups in recent years. 22-29 In this technique, the hydrophobic domains, acting as a multifunctional cross-linking agent, within the gel network can efficiently dissipate the crack energy along the hydrogel sample, and thus the growth of the crack to a macroscopic level can be prevented. However, high concentrations of a small molecular surfactant and/or NaCl were needed to dissolve the hydrophobic comonomers. When such a hydrogel is immersed in a large amount of pure water, it becomes fragile and does not exhibit the initial mechanical performance due to the removal of the surfactant from the gel. 24

On the other hand, soft tissues or many biological hydrogels, such as elastin and resilin, are not only strong but also able to undergo significant reversible deformation without energy loss. These hydrogels are well-known as having resilience – an important feature developed by nature for mechanical energy storage that facilitates movement. 8,30,31 Although extensive methods have been developed to prepare hydrogels with high mechanical performance to match natural tissues, and indeed the modulus and extensibility of many reported tough hydrogels can match or are even better than many natural soft tissues, they often exhibit high stress–strain hysteresis. 8,10,32 In contrast, there are only very few recent reports on highly stretchable and resilient synthetic hydrogels. 8,33

In this paper, we report for the first time, a versatile method capable of preparing highly stretchable and resilient hydrogels with tunable properties, including breaking elongation ratio, modulus and fracture toughness, etc. The hydrogels are produced by free-radical copolymerization of water soluble acrylamide and polymerizable macromolecular surfactants, i.e., amphiphilic polyurethane (PU) macromonomers. The polymerizable PU macromolecular surfactants can self-assemble into reactive micelles and act as multifunctional cross-linkers. Different from the previously reported micellar copolymerization technique which always needs additional small molecular surfactants and/or NaCl to dissolve the hydrophobic co-monomers, the present method is a small molecular surfactant-free approach. Naturally, hydrogels made by such a methodology are expected to display superior mechanical performance and stability in water.

Experimental

3-Isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate (IPDI), polyethylene glycol (Mw = 1000 g mol⁻¹, PEG 1k) and acrylamide (Am) were purchased from Sinopharm Chemical Reagent Co. Ltd. The photo-initiator z-ketoglutaric acid (z-ka, 99%) was purchased from Fluka. 2-Isocyanatoethyl acrylate (AOI) was kindly donated by Showa Denko Company. The catalyst dibutyltitan dilaurate (DBTDL) was purchased from TCI. All reagents were used without any further purification.

Fig. 1 Synthetic procedure of polyurethane (PUI and PUII) macromonomers.

Synthesis of the amphiphilic PU macromonomer

The amphiphilic polyurethane macromonomers were synthesized according to the procedure shown in Fig. 1. Firstly, 0.02 mol (20.0 g) PEG 1k was added to a three-necked flask and dried under vacuum at 80 °C overnight in the presence of P₂O₅. Catalytic amount of DBTDL (0.12 g) was then added into the flask and stirred for 20 min at 60 °C. After that, acetone (2.0 mL) solution of IPDI (0.01 mol) was added dropwise into the flask and the reaction was continued at 40 °C for 0.5 h (the completion of the reaction was monitored by IR with the disappearance of the –NCO groups) to get PUI and PUII (as shown in Fig. 1), respectively. The crude products were purified by precipitation in a large amount of ether and dried under high vacuum at 30 °C.

Micellization of PUI and PUII

10 wt% aqueous solution of PUI or PUII was prepared as follows: 10 g of solid PUI or PUII was added in portions to 90 g H₂O at room temperature. The mixture was sonicated for 30 min until there were no observed precipitates, and then vigorously stirred for another 12 h before further use.

