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ARTICLE

De Novo Design of a Shear-Thin Recoverable Peptide-Based Hydrogel Capable of Intrafibrillar Photopolymerization

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ABSTRACT: A *de novo* designed peptide-based gel has been prepared whose mechanical rigidity can be modulated after shear-thin recovery. The photopolymerizable β-hairpin peptide named MLD undergoes temperature-induced folding and self-assembly to afford a network of β-sheet-rich fibrils that constitutes a moderately rigid hydrogel ($G' = 220 \pm 50$ Pa, 1 wt %). The MLD hydrogel can be shear-thinned into a low-viscosity gel upon application of shear stress and immediately recovers its mechanical rigidity upon termination of stress. MLD peptides contain non-natural sorbamide derivatives of lysine that allow the mechanical rigidity of its hydrogels to be enhanced through polymerization of dienes displayed along the surface of the fibrils constituting the gel. Irradiation of the gel network increases its mechanical rigidity ~2.5-fold. Circular dichroism (CD) spectroscopy shows that MLD folds and self-assembles into β-sheet-rich fibrils and that photo-cross-linking does not influence the secondary structure contained within the assembly. The MLD hydrogel shows potential as an injectable material whose mechanical properties can be modulated after delivery.

Introduction

The development of three-dimensional scaffolds with suitable architecture as well as mechanical properties that mimic the natural extracellular matrix (ECM) has been a challenge to material scientists. Hydrogel materials are attractive candidates as ECM mimics due to their high water content, porous nature, and mechanical rigidity.[1−10] There is a large number of both natural and synthetic gels either currently in use or being developed for tissue engineering applications.[11−13] One important consideration of hydrogel design is that of the method of implantation or delivery. Many polymeric hydrogels are fabricated *ex vivo* and subsequently implanted into a targeted site such as the liver,[14,15] cartilage,[16,17] or bone[18,19] to aid in tissue repair. This approach can be invasive and result in poor implant fit. In addition, this method of material delivery can be susceptible to infections since large incisions often accompany implantation.

Alternatively, hydrogel precursors can be introduced as liquids through small incisions to a site of interest via a syringe and gelation can be initiated *in vivo*. Minimal invasive delivery via a syringe not only limits the possibility of infection at the tissue site but also allows the gel forming solution to fill irregular-shaped cavities. Subsequent to delivering the polymer solution, hydrogelation can be induced *in vivo* through a sol−gel phase transition triggered environmentally or by initiating chemical cross-linking.[19−22] Photopolymerization can be especially convenient as it can provide spatial and temporal control over the *in situ* hydrogelation process. Many light-triggered hydrogels have been developed for various applications such as drug delivery,[23−27] wound healing,[28,29] and tissue engineering.[30−32] Although promising, a potential limitation of the delivery of liquid polymer solutions is the possibility that the solution can leak to neighboring tissues if the rate of triggered gelation is slow. Hydrogels that can be prepared *ex vivo* and subsequently delivered by syringe have the potential to be acutely retained at the point of application.

Using self-assembling peptides to prepare hydrogels is an attractive alternative to traditional chemically cross-linked polymers since these networks contain physically cross-linked fibrils that can be disrupted under high strain. In addition, peptides offer nearly infinite design space from which novel functional materials can be prepared.[33−44] We have developed a family of β-hairpin peptides capable of undergoing triggered folding and self-assembly to form hydrogels that can be subsequently shear-thin delivered via syringe with spatial and temporal resolution.[45−48] The hydrogels prior to shear-thin delivery display moderate mechanical stiffness and low yielding strains.[47,49−51] During the application of shear force, such as that delivered from depressing a syringe barrel, some of the noncovalent cross-links break, allowing the gel to flow. After delivery, the applied shear is terminated, and the gel quickly recovers its original mechanical stiffness. This hydrogel system allows gels to be prepared directly in a syringe and subsequently delivered to a target site in a minimally invasive manner.

