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Therapeutic-Ultrasound-Triggered Shape Memory of a Melamine-Enhanced Poly(vinyl alcohol) Physical Hydrogel

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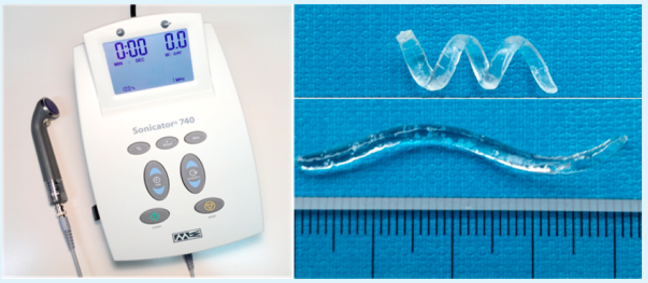
Supporting Information

ABSTRACT: Therapeutic-ultrasound-triggered shape memory was demonstrated for the first time with a melamine-enhanced poly(vinyl alcohol) (PVA) physical hydrogel. The addition of a small amount of melamine (up to 1.5 wt %) in PVA results in a strong hydrogel due to the multiple H-bonding between the two constituents. A temporary shape of the hydrogel can be obtained by deformation of the hydrogel (~65 wt % water) at room temperature, followed by fixation of the deformation by freezing/thawing the hydrogel under strain, which induces crystallization of PVA. We show that the ultrasound delivered by a commercially available device designed for the patient's pain relief could trigger the shape recovery process as a result of ultrasound-induced local heating in the hydrogel that melts the crystallized PVA cross-linking. This hydrogel is thus interesting for potential applications because it combines many desirable properties, being mechanically strong, biocompatible, and self-healable and displaying the shape memory capability triggered by a physiological stimulus.



KEYWORDS: *shape memory polymer, physical hydrogel, ultrasound trigger, stimulus-responsive polymer, melamine*

INTRODUCTION

Shape memory polymers (SMPs) have the ability to fix a deformation and afterward recover to the original shape upon exposure to a stimulus, such as temperature change, light, moisture, electric field, and ultrasound.[1−5] They hold promise for applications in many areas, including medical devices, textiles, aerospace, and so on.[6−11] So far, most research on SMPs has been focused on solid polymers. Only in recent years has there been regained interest in shape memory hydrogels that are swollen 3-D hydrophilic polymer networks containing a large amount of water and are particular attractive for biomedical applications due to their elastic properties comparable with those of biological tissues.[12] The shape memory effect in the reported hydrogels is generally enabled by some kind of side chain, such as *n*-stearyl acrylate (SA), two cooperatively cross-linkable DNA elements and oligomeric chain segments, addition of metal ions as functional cross-linkers, or use of copolymers with crystallizable segments.[13−17] Nevertheless, hydrogels that can undergo the temporary-to-permanent shape transition while containing a large amount of water and being triggered by a physiological stimulus remain very rare. Herein we report such a hydrogel.

The hydrogel studied in the present work was designed on the basis of consideration of the following important aspects. A first challenge is to find out a way that allows one to process the temporary shape of a hydrogel with high water content and fix it. This cannot be done by using the typical procedure for solid SMPs, for which the polymer can simply be deformed above the phase transition temperature T_{tr} (glass transition temperature T_g or melting temperature T_m) followed by cooling below T_{tr} to freeze the temporary shape. For hydrogels, the temporary shape needs to be preserved by a second network structure that is formed within the deformed hydrogel to retain the strain energy.[15,18,19] A second requirement is that the shape memory effect can be triggered by a physiological or physiologically tolerable stimulus. Most known shape memory hydrogels were thermally activated, and their shape recovery process was triggered by either hot water or hot gas,[12,14,17,18] while for those with ionic cross-linkers or supramolecular interactions, a change in ionic strength or pH can activate the shape memory effect.[16,17] It is not obvious how those triggers can be applied in biomedical applications.[20] By processing the temporary shape in the dried state, the shape recovery of a hydrogel can also be triggered by absorption of water, which reduces T_{tr} by a plasticization effect.[21,22] The latter mechanism is fundamentally different from fixation of a temporary shape of a wet hydrogel. Previously we reported the use of high-intensity focused ultrasound (HIFU) to trigger shape memory of solid polymers.[5,23,24] This stimulation mode has spatiotemporal control and can propagate much deeper in human tissues and organs than light or other stimuli, making it particularly appealing for triggering the shape recovery of a hydrogel in the