Hydrogel preparation

As shown in Scheme 1, the hydrogels were prepared by free-radical micellar cross-linking copolymerization of acrylamide and PUI or PUII at room temperature using reactive PUI or PUII micelles as a multifunctional cross-linker and z-ka as the photoinitiator. First, 0.25 wt%, 0.5 wt%, 1.0 wt%, 2 wt% and 4 wt% of PUI or PUII aqueous solutions were prepared by dilution of the above obtained 10 wt% solution. Next, acrylamide and z-ka were added into these solutions and sonicated for 5 min, and then the mixed solutions were transferred into plastic syringes and sealed. Finally, the sealed plastic tubes were irradiated by 365 nm UV light (Spectroline UV lamp, EBF-260C, 6 W, the
distance between the samples and the lamps was 10 cm) for 1 h. For all the samples, the concentrations of acrylamide and α-ka were fixed at 10 wt% and 0.4 wt%, respectively.

**Measurements**

$^1$H NMR spectra in deuterated chloroform were recorded using a 400 MHz Inova NMR spectrometer. The light transmittance of the PUI or PUII aqueous solution was monitored as a function of concentration at a fixed wavelength of 500 nm by means of a Hitachi U-3900/3900H UV/vis spectrophotometer using water as the reference. The average size of the PUI and PUII micelles in water (2 wt%) was measured by using a Malvern HPP5001. Rheology measurements were performed on a HAAKE rheometer (RS 6000) with a parallel plate accessory (20 mm in diameter). In particular, the dynamic shear modulus was measured over the frequency range $0.1 < \omega < 20$ rad s$^{-1}$ at 25 °C for all the samples. The existence and extent of the linear viscoelastic regime were determined by measuring the dynamic shear storage and loss modulus, $G'$ and $G''$, as a function of strain ($0.01 < \gamma < 10$) at an angular frequency of 6.28 rad s$^{-1}$. All the measurements were carried out within the linear viscoelastic range, where $G'$ and $G''$ are independent of strain. All the tensile and compression tests were carried out in air, at room temperature, using a universal tensile machine (KJ-1065B, Kejian-tech, China) with a 50 N loading cell. The cross-head speeds of the tensile and compression measurements were 50 mm min$^{-1}$ and 3 mm min$^{-1}$, respectively.

**Results and discussion**

**Characterization and micellation of PUI and PUII**

PUI and PUII were synthesized according to the procedure described in Fig. 1. $^1$H NMR spectra in deuterated chloroform were recorded to confirm the chemical structures of PUI and PUII and are shown in Fig. 2. As shown in Fig. 2, peaks at 0.8–1.0 ppm and 5.8–6 ppm were assigned to the protons of –CH$_3$ and –CH=CH$_2$ in IPDI and AOI units, respectively. It should be noted that although the completion of the reaction was monitored by IR with the disappearance of the –NCO groups in the first step (Fig. 1) and oligomers with two PEG 1k blocks should be the main product, there still may be a small amount of products containing more than two PEG 1k blocks, so that some PEG 1k was still free. Thus, in the second synthetic step of PUI, some of the final products may contain two acrylate end groups and a tiny amount of oligomers without any acrylate end groups may also exist. Though there is indeed no efficient method to separate these side products, the as prepared PUI macromolecular surfactants still can be used as a cross-linker for the hydrogel formation as demonstrated below.

The PUI and PUII macromonomers are in fact amphiphiles because the IPDI unit is very hydrophobic. Thus the light transmittance of the PUI and PUII aqueous solutions was recorded as a function of concentration at a fixed wavelength of 500 nm by UV-Vis to monitor the critical aggregation concentrations of PUI and PUII. As shown in Fig. 3, in both cases, the transmission remains constant at ~97% until the concentration reaches 0.001 g mL$^{-1}$, then begins to drop down over the concentration range of 0.001–0.5 g mL$^{-1}$, and then reaches a constant value of ~5%. These results indicate that the starting concentration of aggregate (micelle) formation for both PUI and PUII is about 0.001 g mL$^{-1}$.