Although these systems provide a convenient mode of material formation and delivery, they do not allow the mechanical properties of the gel to be manipulated after the gel has been delivered. Such a gel could be delivered and its mechanical properties fine-tuned at the application site to customize its performance for the task at hand. Herein, we describe a new peptide-based hydrogel whose mechanical rigidity can be enhanced post shear-thin delivery. The new peptide, named MLD, undergoes triggered self-assembly to form a physically cross-linked network of morphologically well-defined fibrils. Hydrogels formed from MLD shear thin and self-heal allowing facile delivery. Importantly, the primary sequence of MLD contains non-natural residues whose photopolymerizable side chains are precisely displayed along the solvent exposed surfaces of the fibrils. Exposure of an MLD gel to UV radiation post delivery yields

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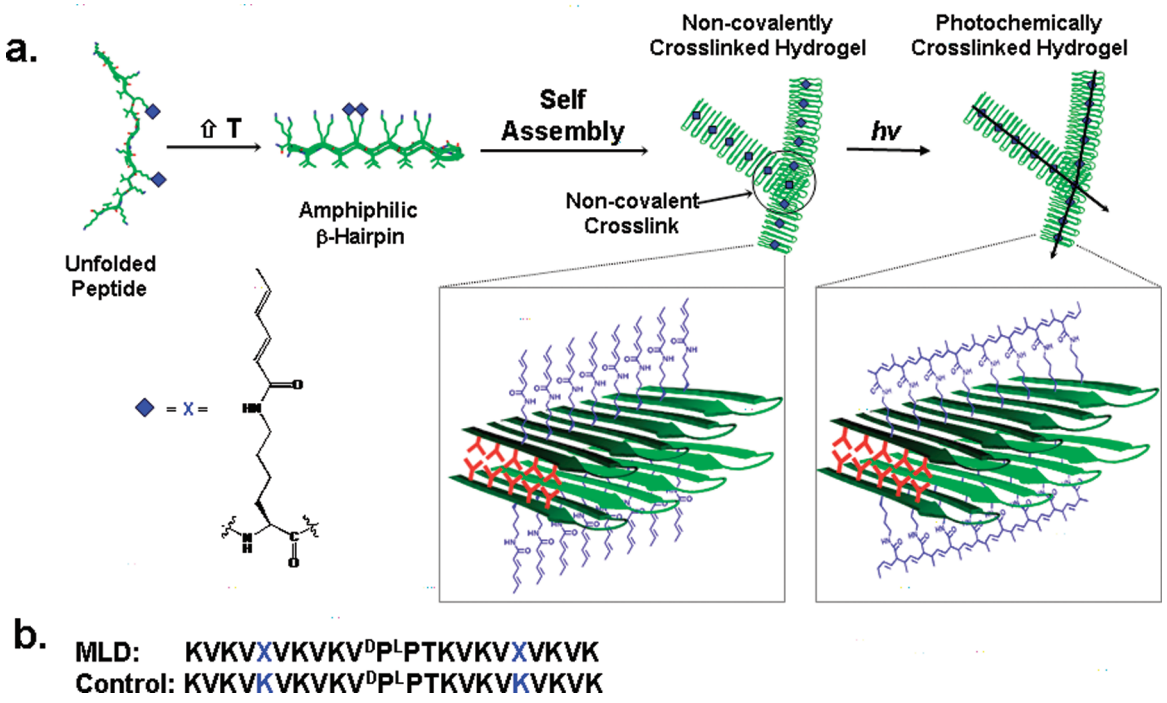

Figure 1. (a) Proposed mechanism of MLD folding and self-assembly leading to hydrogelation and subsequent photopolymerization of its fibrillar network (X = lysyl sorbamide). (b) Primary sequence of MLD and its control peptide.

the formation of intrafibrillar cross-links and the consequent modulation of the hydrogel's rigidity (Figure 1).

Results and Discussion

MLD is a 22-residue peptide designed to intramolecularly fold and subsequently self-assemble in response to an increase in temperature to form an extensive network of β-sheet-rich fibrils leading to hydrogelation. This mechanism allows photoreactive amino acid side chains to be incorporated at the level of the peptide monomer that are eventually displayed in high copy number and with spatial control from the fibrils formed from self-assembly. Previous reports indicate that self-assembling peptides can serve as templates to display photoreactive groups in both the aggregated[52] and cystalline[53] states. The primary sequence of MLD consists of two β-strands composed of alternating high β-sheet propensity valine and lysine residues (Figure 1b).[48] The two strands are connected by a type II′ β-turn composed of -V^DP^LPT-.[46,48,54,55] The primary sequence of MLD contains eight lysine residues and an N-terminal free amine that are protonated at pH 7.4. The peptide also contains nine hydrophobic valine residues. As will be shown, when dissolved in buffer of low ionic strength at low temperatures, the peptide remains unfolded. This is due to both intramolecular charge repulsion between positively charged residues and the ability of water to solvate the hydrophobic valine side chains at low temperature.[56,57] Both of these factors favor the unfolded state. Adjusting the ionic strength of the solution by adding 150 mM NaCl screens the positive charge and poises MLD for folding. Under these conditions, increasing the temperature drives the hydrophobic effect,[56,57] which desolvates the hydrophobic residues, promotes intraresidue hydrophobic interactions, and triggers folding.

