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Review

Self-healing gelatin ionogels

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ABSTRACT

We demonstrate room temperature (20 °C) self-healing, and substantial recovery (68–96%) of gel rigidity of gelatin, a polypeptide, ionogels (made in 1-ethyl-3-methylimidazolium chloride ionic liquid (IL) solutions via thermal treatment, IL ≤ 5% (w/v)) after they were cut using a surgical blade. The recovery process did not require any stimuli, and the complete healing under ambient condition required about 10 h.The self-healing owed its origin to the reformation of network structures via imidazolium ion mediated charge quenching of deprotonated residues, and hydrophobic interaction between neighbouring alkyl tails of IL molecules. The rate of healing determined from the growth of rigidity modulus was 20 ± 5 mPa/s independent of ionic liquid content of the gel. This was true regardless of the fact that ionogels containing more IL had a lower gel modulus due to propensity of hydrophobic linkages, but these were agile enough to recover their network structures to a higher degree during the healing process. These features indicate that the gelatin ionogel being biocompatibile, and biodegradable holds great potential for applications in the field of biomedical engineering.

Contents

1. Introduction

Self-healing is a key property of living tissues that allows them to sustain repeated damage. Physical hydrogels are solvent-filled networks, formed by physically crosslinked biopolymers, in which secondary interactions such as hydrogen bonds, electrostatic interactions, hydrophobic interactions or van der Waals forces are responsible for formation of reversible crosslinks (entanglements). Hydrogels are crosslinked hydrophilic polymer assemblies classically made from high molecular weight biopolymers such as gelatin, fibrin, chitosan, pectin, carrageenan, cellulose etc to name a few. Gelatin, in particular is an interesting biomaterial that is available in plenty in the biosphere, and this material has been extensively studied in the past. Chemical composition of this biopolymer depends on its source of origin. Hydrophobic amino acids like proline (Pro), hydroxyproline (Hyp), and glycine (Gly) are in propensity in gelatin. The general primary sequence is given by of (Gly-X-Pro) and (Gly-X-Hyp), in which X represents other amino acids [1]. Due to the self-assembled origin of these gels, the gel strength quickly recovers after the material experiences mechani-

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cal deformation [2]. Thus, physical polymer networks offer unique advantages, over the chemical gels that are difficult to manipulate. In mammals self-healing is provided by fibrous tissues, like cartilage that are structured by non-covalent crosslinked biopolymers.

In the recent past, major attempts have been made to introduce non-covalently crosslinked biopolymers and their supramolecular assembly to develop self-healing materials. Sometimes, an external trigger in the form of energy or healing moiety is needed for a self-healing to occur [2]. Dynamic-reversible materials (efficiency in detecting and "autonomically" healing damage) displays a wide range of responses from self-healing to mechanical work for applications such as sensors, actuators and various other biomedical applications. Supramolecular chemistry [3] uses non-covalent forces such as hydrogen bonding and π–π stacking giving rise to a variety of stimuli-responsive self-healing materials [4–10]. Macroscopic self-assembly uses the common host–guest molecular recognition [11]. Often external stimuli thermal, radiation, catalytic, and mechanical actions may cause transformations in these structures by thermodynamic reorganization [12–14]. Deng et al have synthesized crosslinked polymer gels with reversible covalent bonds under acidic conditions that showed healable properties [15]. Synthesis of healable polymer gels with trithiocarbonate units in their structures has been proposed by Matyjaszewski and coworkers [16,17]. Similarly, reversible Diels–Alder units have been studied for thermally healable potential[18–20]. It is reported that Diarylbibenzofuranone (DABBF) can reach a state of thermodynamic equilibrium in the absence of any stimuli and the radical species arising from cleaved DABBF was found to tolerant to oxygen [21–26]. Imato et al. prepared crosslinked DABBF containing polymer gels with cleavable properties under ambient conditions [27].

All the above mentioned examples involve chemically crosslinked network gels formed of synthetic polymers that often use toxic crosslinkers. Not many self-healing physical gels made of biopolymers are reported in the literature. Herein, we report the gel recovery process (self-healing) of gelatin ionogels under ambient conditions after their mechanical incision. The extensive physical characterization of gelatin ionogels has been reported by us earlier [28]. The enormous application potential of healable biocompatible gels makes the current report timely and significant, it is more so because these gels are green materials.