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human body. The last requirement is that the hydrogel should be biocompatible and possess sufficient or high mechanical strength. Due to the nature of wet and soft material with a high water content, hydrogels generally have relatively poor mechanical properties. Many approaches have been established to improve the mechanical strength and/or toughness of hydrogels, such as a slide ring, tetra-PEG, a nanocomposite, or double-network gels, to name only a few.[25−28]

In this paper, we show that, by adding a small amount of melamine to poly(vinyl alcohol) (PVA), two types of physical cross-links can be formed in two separate steps, which not only result in a mechanically enhanced and biocompatible PVA gel, but also allow for the deformation of the wet hydrogel (∼65 wt % water) and fixation of the temporary shape. Moreover, we show for the first time that therapeutic ultrasound can be used to trigger the shape memory effect of the hydrogel. The employed ultrasound source is a commercially available device that can be used by a patient for pain relief, reduction of muscle spasm, and increase of blood flow. At the same time, owing to the extensive hydrogen bonding, the melamine-enhanced hydrogel also displays a self-healing function.

RESULTS AND DISCUSSION

Design and Preparation of the Hydrogel. Figure 1 illustrates the formulation of our hydrogel physically cross-linked by two separate steps and whose shape memory can be triggered by therapeutic ultrasound. Knowing that the presence of melamine in PVA can improve both the strength and extensibility of the PVA film due to H-bonded cross-linking,[29] we expected a gelation effect by adding a small amount of melamine to an aqueous solution of PVA. Each melamine molecule has six nitrogen and six hydrogen atoms that can act as H-bond acceptors and donors, respectively. Surrounded by PVA chains, multiple H-bonds can form between melamine and the hydroxyl groups on the PVA chains, which makes melamine an effective physical cross-linker and, together with the H-bonds between PVA chains, generates a strong and stable hydrogel (Figure 1a). To process a temporary shape, the melamine-enhanced, H-bonding cross-linked PVA hydrogel is deformed to the desired state (Figure 1b); then under strain the hydrogel is subjected to the freezing/thawing treatment that results in the second physical cross-linking by the microdomains of crystallized PVA chains.[30−32] Since the second cross-linking develops in the deformed hydrogel, it should be able to retain the deformed state (at least to a significant degree) after removal of the external force (Figure 1c). When the hydrogel of temporary shape is exposed to the therapeutic ultrasound, the shape recovery will be activated if the absorption of the ultrasound energy by the hydrogel gives rise to disruption of the physical cross-links and, consequently, relaxation of deformed PVA chains (back to Figure 1a). As shown below, the targeted property and function of the hydrogel were confirmed.

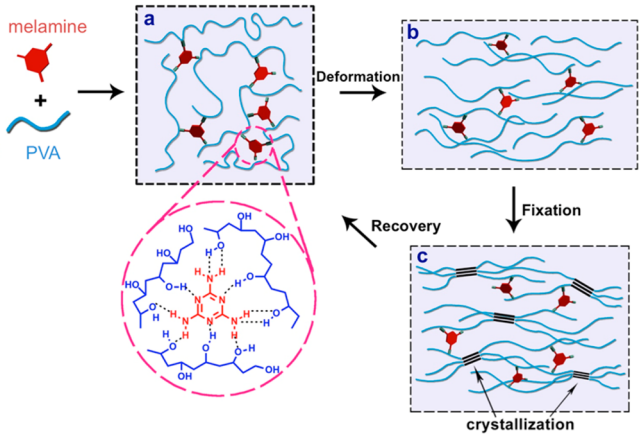

Figure 1. Schematic illustration of the therapeutic-ultrasound-triggered shape memory hydrogel of PVA with added melamine, which is physically cross-linked in two separate steps: (a) the addition of melamine into an aqueous solution of PVA gives rise to the first physical network enhanced by multiple H-bonds between melamine and PVA chains; (b) the hydrogel can be deformed; (c) the deformed shape of the hydrogel can be fixed by freezing/thawing of the hydrogel under strain, resulting in the second network formed by crystallized PVA chains. From (c) to (a) the shape recovery occurs under ultrasound exposure as the crystalline domains of PVA absorb ultrasound energy and melt, releasing the retained strain energy. For the sake of clarity, water molecules as well as H-bonding between PVA chains, PVA−water, and melamine−water in the wet hydrogel are not depicted.