When folded, the periodic arrangement of hydrophobic and charged residues imparts amphiphilicity to the faces of the β-hairpin. This facilitates the association of the valine-rich faces of two distinct hairpins to form a bilayer-like structure, leaving their lysine faces exposed to solvent. Simultaneously, the β-strand edges of the folded β-hairpins assemble laterally via H-bonding with other folded β-hairpins, defining the long axis of a given self-assembled fibril. Thus, folded MLD assembles into fibrils comprised of a bilayer of laterally hydrogen-bonded hairpins. Previous mechanistic studies on other self-assembling β-hairpins from our lab, having similar amphiphilic character, support this proposed mechanism.[5,46,47,49,51,54,58−60] During the self-assembly process, irregular hydrophobic facial associations can occur, leading to packing imperfections.[60] This creates nucleation sites for nascent fibril growth, resulting in the formation of noncovalent interfibril junctions that cross-link the network. The number of these physical cross-links as well as fibril entanglements formed during self-assembly imparts rigidity to the resulting hydrogel.

MLD also contains sorbamide-modified lysines at positions 5 and 18 in its primary sequence. After MLD is folded, these residues are centrally located on the hydrophilic face of the hairpin. When MLD self-assembles, these residues line both solvent exposed faces of each fibril comprising the network (Figure 1a). Irradiation of the hydrogel network should polymerize the sorbamide moieties and install a continuous polyene network along both faces of a given fibril. The formation of this intrafibrillar network should influence the mechanical properties of the hydrogel. Although intrafibrillar polymerization along the fibril faces is designed for, the possibility that interfibrillar cross-links can form between entangled or neighboring fibrils cannot be ruled out. Both intra- and interfibrilar cross-link formation would rigidify the network; however, experimental distinction between these two modes of cross-linking would be extremely difficult. Sorbamide was chosen as the photoreactive moiety based on the known average spacing of residues contained in cross β-sheet structure. Peptide strands in self-assembled β-sheets align ~4.8 Å (0.48 nm) apart; this distance varies slightly depending upon the peptide sequence.[61] Therefore, to successfully photo-cross-link the fibrils in the self-assembled state, the photopolymerizable group should not only be able to traverse across this distance but also maintain this separation after the photo-cross-linking reaction without distorting the peptide secondary structure. In this regard, 1,3-diynes[53] and 1,3-dienes[52,62] are ideal since successful topochemical polymerization has been shown to occur

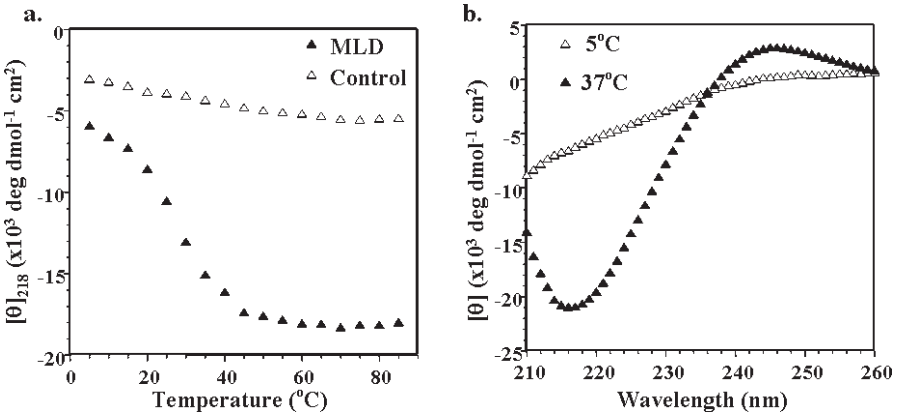

Figure 2. (a) CD spectroscopy of 150 μM peptide solutions at pH 7.4 (50 mM BTP, 150 mM NaCl) showing temperature-dependent β-sheet formation monitored at 218 nm. (b) Wavelength spectra of a 150 μM MLD solution at pH 7.4 (50 mM BTP, 150 mM NaCl) showing transition from random coil at 5 °C (△) to β-sheet at 37 °C (▲).