**Fig. 2** $^1$H NMR spectra of PUI (a) and PUII (b).

**Fig. 3** Turbidity dependence of PUI and PUII aqueous solutions on concentration.
Dynamic light scattering (DLS) measurements of the PUI and PUII micelles in water were performed on a Malvern HPP5001 instrument to investigate the size distributions. As shown in Fig. 4, there is not much difference between the two size distribution curves of PUI and PUII micelles, and the number average diameter of both micelles is about 30 nm. The appearance of a small broad peak (~80 to 200 nm) in the PUII system may be due to the collapse between PUII micelles which have a higher periphery hydrogen-bonding group (urethane) density than PUI micelles.

Rheology measurements

The mechanical properties of the as prepared hydrogels were firstly determined in shear using dynamic oscillation rheometry. Fig. 5 shows the log–log plots of shear modulus $G'$ as a function of frequency $\omega$. The shear modulus of the hydrogel made from PUI or PUII at 1 rad s$^{-1}$ increased from ~50 to ~4000 Pa or ~300 to 5000 Pa, respectively, as the concentration of PUI or PUII increased from 0.0025 to 0.04 g mL$^{-1}$. This is because the increased content of PUI or PUII increases the cross-linking density of the gel network which mainly determines the stiffness of the hydrogel. These results also demonstrate that the mechanical property of the hydrogel can be easily turned by variation of the contents of PUI and PUII. On the other hand, from Fig. 5a and b, one can see that, at the same concentration of PUI and PUII, the modulus of the PUII cross-linked hydrogels is always almost double that of the PUI cross-linked ones. This is because PUI and PUII have a similar chemical structure and molecular weight (as shown in Fig. 1), but there are two double-bonds in PUII and only one in PUI.

Tensile test

Fig. 6 represents the tensile stress–strain data of the hydrogels cross-linked by various amounts of PUI (Fig. 6a) and PUII (Fig. 6b). In PUI cross-linked hydrogels (Fig. 6a), with increasing concentration of PUI from 0.0025 g mL$^{-1}$ to 0.04 g mL$^{-1}$, elongations at break decrease from 3500% to 370%, but the tensile strengths at the same elongation ratio increase. Similar trends can be observed in PUII cross-linked hydrogels (Fig. 6b). However, comparing Fig. 6a with b, one can see that at the same concentration of PUI and PUII, the elongations at break of the former ones are obviously higher than those of the latter ones, but the tensile strengths at the same elongation ratio are reversed. For example, as shown in Fig. 6c, where the concentration of PUI and PUII is identical (0.005 g mL$^{-1}$), the elongation at break of the PUI cross-linked hydrogel is 1600%, and that of the PUII cross-linked hydrogel is 850%, but the tensile strength of the former one is always lower than that of the latter one in the whole range of measurement. It is well known that cross-linking density is one of the most important parameters that determines the stiffness and strength of a three-dimensional cross-linked network. The network's strength will increase with increasing cross-linking density, but its extendibility will decrease. And so, all the above discussed results as shown in Fig. 6 can be essentially attributed to the different cross-linking densities of the hydrogels.

As previously mentioned, the biomedical and also many other industrial applications of hydrogels often require them to have excellent deformation resilience, since artificial organs, such as artificial muscles, or mechanical parts made of hydrogels should be able to withstand repeated deformations for a long time. In addition, previous reports showed that most soft tissues only experience relatively small passive deformations under normal physiological conditions (cardiac muscle < 30%, blood vessel < 25%, bladder < 30%, esophagus < 200%), and an implant capable of being resilient over a larger deformation range of 400% is enough to minimize the possibility of rupture of the implant under abnormally increased stress or fatigue failure under dynamic cyclic loading. Thus, to further investigate the resilient property of the hydrogels, cyclic tensile-test
loading with a maximum strain of 200 or 400% for 10 run cycles were performed. As shown in Fig. 7 (see also Movie-1 and 2 in the ESI†), with a maximum strain of 200% (Fig. 7a and c), both PUI (0.01 g mL\(^{-1}\)) and PUII (0.005 g mL\(^{-1}\)) cross-linked hydrogels show almost negligible hysteresis. Even with an increased maximum strain of up to 400% (Fig. 7b and d), the resilience of these hydrogels is still higher than 96%, which is comparable to that of a dragonfly tendon (92–97% resilience) and the two recently reported highly resilient synthetic hydrogels prepared by double-network and \(\gamma\)-ray induced \textit{in situ} grafting polymerization methods, respectively.\(^8,33\)

Fig. 6  Tensile stress–strain curves of PUI (a) and PUII (b) cross-linked hydrogels with various concentrations and at the same concentration (c).