Details on the preparation and characterization of the hydrogel are given in the Supporting Information. Typically, PVA (99+% hydrolyzed, M_w = 146000−186000 g/mol) was dissolved in deionized water at a concentration of 35 wt %; after complete dissolution upon heating to 90 °C, a certain amount of melamine was added and mixed with the PVA solution at the same temperature. During the whole process the system was sealed to prevent water evaporation. Afterward, the solution was cast into a Teflon mold before the mold was sealed and left overnight. For the freezing/thawing treatment the hydrogel was cooled to −15 °C for 30 min and then thawed at room temperature for at least 6 h. This procedure can be repeated for various cycles. In the discussion below, the investigated samples are labeled either as *x*MA for the PVA hydrogel with *x* weight percentage of added melamine (MA) or as *x*MA-*y* for the hydrogel subjected to *y* cycles of the freezing/thawing treatment.

Mechanical Properties of the Hydrogel. Figure 2 shows the mechanical properties of the hydrogels, which confirm the existence of the two types of physical cross-linking of PVA chains in separate steps. By adding melamine in PVA aqueous solution, the resulting hydrogel feels more solid and tough than the hydrogel without melamine on touching. The difference can be visually noticed by putting solutions of PVA or PVA with added melamine into a cuboid mold, sealing the mold for 1 h, and gently removing the PVA or PVA with added melamine from the mold. As is seen in Figure 2a, the 1.5MA hydrogel retained the rectangular shape well, but 0MA deformed a lot after removal, revealing the network-strengthening effect of melamine due to its H-bonded cross-linking of PVA chains. After freezing/thawing, the 1.5MA-3 hydrogel appeared translucent due to light scattering from crystallized PVA microdomains. To observe the effect of melamine, dynamic mechanical measurements were carried out on the samples of 0MA and 1.5MA, showing changes in the storage (G') and loss (G'') moduli vs frequency at room temperature and vs temperature at a fixed frequency of 1 Hz, respectively (Figure 2b,c). It is seen that the presence of 1.5 wt % melamine raises the moduli and enhances the elastic response of the hydrogel, with the elastic modulus G' exceeding the viscous modulus G'' over the entire frequency or temperature range. The variations in the moduli upon frequency or temperature change are

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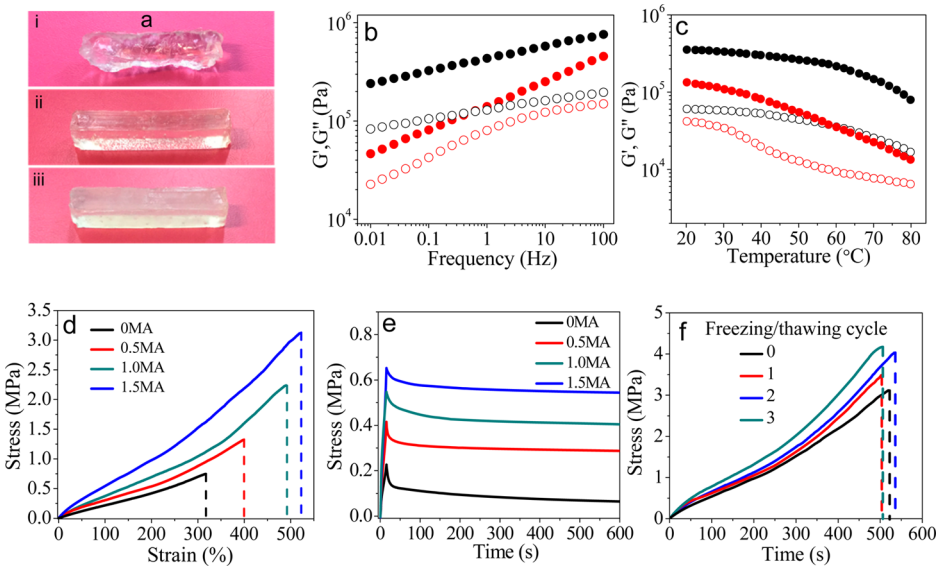