when their respective functionalities are aligned at a distance of 4.9−5.1 Å in the crystalline state. Importantly, this distance is maintained throughout the photopolymerization process. Sorbic acid, or 2,4-hexadienoic acid, was specifically chosen as the diene since lysine derivatives can be easily prepared with this moiety.[63] A sorbamide derivative of lysine (Figure 1a) can be prepared by conjugating the *N*-hydroxysuccinimide ester of sorbic acid to the ε-amine of Fmoc-Lys-OH.[64,65] This functionalized lysine can then be incorporated into a peptide sequence via Fmoc-based solid phase peptide chemistry at specific positions to achieve controlled polymerization of the peptide upon UV irradiation. In addition to MLD, a control peptide was prepared to assess the importance of the sorbamide functionality. The control peptide contains unmodified lysine residues at positions 5 and 18 in place of the sorbamide residues. An alternative control peptide would be a hexanamide-containing sequence, but on the basis of the degree of difficulty in purifying the parent MLD peptide, we opted for the more easily purified lysine-containing control.

MLD is designed to undergo triggered folding and self-assembly to promote β-sheet formation in response to an increase of temperature. At pH 7.4 under low ionic strength conditions, the lysine side chains are protonated, preventing peptide folding and self-assembly even at elevated temperatures. Increasing the ionic strength of the peptide solution by adding 150 mM NaCl promotes the screening of the positively charged lysines and makes thermally triggered folding possible. Circular dichroism (CD) spectroscopy was used to assess the potential of MLD and the control peptide to fold and self-assemble as a function of temperature at pH 7.4 (150 mM NaCl). CD spectra of MLD were collected at a concentration of 150 μM. At this low concentration, the peptide is capable of folding and self-assembling but is unable to gel the sample volume. This limits light scattering and facilitates data acquisition for these spectroscopic measurements. Figure 2a shows the mean residue ellipticity at 218 nm, $[\theta]_{218}$, an indication of β-sheet formation, for 150 μM solutions of MLD and the control peptide as a function of temperature. At low temperatures, MLD is unfolded but begins to fold and self-assemble at ∼15 °C. The evolution of β-sheet structure is complete by 40 °C. Figure 2b shows the wavelength spectra for MLD as a function of temperature, verifying that the peptide exists in an ensemble of random conformations at 5 °C and folds and self-assembles into β-sheet-rich structure at higher temperatures. At 37 °C, a clear minimum at 218 nm is observed, indicative of β-sheet secondary structure. In addition to the minimum at 218 nm, an interesting positive absorption at ∼245 nm is also evident in the spectrum of the folded and assembled peptide. On the basis of literature CD data[66] as well as UV spectra collected herein, this absorption can be assigned to the diene chromophores of the sorbamide side chains having been placed in a chiral environment afforded by MLD in the folded and assembled state.

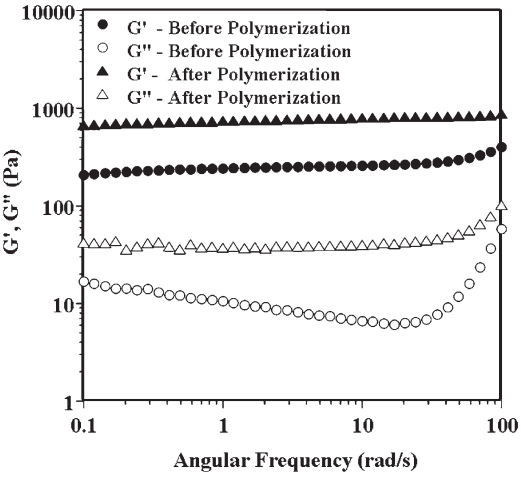

Figure 3. (a) Dynamic frequency sweep of 1 wt % MLD hydrogels formed at pH 7.4 (50 mM BTP, 150 mM NaCl, 0.025 wt % Irgacure 2959) and 37 °C before (●) and after (▲) photopolymerization.

The control peptide remains largely unfolded under identical buffer conditions, even at elevated temperatures. This is not surprising given that the control peptide contains two unmodified lysine residues at positions 5 and 18 that are protonated at pH 7.4. As a result, the control peptide has an overall charge of +11 (10 lysines and the N-terminal amine) as compared to +9 for MLD. Even in the presence of 150 mM NaCl, the temperature-dependent hydrophobic effect is unable to overcome the electrostatic repulsions inherent to the control peptide. Thus, the sorbamide residues of MLD not only enable photopolymerization but also are essential for its folding and self-assembly.

