TANNIN-INSPIRED HYDROGELS WITH CONSIDERABLE SELF-HEALING AND ADHESIVE PROPERTIES

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Hydrogel materials are attracting considerable attention owing to their wide applications such as wound closure, drug delivery, tissue engineering, cell therapy, wrinkle fillers, etc. Considering the unique tannin chemistry including excellent chelating properties to metals, easily oxidability and superior ability to bind proteins, herein, the natural gallol-containing tannic acid (TA), an extract of plant materials such as Chinese gallnuts, cacao, green tea leaves and fruit peels, was used as a natural phenolic crosslinker to fabricate the self-healing and adhesive hydrogels based on the oxidation of polyphenol groups with the aid of NaIO₄ under alkaline condition. The properties of the obtained hydrogels were well characterized by rheometer, universal testing machine, thermogravimetry (TG), dynamic mechanical analysis (DMA) and scanning electron microscope (SEM). The feed molar ratio of NaIO₄ to TA was found to play an essential role in gelation time (3-15 min), physical properties (MPa range of tensile strength and 50-220% of elongation at break), adhesive strength (up to 36KPa) as well as self-healing efficiency (up to 73%) of the fabricated hydrogels. By using TA and gelatin with complete natural origin, this study opens a new path toward the preparation of biocompatible self-healing and adhesive hydrogel materials with improved properties.

Keywords: gelatin; tannic acid; hydrogel; self-healing; adhesives

INTRODUCTION

Recently, inspired by the catecholic chemistry of dopamine (DOPA), mussel-inspired hydrogels for self-healing and tissue adhesive have drawn increasingly attention owing to their biomedical applications such as wound dressing, tissue sealants, scaffolds for tissue engineering and encapsulation of drug (Mehdizadeh *et al.*, 2012). However, the costly price and potential neurotransmission effect of DOPA limit its application in commercial filed, and thus the seeking of alternatives to DOPA is extraordinary necessary (Guo *et al.*, 2018).

Hence, tannic acid (TA), a natural plant-derived polyphenolic compound with extensive sources, is employed as a desired alternative for mussel-inspired self-healing materials. TA is capable to precipitate proteins (collagen and gelatin) by multi-point hydrogen-bond and hydrophobic actions. The two adjacent phenolic hydroxyls of gallols in TA can also chelate metal ions (e.g. Fe³⁺, Al³⁺, Cr³⁺) in the form of oxygen anion (O⁻) to form a stable pentacyclic complex, and although the third phenol hydroxyl is not involved in the formation of pentacyclic complex, it can promote the dissociation of the other two adjacent OH groups, and thus accelerating the formation of pentacyclic complex and promoting its stability (Fan *et al.*, 2017). In addition, TA has good antioxidant capacity. Its gallols can also be oxidized to form quinones that further take placenucleophilic addition reactions. Thus, like the versatile DOPA containing

catechol, TA could also be used to fabricate functional materials including self-healing and adhesive hydrogels.

Herein, a one-pot method is described to fabricate TA-modified gelatin hydrogels through supramolecular interactions as well as covalent bonds under oxidizing conditions. The strong multi-point hydrogen-bond and hydrophobic interactions between TA and gelatin are first inhibited to a large extent in alkaline conditions to obtain their homogeneous mixture, and sodium periodate (NaIO_4) was then added as oxidant to prepare oxidation-crosslinked gelatin hydrogels with considerable self-healing and adhesive properties. The effect of NaIO_4 dosage was systematically investigated on the gelling time, self-healing adhesive, viscoelastic and thermal properties and morphology of the obtained hydrogels.

MATERIALS AND METHODS

Gelatin (10 g) and TA (0.5 g) was blended in 100 ml deionized water and heated at 70 °C for 1 h to get a mixed solution with an ultimate gelatin concentration of 10% (w/v), then the pH value was adjusted to 11 using 2 M NaOH. The obtained solution was further stirred for 24 hours at 70°C to yield the wine-red transparent precursor solution of hydrogel. Various amounts of NaIO_4 solutions (10 %, w/v) were added to the precursor solution under vigorous stirring at 50°C. The reaction mixture was further stirred at 50°C until the sol-gel transformation. The feed molar ratios of NaIO_4 to TA are 5:1, 10:1, 15:1, 20:1 and 25:1, respectively, and the obtained hydrogels are named as NA-5, NA-10, NA-15, NA-20 and NA-25, respectively.

RESULTS AND DISCUSSIONS

Gelling Time

Gelling time of the hydrogels was measured by inverting test tube method (Fig 1 A) at 50°C, and it was determined at the time when there was no visual flow observed by inverting the vial. As shown in Fig 1B, the feed molar ratio of NaIO_4 to TA played an essential role in the process of gelling. Along with the increase of NaIO_4 dosage, the gelling time is decreased from 15 min for NA-5 to the shortest 2.35 min for NA-15, and then slighted improved to 3 min for NA-20, which is probably due to the improved density of crosslinking of the hydrogel.