Figure 2. (a) Photos showing the visual difference between the PVA hydrogels of (i) 0MA, (ii) 1.5MA, and (iii) 1.5MA-3. (b) Storage modulus (G', solid symbols) and loss modulus (G'', open symbols) vs frequency at room temperature for the PVA hydrogels of 0MA (red) and 1.5MA (black). (c) Storage and loss moduli vs temperature at a fixed frequency of 1 Hz for the same samples as in (b). (d) Stress–strain curves of PVA hydrogels with different melamine contents at room temperature. (e) Stress relaxation curves (100% elongation) for the same samples as in (d). (f) Stress–strain curves of the 1.5MA hydrogel after different cycles of freezing/thawing.

significantly smaller for 1.5MA, which is indicative of a more stable and elastic-like network in the sample.

Moreover, tensile tests were performed on samples with different melamine contents. From the stress–strain curves (Figure 2d), it is evident that adding even a small amount of melamine, such as 0.5 wt %, to the PVA hydrogel can enhance the mechanical properties such as the Young modulus, elongation at break, tensile strength, and, as a result, toughness. This beneficial effect is proportional to the melamine content over the range investigated. For instance, while 0MA breaks at about 325% elongation with a tensile strength of 0.74 MPa, the 1.5MA sample displays a 525% elongation at break and a tensile strength of 3.11 MPa, which represent about 160% and 420% increases, respectively. The action of melamine can also be observed from the stress relaxation results (Figure 2e). Although for all samples once the elongation (100%) stops the stress drops rapidly and then continues to decrease slightly over time, the stress remaining after 10 min is much higher with MA even at 0.5 wt %, being ∼29% for 0MA while jumping to 69%, 74%, and 83% for 0.5MA, 1.0MA, and 1.5MA, respectively. All these results can only be explained by the formation of a large amount of H-bonds between the melamine molecules and PVA chains.[29] The multiple H-bonded cross-linking in the hydrogel leads to a stable and mechanically strong physical network of PVA.

Lastly, what happens to the mechanical properties when further physical cross-linking by crystallization of PVA occurs in the melamine-enhanced hydrogel subjected to the freezing/thawing treatment? The answer can be found from the tensile test results obtained with the 1.5MA hydrogel after various cycles of freezing/thawing (Figure 2f). While the elongation at break remains essentially the same, the tensile strength further increases with increasing number of freezing/thawing cycles. It reaches about 4.2 MPa for 1.5MA-3 as compared to 3.11 MPa for 1.5MA, meaning also increased toughness of the hydrogel. Therefore, the second physical cross-linking added to the melamine H-bonded network further impacts the mechanical properties, and the result is a mechanically strong and tough PVA hydrogel.

Thermally Activated Shape Memory. The shape memory effect of the melamine-enhanced hydrogel was then investigated. As pointed out above, if the second physical cross-linking by crystallized PVA chains can retain the deformation of a wet hydrogel, subsequent disruption (melting) of the second network should give rise to the recovery of the permanent shape. Figure 3a shows a visual observation. A piece of the 1.5MA hydrogel was first stretched to 100% elongation (photos i and ii in Figure 3a). After three cycles of freezing/thawing under strain, a substantial elongation indeed remained upon removal of the external force (photo iii), and the recovery to the permanent shape was achieved by immersing the hydrogel in water at 60 °C (photo iv), implying that 60 °C is sufficiently high to melt the crystallized PVA microdomains formed in the freezing/thawing treatment. The characteristics of thermally activated shape memory were measured for the 1.5MA hydrogel subjected to different freezing/thawing cycles. For a given sample, after freezing/thawing, the external force was removed and the change in the elongation degree was followed as a function of time until the stable fixation was reached. Afterward, the hydrogel of temporary shape was placed in a water bath heated to different temperatures, and the shape recovery, i.e., decrease in the elongation, was monitored at various temperatures. From the results shown in Figure 3b, it is seen that both the retained elongation (fixity) at 25 °C and the temperature for complete shape recovery increase with increasing number of freezing/thawing cycles. These observations are no surprise and in accord with our expectations. As a matter of fact, freeze/thawed PVA hydrogels have been much studied, and it is known that more cycles of freezing/thawing will result in higher crystallinity and larger crystallites of PVA as well as more stable crystalline microdomains with higher melting temperature.[30,31] In other words, a stronger physical cross-linking not only preserves better the deformed state of the wet hydrogel after removal of the external force, but also is