MLD solutions of higher concentration (1 wt %) undergo hydrogelation after peptide folding and self-assembly is triggered in response to an increase in temperature. Figure 3 shows a dynamic frequency sweep measurement from 0.1 to 100 rad/s for an MLD hydrogel formed on the rheometer after warming a 1 wt % solution (pH 7.4, 150 mM NaCl, 0.025 wt % Irgacure 2959) of the peptide for 3 h. The MLD hydrogel is characterized by a storage modulus (G', the elastic response of a material to applied strain) of 220 ± 50 Pa at 6 rad/s. The value of G' is over an order of magnitude greater than the loss modulus (G'', the viscous response of a material to applied strain) at this frequency, indicating the formation of a moderately rigid gel. The values

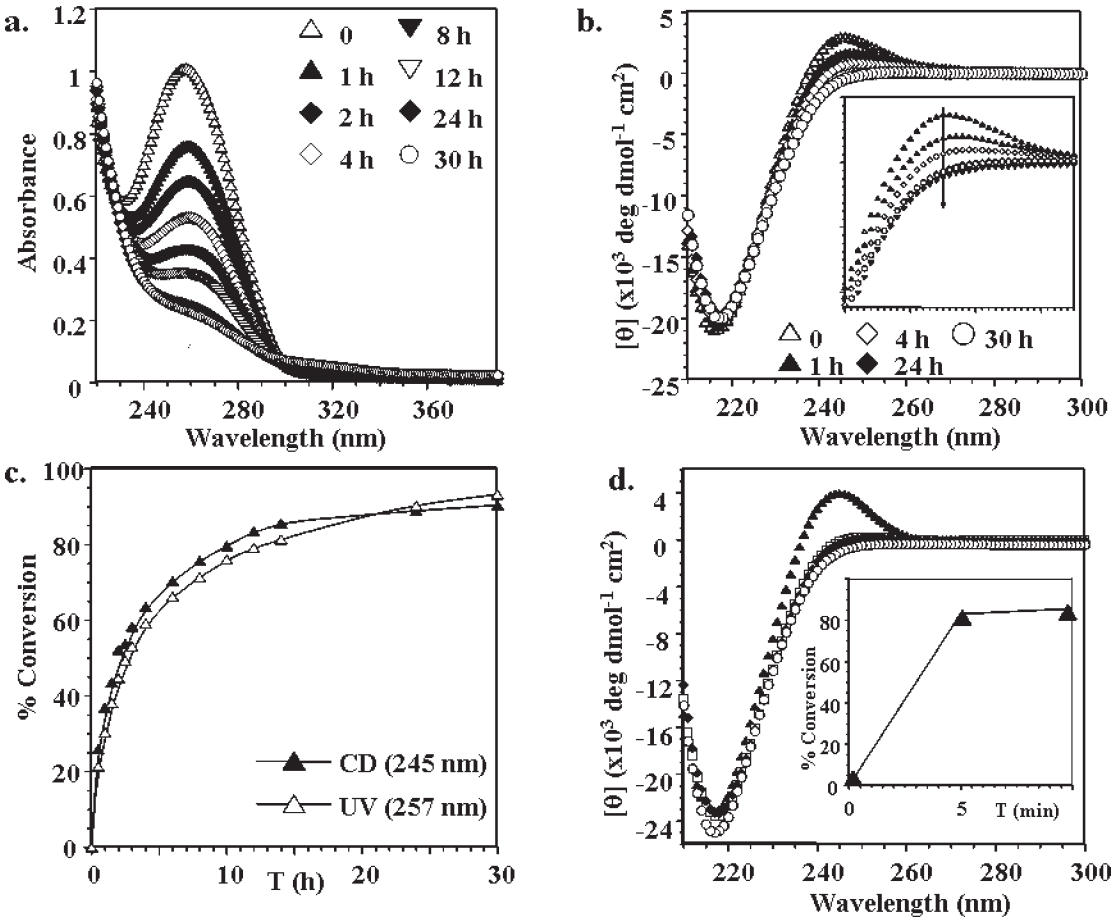

Figure 4. (a) UV absorption spectra of 0.1 wt % MLD solution at pH 7.4 (50 mM BTP, 150 mM NaCl) as a function of UV irradiation time (0−30 h). (b) CD wavelength spectra of 0.1 wt % MLD solutions at pH 7.4 (50 mM BTP, 150 mM NaCl) as a function of UV irradiation time (0−30 h). Inset: magnified view showing the decrease in intensity at 245 nm upon irradiation. (c) UV and CD time-dependent conversion of the sorbamide side chains of 0.1 wt % MLD on irradiation at pH 7.4 (50 mM BTP, 150 mM NaCl). (d) CD wavelength spectra of 1 wt % MLD hydrogel at pH 7.4 (50 mM BTP, 150 mM NaCl, 0.025 wt % Irgacure 2959) and 37 °C before and after UV irradiation at 365 nm. A wavelength scan of 1 wt % control peptide under identical conditions is also shown. Inset: percent conversion of sorbamides as a function of time.

of both G' and G'' show a gradual slope upward with increasing frequency evident at the highest frequencies examined. This behavior is reminiscent of soft cross-linked elastomers as opposed to viscoelastic liquids.[67] These data taken together indicate that MLD self-assembles to form a moderately rigid, but loosely cross-linked, physical network.

The MLD gel was designed as a shear-thin delivered material whose mechanical properties could be modulated post delivery. However, before the shear-thin properties of the hydrogel were examined, we first investigated the gel's response to photo-cross-linking prior to thinning. This provided insight into the native network's ability to support efficient photo-cross-linking. When the MLD hydrogel is irradiated for 15 min at 365 nm (~16 mW/cm^2) after its formation, an average G' of 500 ± 75 Pa is realized at 