Figure 1. Photographs of gelation (A) and gelling time (B) at different amount of NaIO_4

Self-healing and Adhesive Properties

Cylindrical hydrogels with a diameter of 10mm and height of 100mm were prepared and immersed into 30% (w/w) $(\text{NH}_4)_2\text{SO}_4$ for one day before performing the tensile test. The aim of immersion operation is to improve the mechanical strength of hydrogels so that the gels could be strong enough to withstand the clamp of tensile test machine. A cylindrical piece of hydrogel was cut in half, and the two halves were then reattached to one another. After 2 h under wet conditions, the separated hydrogel pieces had adhered again to form one hydrogel, indicating its preliminary self-healing ability. The stress-strain curves (Fig.2A) were then recorded for the original and self-healed hydrogels, and the self-healing rate was calculated by the following equation:

$$\text{Self-healing rate (\%)} = S_{\text{after}}/S_{\text{before}} \times 100\% \quad (1)$$

Where S_{before} is the tensile stress of original hydrogel at break, and S_{after} is tensile stress of self-healed hydrogel at break. The self-healed hydrogel **NA-15** recovers 72.84% tensile strength compared with the original hydrogel (Fig.2B).

A lap shear test was also performed to evaluate the adhesive strength of the hydrogel. A piece of cow-skin with the shape of 1.5 cm × 10 cm rectangle was smeared with 1ml of the gelatin/TA/NaIO₄ mixture. Then another piece of cow-skin was placed on the treated one, and the contacted area was kept as 1.5 cm × 8 cm. 24 h later, the samples were measured by the lap shear test, and the results were shown in Fig. 2C. Along with the increase of NaIO₄ used, the average adhesive strength of hydrogel shows similar change tendency to the self-healing rate (Fig.2B). Specially, it firstly increases from 8.52 KPa of **NA-5** to 36.31 KPa of **NA-15** and then decreases to 9.79 KPa of **NA-20**, which suggested an optimal amount of NaIO₄ for leather adhesive.

Figure 2. Stress-strain curves of NA-15(A), self-healing rates (B) adhesive strength (C) of hydrogels

Rheological Analysis and DMA

Rheological analysis was also performed for the **NA-10** hydrogel to qualitatively monitor its viscoelasticity. A strain amplitude sweep was firstly measured to investigate the linear viscoelastic region and the crossover point where storage modulus (G') is equaled to loss modulus (G''). As shown in Fig.3A, both G' and G'' remain constant at a low strain amplitude (0.1%-25%), and after that, when the strain further increases, the G'' value firstly starts to improve, and G' value subsequently shows a dramatic decrease, indicating a shear-thinning behavior of hydrogel. As a result, a cross over point is observed at the strain of approximately 700%, implying the destruction of the hydrogel network. Besides, the value of G' is consistently much higher than that of G''

in the frequency sweep test range (Fig.3B), showing a Hooke an-like frequency-independent behavior and further indicating a stable formation of hydrogel (Fan, 2017).

Figure 3. Strain amplitude sweep test (0.1-1000%) of **NA-10** hydrogel at a fixed frequency of 1 rad s⁻¹ (A) and its frequency sweep test (0.1-100rad s⁻¹) at a fixed strain of 1% (B)

In the DMA curves (Fig.4A) both G' and G'' values of **NA-10** hydrogel precipitously decrease with the growth of temperature, indicating the hydrogel gradually became soft. The crossing point of G' and G'' is observed at 54 °C, corresponding to the transformation of gel to sol.

TG Analysis

Fig. 4B provides the TG curves of hydrogels at various amount of NaIO₄. In general, all the hydrogels decompose in a two-step mode. The first weight loss occurs below 100°C, which is probably due to the volatilization of water and other small molecules in hydrogels. The second stage of weight loss is observed at 250 °C or so, which is associated with the degradation and carbonization of hydrogel network. Notably, at the same testing temperature, the higher the dosage of NaIO₄ is, the smaller the weight loss of the obtained hydrogel is, namely, the more stable the hydrogel is.

Figure 4. Dynamic thermo mechanical properties (A) of **NA-10** and TG curves (B) of various hydrogels

SEM Analysis

Figure 5. SEM images of **NA-5** (A), **NA-10** (B), **NA-15** (C), **NA-20** (D) hydrogels

The interior structure of the obtained hydrogels was investigated by SEM analysis. As shown in Fig.5, all the lyophilized hydrogels exhibited a porous three-dimension structure with different shape and porosity. The pore size progressively decreases with the increase of NaIO₄ used. For **NA-5** hydrogel, the SEM image (Fig.5A) provides a petal-shaped porous structure with a pore diameter of $213 \pm 58 \mu\text{m}$. In the SEM of **NA-10** hydrogel (Fig. 5B), there are clear thick boundary between the pores, and the pore diameter is decreased to $73 \pm 21 \mu\text{m}$. For **NA-15** and **NA-20** hydrogels, the pore diameter is further declined to $35 \pm 10 \mu\text{m}$, and the number of pores is greatly reduced, too. Furthermore, thick cracks are found for **NA-20**, which is attributed to its high crosslinking density.

CONCLUSIONS

In conclusion, we successfully fabricated tannin-inspired self-healing hydrogels through a facile one-pot method in which TA was introduced to gelatin via both supramolecular interaction and covalent bonds in alkaline condition. The crosslinking of these hydrogels was easily accomplished by oxidizing the homogeneous gelatin-TA solution in the presence of NaIO₄. Similar to mussel-inspired hydrogels, the resulting product exhibited sticky and self-healing nature. The amount of NaIO₄ added can be used to modulate the gelling time, self-healing, mechanical property, adhesive strength as well as the interior pore size of gelatin hydrogels. Besides, owing to the remarkable thermal properties, viscoelasticity and porosity the present hydrogels will be an excellent candidate for wound closure, tissue adhesive and cell delivery. Additionally, considering the accessibility and low price of TA as well as the biocompatibility of gelatin, the simple and feasible method developed in this work offers a practical strategy for the preparation of self-healing and adhesive materials in biomedical field.

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