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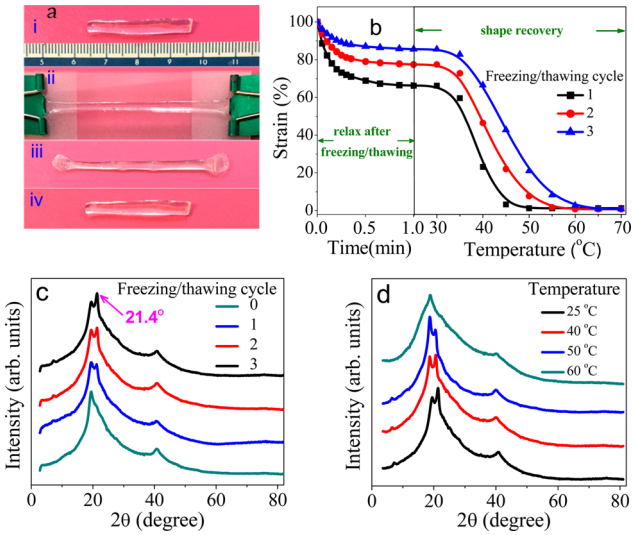

Figure 3. (a) Thermoresponsive shape memory behavior of the 1.5MA hydrogel: (i) the original shape; (ii) stretched to 100% elongation at room temperature; (iii) the retained shape after three cycles of freezing/thawing and removal of the stress; (iv) after immersion in 60 °C water without external stress. (b) Temporary shape fixation after 100% elongation followed by removal of the external force as well as shape recovery on heating for the 1.5MA hydrogel subjected to various cycles of freezing/thawing. (c) X-ray diffraction (XRD) patterns of the 1.5MA hydrogel after various cycles of freezing/thawing and (d) XRD patterns of the 1.5MA-3 hydrogel at different temperatures.

disrupted at the higher temperature required for the shape recovery. The effect of the melamine content on the shape recovery was also investigated (Figure S3, Supporting Information).

The above analysis for the observed thermoresponsive shape memory behavior was confirmed by X-ray diffraction (XRD) measurements on the 1.5MA hydrogel treated with different cycles of freezing/thawing (Figure 3c) and on the 1.5MA-3 hydrogel heated to different temperatures (Figure 3d).

On one hand, the initial hydrogel prior to freezing/thawing already displays a small diffraction peak at 19.4° corresponding to the $10\bar{1}$ reflection of a typical crystalline PVA hydrogel (reflection plane spacing 4.68 Å).[33] This feature was observed for the hydrogels either with or without melamine (Figure S1, Supporting Information). Thus, it appears that some crystallized aggregates of PVA exist before freezing/thawing, likely due to the high molecular weight and high concentration (35 wt %) of the PVA sample, while most diffraction around the peak arises from "free water" and swollen amorphous PVA chains.[30] Quite surprisingly, unlike PVA alone, for which the freezing/thawing-induced crystallization results in an increased diffraction intensity of the 19.4° peak, i.e., enhanced crystallinity of the same crystalline structure (Figure S1), the 1.5MA hydrogel displays a new diffraction peak at 21.4° following the freezing/thawing treatment, and its intensity grows with increasing number of freezing/thawing cycles (marked by an arrow in Figure 3c). This observation reveals that melamine molecules not only create H-bonded cross-linking with the surrounding PVA chains but might also modify the ordered structure of the crystallizing PVA chains under the freezing/thawing treatment, since the new peak at 21.4° implies a more compact crystalline structure (plane spacing 4.25 Å). This result suggests that melamine in the PVA hydrogel could act as both a physical cross-linker via the multiple H-bonds with PVA and a structuring molecule impacting the ordered structure of the polymer. One speculation is that H-bonded melamine molecules could change the direction of the −OH groups on the PVA chains, which has a drastic effect on the unit cell parameters.[33] However, the exact crystalline structure corresponding to the peak at 21.4° and the role of melamine remain to be clarified by future studies.