6 rad/s. This is about a 2.5-fold increase in material rigidity. The variance of both G' and G'' with frequency is less than that observed for the unirradiated MLD hydrogel, indicating the formation of a less structurally flexible gel after irradiation. Although this data suggests that the fibrils comprising the MLD hydrogel are capable of undergoing photoinduced cross-linking as designed, control experiments were performed to ensure that local temperature increases during irradiation were not responsible for the apparent increase in G'. Experiments employing the temperature-sensitive standard viscosity oil S200 were performed to determine the UV intensity at which minimal change in temperature and resultant viscosity is observed upon irradiation (Supporting Information, Figure S-4). These studies indicated that a UV intensity of 10% (365 nm), which corresponds to about 16 mW/cm^2, incurs a minimal rise in temperature (~2 °C) at the sample position after 30 min of irradiation. UV intensities of this magnitude are widely employed for the fabrication of hydrogels via photopolymerization for biomedical applications.[68−70] This small increase in local temperature should not grossly affect the material properties of the MLD self-assembled hydrogel. Thus, the increase in storage modulus (G') observed for the MLD hydrogel when irradiated is due to the formation of chemical cross-links into the network and not simply local changes in temperature.

Next, the reactivity of the sorbamide functionalities was examined. UV and CD spectroscopy were used to both follow the consumption of the 1,3-dienes upon lumination as well as monitor any changes in secondary structure that might occur during polymerization. Sorbate chromophores exhibit a broad UV absorption at around 260 nm in the crystalline state that decreases when photopolmerized.[63] Figure 4a shows an absorption spectrum of self-assembled 0.1 wt % (300 μM) MLD peptide at pH 7.4 prior to irradiation (△). Although Irgacure 2959 photoinitiator will ultimately be used for bulk material formation, it has not been included in this experiment since its absorption complicates the sorbic acid spectra. In addition, a low concentration of peptide is used in this experiment to satisfy the linear range of the UV spectrometer. As can be seen, MLD displays an absorption band at ~255 nm due to the conjugated π system of the dienes. When the sample is irradiated at 365 nm (6 mW/cm^2), the