Besides the cyclic tensile tests, 5-run cyclic compression tests were also performed on cylindrically shaped PUI (0.01 g mL\(^{-1}\)) and PUII (0.005 g mL\(^{-1}\)) cross-linked hydrogels with a thickness of 15 mm and a diameter of 13 mm, at a crosshead speed of 3 mm min\(^{-1}\) with a maximum force of 50 N (the upper limit of the machine used). As shown in Fig. 8 (see also Movie-3 and 4 in the ESI†), with a maximum compression stress of 300 and 350 kPa, respectively, no compression fractures are observed for both PUI and PUII cross-linked hydrogels even at a compressing strain of 90% and 85%, respectively, indicating excellent compression-resistant property. Although, unlike the cyclic tensile tests, hysteresis or energy loss is observed during the loading and unloading compressing process, all immediately subsequent cycles almost follow exactly the same procedure as for the first cycle. This observation reveals that loading–unloading curves for both PUI and PUII micelle cross-linked hydrogels are identical over a series of five cycles, and a full recovery to the initial state is reached during the time scale of the experiment. The above facts prove that these hydrogels show fully reversible behaviour under repeated compression.

As shown in Fig. 7 and 8, the present hydrogels show comparable high stretchability to that made by micellar copolymerization.\(^22–26\) In addition, the present hydrogels also show highly resilient and reversible behavior under repeated tensile or compression stress, demonstrating excellent elastic property. In addition to the reversible hydrophobic association effect,\(^22–26\) dynamic hydrogen-bonding interaction between the urethane groups in PUI and PUII micelle cross-linked hydrogels may also play an important role in the excellent mechanical property of these hydrogels. This is also why we chose the polymerizable polyurethane, a well-known excellent elastomeric surfactant micelle as the multifunctional cross-linker.

Fig. 7  Cyclic tensile test curves (a–d) and photo images (e) of PUI (a and b) and PUII (c and d) micelle cross-linked hydrogels.
Micellar copolymerization technique has been one versatile method to greatly improve the stretchability of hydrogels in recent years. However, the prepared hydrogels become fragile and do not exhibit the initial mechanical performances with the removal of small molecular surfactants from the gels. The aim of this work is to develop a micellar cross-linking copolymerization method without small molecular surfactants. To this end, polymerizable macromolecular surfactants, i.e., amphiphilic PU macromonomers which self-assemble into reactive PU micelles acting as multifunctional cross-linkers have been used. Using this technique, hydrogels with tunable mechanical properties including breaking elongation ratio, modulus and fracture toughness can be easily prepared by adjusting the content of the PU micelles. Most importantly, the present hydrogels show fully reversible behavior under cyclic tensile and compression experiments. These findings demonstrate a strategy for the preparation of hydrogels that combine high extendibility with excellent resilience and may greatly benefit the further use of hydrogels in tissue engineering and other soft materials research fields.

On the other hand, the presently obtained hydrogels are in fact both non-covalent and covalent cross-linked hydrogels, especially for the PUII series which have two polymerizable double-bonds at both ends. Even for the PUI series, there may still be trace amounts of PUII molecules due to the simple but rough synthetic procedure of PUI. And thus they have superior stability upon immersing in a large amount of water thanks to their chemical cross-linking character. Detailed stability studies of the hydrogels and the copolymerization behaviour of polymerizable polyurethane surfactants with other water soluble monomers are still under progress in our lab.

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Notes and references