On the other hand, the change in the diffraction pattern of the 1.5MA-3 hydrogel at different temperatures (Figure 3d) provides more insight into what leads to the shape recovery of the hydrogel. The intensity of the new peak at 21.4° starts to decrease at 40 °C, reduces more significantly at 50 °C, and essentially vanishes at 60 °C, whereas the peak at 19.4° appears unchanged during the heating process. This observation clearly indicates that the crystalline microdomains of PVA formed in the course of freezing/thawing have lower thermal stability, i.e., a lower melting temperature, than the crystallized PVA existing prior to freezing/thawing. Since the crystallization of PVA occurring during freezing/thawing is responsible for the fixation of the temporary shape of the hydrogel, the apparent melting of the crystalline microdomains, around 50 °C, disrupts the network and results in a release of the strain energy stored in the temporary shape, thus activating the shape recovery process.

Therapeutic-Ultrasound-Triggered Shape Memory. Having understood how the shape memory effect works for our melamine-enhanced PVA hydrogel and knowing that the transition temperatures for the shape recovery are in a quite broad range of 40−60 °C, we investigated the use of a therapeutic ultrasound device (sonicator 740, Mettler Electronics Corp.) to trigger the shape memory process. The used device is designed to generate a deep tissue temperature increase for the patient's well being by causing an effect of pain relief, muscle spasm reduction or increase in blood flow. It has a tunable frequency between 1 and 3 MHz with a maximum power output of 2.2 W/cm^2.

The photo in Figure 4a shows how the ultrasound-triggered shape recovery experiment can be carried out. The hydrogel sample is placed in a water bath (400 mL) in front of the ultrasound probe. Once the device is turned on, ultrasound waves are transmitted from the probe to the water and can be absorbed by the hydrogel. The viscoelastic nature could convert the ultrasound energy onto heat and thus raise the temperature of the hydrogel.[34] The photos in Figure 4b show an example of visual observation of the ultrasound-triggered shape recovery. A rod of 1.5MA was deformed into a helix and fixed by one cycle of freezing/thawing; under ultrasound exposure (3 MHz, 2 W/cm^2), the hydrogel helix started to unwind. The shape recovery after 5 min was substantial but not complete, indicating either some chain relaxation during the helix processing or some unreleased strain energy in the hydrogel under the used ultrasound conditions. In this experiment, the unwinding of the helix was halted once the ultrasound was turned off, which allowed the hydrogel to be taken out of the water bath for picture-taking. Figure 4c shows the XRD patterns of the 1.5MA-3 hydrogel before and after the ultrasound exposure (2 W/cm^2). After 10 min of ultrasound exposure, the diffraction peak at 21.4° almost disappears, while the peak at 19.4° remains. These changes are similar to those observed following direct heating of the hydrogel to 50−60 °C (Figure 3d), confirming that the mechanism of therapeutic-ultrasound-triggered shape recovery is due to the melting of the crystalline

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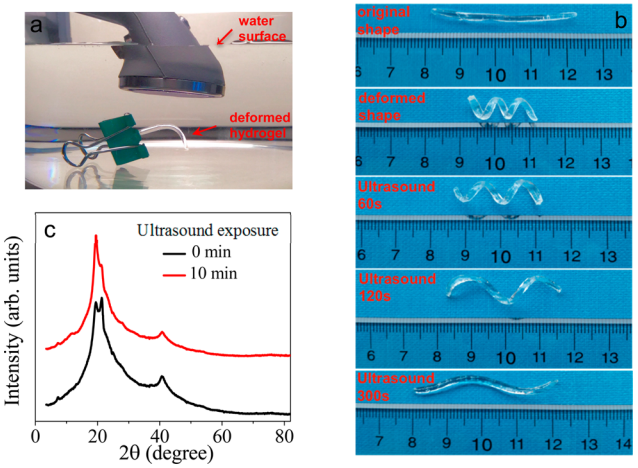

Figure 4. (a) Photo showing the experimental setup used for monitoring therapeutic-ultrasound-triggered shape recovery of the hydrogel. (b) Photos showing the shape recovery of the 1.5MA-1 hydrogel under ultrasound irradiation, with the sample of original shape being first processed to a temporary twisted shape and then subjected to therapeutic ultrasound (2.0 W/cm^2) for different times (1−5 min). (c) XRD patterns of the 1.5MA-3 hydrogel before and after 10 min of ultrasound exposure (2.0 W/cm^2).

microdomains formed by the PVA chains in the presence of melamine during the freezing/thawing treatment. It should be noted that ultrasound irradiation also raises the temperature of the aqueous solution as a whole. However, the temperature rise of the used large-volume solution (400 mL) surrounding the hydrogel sample after 10 min of ultrasound exposure is too small (about 2°) to account for the melting of crystallized microdomains. Efficient heat generation by the viscoelastic hydrogel upon ultrasound energy absorption is necessary for the therapeutic-ultrasound-triggered shape memory behavior. It should be noted that all ultrasound tests were performed with the hydrogel sample in water for up to 10 min, and within this period of time the temporary shape of the hydrogel remained stable in the absence of ultrasound exposure, showing no water-induced plasticization effect.