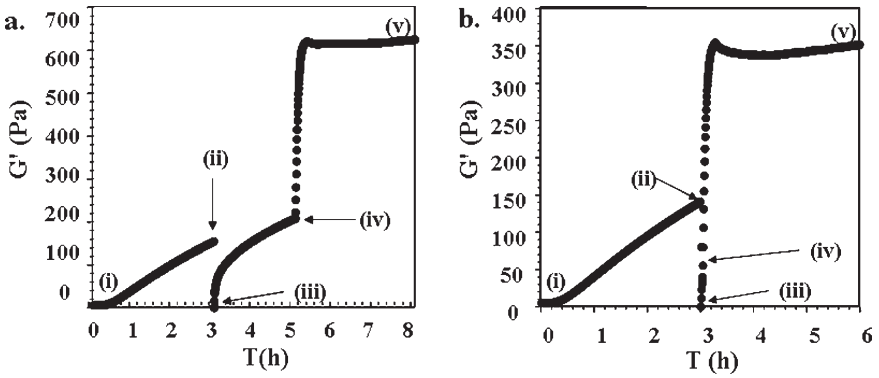

Figure 5. (a) Oscillatory shear rheology of 1 wt % MLD hydrogels at pH 7.4 (50 mM BTP, 150 mM NaCl, 0.025 wt % Irgacure 2959) and 37 °C: (i) Hydrogelation at pH 7.4 for 3 h at 6 rad/s and 0.2% strain. (ii) Application of high strain (1000%, 30 s). (iii) Gel recovery for 2 h at 6 rad/s and 0.2% strain. (iv) Photopolymerization for 15 min at 365 nm. (v) Monitoring of storage modulus at 6 rad/s and 0.2% strain after UV irradiation. (b) Oscillatory shear rheology of 1 wt % MLD hydrogels at pH 7.4 (50 mM BTP, 150 mM NaCl, 0.025 wt % Irgacure 2959) and 37 °C: (i) Hydrogelation at pH 7.4 for 3 h at 6 rad/s and 0.2% strain. (ii) Application of high strain (1000%, 30 s). (iii) Cessation of high strain to 0.2% strain. (iv) Photopolymerization for 15 min at 365 nm. (v) Monitoring of storage modulus at 6 rad/s and 0.2% strain after UV irradiation.

absorption intensity at 255 nm progressively decreases with time. In the absence of photoinitiator, the signal ceases to change after 24 h.

Figure 4b shows CD spectra of a solution of self-assembled 0.1 wt % (300 μM) MLD peptide at pH 7.4 as a function of irradiation time. A low concentration of MLD was employed so direct comparison to the UV data could be made. Before polymerization, the spectrum is similar to the one in Figure 2b and shows the signature β-sheet minimum at 218 nm (△, 0 h). The positive band at ~245 nm due to the 1,3-diene of the sorbamide residue is also evident. During UV irradiation, the intensity of the CD signal at 245 nm decreases with time due to the photoreaction converting the 1,3-diene to the polyene (inset, Figure 4b), eventually reaching $[\theta] \approx 0$. Figure 4c plots the percent conversion as a function of time for the polymerization reaction in the absence of photoinitiator. Satisfyingly, there is excellent agreement in the rates of conversion as measured by the distinct spectroscopic methods. The extent of diene conversion is ~93% (for equation see Figure S3). Attempts to measure the extent of cross-linking along the fibril long axis by MALDI-TOF MS failed, presumably due to poor ionization of the large cross-linked fibrils. Collectively, the UV and CD data suggest nearly quantitative conversion of the diene. Importantly, the photopolymerization reaction does not grossly distort the β-sheet secondary structure as observed by a minimal change in intensity at 218 nm. This indicates that that the distance between the sorbamide moieties displayed from the fibrillar network is conducive to the reaction coordinates of the polymerization and thus does not disrupt the structure of the native β-sheet-rich fibrillar network when cross-linked.

Importantly, Figure 4d monitors the extent of photo-cross-linking for a 1 wt % MLD hydrogel in the presence of Irgacure 2959 at pH 7.4 by CD spectroscopy. Control experiments demonstrate that the photoinitiator does not contribute to the CD signal. Similar to the CD data collected at low peptide concentrations in the absence of photoinitiator, irradiation results in a decrease of $[\theta]_{245}$. The signal at 218 nm is unaffected, indicating that the secondary structure is unperturbed during photopolymerization even in the gelated state. The inset shows that in the presence of photoinitiator the reaction is complete within minutes.