2. Materials and methods

Gelatin (GB) (225 bloom, pI ∼ 4.9 ± 0.2) having nominal molecular weight of 50 kDa and ionic liquid (IL) 1-ethyl-3-methylimidazolium chloride were purchased from Sigma-Aldrich, USA, and used as received. The molecular structure of gelatin and the ionic liquid used are shown in Fig. 1. Gelatin ionogel was prepared by dissolving 5% (w/v) of GB in IL solution with varying percentage of IL [0–5% (w/v)] made in deionized water maintained at 60 °C. Continuous stirring for 30 min produced a clear solution, which was then cooled to room temperature (20 °C). After a lapse of gelation time, the contents turned into a rigid gel which was checked by, inversion of the sample holder, and the observation of a non-flowing meniscus implying that it could support the weight of the gel. Concentrations are in (% w/v) unless otherwise stated.

The dynamic rheological profiling of the samples were done on a stress controlled rheometer (AR-500, T.A. Instruments, UK). A2° cone-plate geometry of 20 mm radius and a truncation gap of 500 μm was used, and the oscillatory stress value was fixed at 4.775 Pa. About, 100 mL of the sample was placed on the peltier plate and it was to equilibrate for 5 min before proceeding with measurements. Silicone oil was applied to the outer circular edge of the paltier plate and wet sponge was used as solvent trap to prevent loss of solvent due to evaporation. Bright field biological microscope (Leedzmicro-imaging LTD, U.K.) was used for imaging of the samples.

3. Results and discussion

Gelatin, a biopolymer, is produced by denaturation of collagen through either alkaline or acid processing, during which the interconnected triple-helix units are melted into three distinct single strand gelatin chains [29]. When gelatin is dissolved in warm water these random-coil chains form a homogeneous sol. Upon cooling it to room temperature, these molecules undergo a coil–helix transition, and gradually get physically crosslinked by entanglements to form thermoreversible physical gels with a typical gelation temperature of $T_{gel} \approx 28\,^{\circ}C$ [30].

3.1. Time-dependent microscope imaging

First we prepared thin films of gels on cover slip glass plates by pouring about 0.5 mL of the sol on the plate surface. The plate was stored in a constant temperature incubator over night at a temperature of 20 °C. A transparent gel was set during this period. The ionogel film was then cut into two pieces by using a surgical blade. These samples were placed in the incubator maintained at the same temperature for about 10 h without disturbance. Their recovery pattern was recorded using an optical microscope. These images are depicted in Fig. 2 for two representative ionogels(IL = 1% and 5%). It is clearly seen from the time-sequence of these images that the incision scar disappears typically over a period of 10 h, after which the two pieces are visually unidentifiable and the gel pieces fuse to become one unit again.

3.2. Time-dependent rheology

The healing process was monitored by following the time dependent rigidity modulus of the gels. For the recovery analysis of the ionogel samples, a four-step program on stress controlled rheometer was used. In the first step, the hot sol samples were poured onto the peltier plate maintainedat 10 °C, and kept isothermal at the room temperature for 3 min, and then time sweep measurement was performed at an angular frequency of 1 rad s^{-1} at the oscillatory stress value of 4.775 Pa to observe the temporal growth of low frequency storage modulus, G_0. When storage modulus became constant, we stopped the measurement (generally after 4–5 h). This characterized the ionogel sample. In the second step, the sample was cut into two pieces by using a surgical blade and these pieces were placed touching face to face for 10 h without disturbance. In the third step, we repeated the time sweep measurement on the healed gel sample until its G_0 value reached a plateau. For this measurement, the reference to initiation of healing was defined as the time when the sample wasloaded onto the geometry of the rheometer, which was set as t = 0.

Fig. 3(A) shows the data of isochronal time sweep experiment at constant strain during which the temporal growth of the low frequency storage modulus was monitored for the gel samples. Rheology data shows the self-assembly of the ionogels progressed, and the formation of networks continued to reach a matured state typically after t_{sat} = 4 h of gelation. The saturation values of G_0 are depicted in Fig. 3(A) for various ionogels samples. The time sweep experiment was halted after when saturation in storage modulus values was observed, this equilibrium G_{0max} values are clearly shown in Fig. 3(B). Next the gel was cut into two pieces using a surgical blade (t_{cut} in Fig. 3(A)). A sharp drop in storage modulus after incision resulted from the disruption of physical crosslinks is clearly seen in this figure. For instance, the saturation modulus of