Obviously, a number of parameters can affect the efficiency and speed of the ultrasound-triggered shape recovery of the hydrogel. We investigated the effect of the number of freezing/thawing cycles as well as the effect of the ultrasound intensity in two separate experiments (Figure 5). Here the temporary shape was obtained by folding a 1.5MA hydrogel by 90° followed by

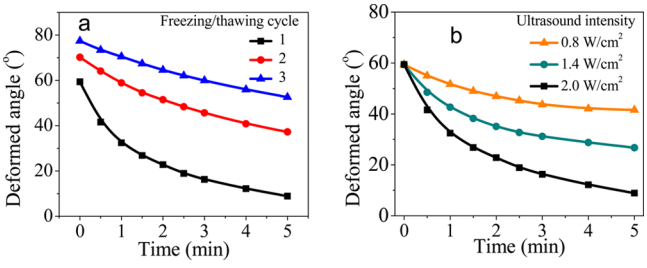

Figure 5. (a) Ultrasound-induced shape recovery of the 1.5MA hydrogel subjected to various freezing/thawing cycles. The different initial deformation angles (at 0 min) reflect different fixation degrees of the temporary shape, and the ultrasound output intensity is 2.0 W/cm^2. (b) Shape recovery behaviors of the 1.5MA-1 hydrogel under ultrasound irradiation of different output intensities.

fixation through freezing/thawing, and the ultrasound-induced shape memory was monitored by measuring changes in the bending angle. First, for samples subjected to different cycles of freezing/thawing (Figure 5a), it is seen that, under the same ultrasound irradiation (2 W/cm^2), the final shape recovery ratios after 10 min of exposure are very different. While the recovery ratio for the sample with three cycles of freezing/thawing is only ∼30%, the shape recovery of the sample with one cycle reaches more than 80%. This situation is the opposite that for the fixation degree of the deformed angle (deformed angle before recovery), which is higher for the hydrogel with more freezing/thawing cycles. This result suggests that more cycles of freezing/thawing result in higher crystallinity and more stable physical cross-linking, which is good for temporary shape fixation but renders the shape recovery more difficult under ultrasound irradiation, probably because of the difficulty of melting the crystalline microdomains. Second, when the 1.5MA-1 hydrogel was exposed to ultrasound at different intensities (Figure 5b), not surprisingly, the shape recovery process was faster and the achievable shape recovery ratio higher with increasing ultrasound intensity from 0.8 to 2 W/cm^2. Clearly this is also about the melting of the crystalline microdomains in the hydrogel as a higher ultrasound intensity means more ultrasound energy absorbed by the hydrogel and thus a greater ultrasound-induced heating effect.

The above results imply that the therapeutic-ultrasound-induced heating mainly disrupt the second physical network of the hydrogel by melting crystallized domains acting as the cross-linking points. What follows appears to be a reasonable explanation. The ultrasonic waves propagate through the hydrogel by motions or vibrations of water molecules and PVA chains. The first physical network is mainly formed by H-bonds between PVA chains and melamine molecules in noncrystalline regions. Under ultrasound irradiation, most ultrasonic waves can propagate through those regions without disrupting H-bonds and without generating a significant amount of heat, because intermolecular friction among PVA chains is unlikely to occur due to the large amount of surrounding water molecules. By contrast, the second networking is mainly formed by crystallized PVA in the presence of melamine. Upon exposure to ultrasound, the propagation of ultrasound waves in the crystalline regions could result in vigorous intermolecular friction of the PVA chains, which generates efficient heat and allows heat to be confined in the crystalline domains. Consequently, the absorption of ultrasound energy by the hydrogel with two types of physical networks would induce a temperature rise mostly centered on the crystalline domains of PVA, i.e., the cross-linking points of the second network formed by the freezing/thawing treatment.