The MLD peptide was designed to fold and self-assemble into a hydrogel that could be shear thin delivered and photo-cross-linked post delivery. Data presented thus far demonstrate that MLD folds and self-assembles at pH 7.4 to form a moderately rigid, physically cross-linked hydrogel that displays sorbamide moieties capable of undergoing photo-cross-linking. The ability of MLD hydrogels to shear-thin, self-heal, and undergo subsequent photopolymerize was investigated using oscillatory rheology as outlined in Figure 5a. In part (i), a 1 wt % MLD hydrogel is formed at pH 7.4 by increasing the temperature to 37 °C. Here, the angular frequency is held at 6 rad/s, and the applied strain is 0.2%. After 3 h of gelation, the storage modulus reaches 200 ± 40 Pa. At this point in time [part (ii)], 1000% strain is applied for 30 s to shear-thin the material, disrupting the hydrogel network and resulting in a rapid decrease in G'. For these networks, the application of shear strain can lead to the disruption of some of the noncovalent cross-links that constitute the network. This transforms the self-supporting hydrogel into a low-viscosity gel that can flow. In part (iii), the applied strain is decreased to 0.2%, and the gel is allowed to recover for a period of 2 h reaching a storage modulus, $G' = 240 \pm 30$ Pa. On removal of the shear strain, the noncovalent cross-links re-form, allowing the gel to recover its original mechanical rigidity. The shear thinning and self-healing nature of the MLD gel allows it to be shear-thinned delivered to a secondary site using a simple syringe where the plunger supplies the shear force necessary for thinning. Following delivery, the MLD hydrogel is designed to undergo photopolymerization to further enhance its mechanical properties at the target site. This was modeled rheologically in part (iv) where the recovered hydrogel is irradiated for 15 min at 365 nm (~16 mW/cm^2), which results in a rapid increase in G'. The photo-cross-linked hydrogel achieves an equilibrium storage modulus of 590 ± 30 Pa and remains constant. The irradiation time of 15 min was chosen based on the CD studies shown in Figure 4d. Photopolymerization of the self-healed MLD hydrogels affords a ~2.5-fold increase in material rigidity, similar to what was observed for the nonsheared gels. The photopolymerized hydrogel is also shear thinning, but its ability to recover is limited (data not shown). This behavior is consistent with intrafibrillar cross-linking that takes place over large, but not infinite, regions along a given fibril. That is, fibrils are probably not cross-linked over their entire length. Thus, under strain, the network can yield at locations along a given fibril where the sorbamide moieties have not efficiently cross-linked.

In practical applications, a 2 h recovery period following the shearing event may not be feasible. The possibility of initiating photopolymerization *during* recovery was investigated to model cases where photopolymerization is initiated directly after the syringe delivery event. Rheology was again used to model this mode of delivery (Figure 5b). For this experiment, parts (i) and (ii) were performed exactly as described for Figure 5a. However, in part (iii), upon reducing the applied strain to 0.2%, the

recovering hydrogel is immediately irradiated for 15 min (365 nm, ~16 mW/cm^2) and the storage modulus monitored. Although the final magnitude of G' is significantly less than the recovered sample (343 ± 26 Pa), it still achieves a reproducible ~2.5-fold increase in rigidity following UV irradiation relative to the modulus prior to the shearing event. This experiment demonstrates that the full recovery of the shear-thinned material is not necessary for photo-cross-linking to occur but plays a role in defining the final modulus.

Conclusion

In summary, a peptide-based gel has been prepared whose mechanical rigidity can be modulated after shear-thin recovery. MLD, a 22-residue peptide, has been designed to undergo triggered folding and self-assembly to form a fibril network composed of β-hairpin peptides. This physically cross-linked hydrogel shear thins but can immediately recover its mechanical rigidity after the cessation of high strain. This property allows for the delivery of preformed gels to a target site in a controlled fashion prior to irradiation. The MLD peptide contains non-natural sorbamide residues that can undergo UV-induced polymerization to modulate the ultimate material properties of the gel after the gel has recovered from a shear-thinned state. The photopolymerizable dienes of the sorbamide groups are displayed along the solvent-exposed faces of the β-sheet-rich fibrils that constitute the gel. CD studies demonstrate that the sorbamides are contained within a chiral environment provided by the self-assembled peptide network and that their polymerization, in the presence of initiator, is nearly quantitative within minutes. Rheological experiments show that irradiation leads to intrafibrillar cross-linking and a ~2.5-fold increase in mechanical rigidity. Typically, the injectable hydrogel is irradiated after it recovers from the shear thinning process. Rheology was used to show that the hydrogel can also be irradiated during the initial recovery process to achieve a significant increase in material stiffness. This gel should find use as an injectable material whose mechanical properties can be easily modulated post delivery.

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Supporting Information Available: Experimental, materials and methods, chromatograms, and mass spectral data for peptides, equation and corresponding CD/UV data for percent conversion determination, and control temperature-dependent viscosity measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

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