Self-Healing Behavior. Finally, we reported previously that a physical PVA hydrogel prepared through freezing/thawing can autonomously self-heal due to the extensive H-bonding between the hydroxyl groups of the polymer.[32] We wanted to know if this function is retained for the melamine-enhanced PVA hydrogel. We carried out measurements by using a standard self-healing test: cut a hydrogel into two pieces, bring the two fracture surfaces into contact without delay, measure the elongation strength at break as a function of the contact time, and normalize it with respect to the initial hydrogel before cutting to yield the self-healing efficiency. The content of melamine and the number of freezing/thawing cycles were considered as two key parameters that influence the self-healing efficiency. The results are summarized in Figure 6.

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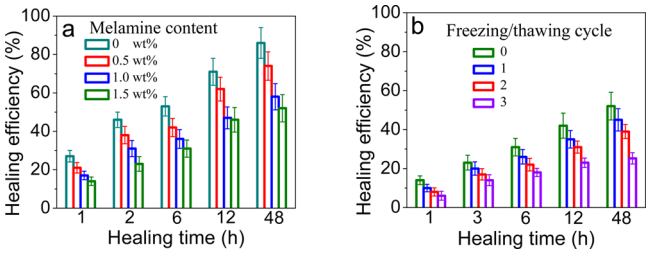

Figure 6. (a) Effect of the melamine content on the self-healing efficiency of PVA hydrogels. (b) Effect of the number of freezing/thawing cycles on the self-healing efficiency of the 1.5MA hydrogel.

As is seen in Figure 6a, a hydrogel with a higher melamine content exhibits a lower self-healing efficiency, with the value decreasing from about 86% to 52% for pure PVA and 1.5MA, respectively, after 48 h of contact. This can be explained by the fact that, by forming multiple H-bonds with PVA, melamine molecules largely enhance the strength and rigidity of the hydrogel, resulting in reduced chain mobility and thus affecting the PVA chain interdiffusion and formation of H-bonds across the fracture surfaces. From Figure 6b, it is seen that when the 1.5MA hydrogel was further strengthened by freezing/thawing, the self-healing efficiency declined further, especially for the hydrogel treated with three cycles of freezing/thawing. The whole of the test results indicate that the melamine-enhanced PVA hydrogel retains the self-healing ability; however, it is less efficient than that of the PVA hydrogel without melamine. The self-healing efficiency appears to be reversely proportional to the strength of the hydrogel. It should be mentioned that PVA-based hydrogels exhibiting both self-healing and shape memory functions are known in the literature. Chen et al. reported a notable example.[35] Supramolecular hydrogels prepared using the dynamic interactions between PVA and phenylboronic acid-modified sodium alginate (Alg-PBA) were shown to be self-healable. As for shape memory, a temporary shape could be fixed quickly by placing the hydrogel into a $CaCl_2$ solution due to the formation of an alginate/Ca^{2+} complex, while the shape recovery was achieved by extraction of Ca^{2+} in a Na_2CO_3 solution. The mechanisms of both self-healing and shape memory obviously are different from those in the present study.

CONCLUSIONS

We have reported the use of therapeutic ultrasound to trigger the shape memory of a PVA hydrogel containing a small amount of melamine (up to 1.5 wt %). Melamine molecules can act as a physical cross-linker by forming multiple H-bonds with the PVA chains, which increases both the strength and elongation at break of the hydrogel. A temporary shape of the melamine-enhanced hydrogel can be processed by deformation at room temperature followed by freezing/thawing under strain, which induces the second cross-linking due to crystallization of PVA chains in the presence of melamine molecules and thus retains the deformation. We showed that the ultrasound delivered by a commercially available device designed mainly for pain relief could trigger the shape recovery of the hydrogel through an ultrasound-induced thermal effect inside the hydrogel that melts mainly the crystallized microdomains formed during the freezing/thawing treatment. The PVA hydrogel based on the two types of physical cross-links possesses a number of appealing properties for biomedical use, such as being mechanically strong and tough, biocompatible, and self-healable and displaying shape memory triggered by a physiological stimulus.

ASSOCIATED CONTENT

Supporting Information

Details of the characterization methods and X-ray diffraction and hydrogel characterization results. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsami.5b02234.

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Notes

The authors declare no competing financial interest.

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