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A Comprehensive Chemical Experiment: Preparation and Performance Analysis of Self-Healing Oxidized Sodium Alginate-Carboxymethyl Chitosan Hydrogels

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Abstract

Through cutting-edge scientific research, an innovative comprehensive chemical experiment has been developed for polymer or chemistry majors: A self-healing oxidized sodium alginate-carboxymethyl chitosan hydrogel (OSA-CMCS) with self-healing properties was synthesized based on dynamic imine bonds. In this study, sodium alginate was oxidized with sodium periodate as an oxidant, and a self-healing OSA-CMCS hydrogel was prepared by reaction with Schiff base of carboxymethyl chitosan. The experimental procedures include the operation of chemical experiments, analysis of instruments, spectral analysis, etc., covering the content of chemistry courses in a comprehensive manner, stimulating students' interest in scientific research. It provides a solid foundation for undergraduate graduation projects, scientific research training projects, and the development of future scientific research.

Keywords: chemistry experiment, self-healing hydrogel

1. Introduction

Experimentation is an integral part of the training of chemistry professionals, however students do not find the experiments engaging because the normal course experiments, experimental procedures, and experimental results are the same. By combining the latest research hotspots with classroom experiments, students' subjective initiatives can be fully explored. The course presents not only the basics of chemical experiments, the use of common analytical instruments, and data analysis methods, but more importantly, the basic methods of chemical scientific research in analyzing and solving problems. The goal of this study is to stimulate students' interest in research and to foster teaching and research synergy.

A hydrogel is a class of polymeric materials with a three-dimensional network structure that exhibits swelling properties when water is absorbed and shrinkage when water is lost. Due to their high water content, excellent flexibility, and good biocompatibility, hydrogels can be used in a variety of biomedical applications (Ayoubi-Joshaghani, M. H. et al., 2020), including wound dressings (Liang, Y., He, J. & Guo, B., 2021), tissue engineering scaffolds (Pascal Bertsch et al., 2023; Zhang, Y. S. et al., 2017), and drug delivery systems (Zhao, Z., Wang, Z., Li, G., Cai, Z. & Cui, W., 2021).

As a new class of intelligent hydrogels, self-healing hydrogels can repair themselves spontaneously or in response to specific stimuli when damaged by the external environment or from within. The self-healing properties of the material enhance its safety, extend its lifespan, and reduce its cost significantly. There are two main mechanisms that are responsible for the reversible properties of self-healing hydrogels: dynamic non-covalent interactions and dynamic covalent bonds. Non-covalent interactions include dynamic hydrogen bonding (Ruru Song et al., 2019), host-guest interactions (Jin, J., et al., 2019), hydrophobic interactions, and metal-ligand interactions (Shi LY, et al., 2018). Nevertheless, the non-covalent forces are generally weak and cannot be used for a wide range of polymeric materials applications. The strength of dynamic covalent bonds is comparable to that of covalent bonds, and they can undergo reversible dissociation/conjugation under certain conditions. In comparison with non-covalent interactions, self-healing hydrogels based on reversible covalent bonds exhibit superior mechanical properties. Covalent dynamics can be divided mainly into two groups: the exchange reaction consists of reactants involved in the exchange of groups, for example, ester exchange reactions (Makafui Y. Folikumah, Marc Behl & Andreas Lendlein, 2021). Second, there are reactions which produce new valence bonds, including addition reactions and condensation reactions, commonly known as Diels-Alder reactions (Hongliang Wei et al., 2020), imine bonds (Honglei Chen et al., 2018), acyl hydrazone bonds (Xueyu Jiang et al., 2022), and disulfide bonds (Wang, Yanan et al., 2017).

In this study, self-healing hydrogels were synthesized by combining sodium alginate oxide with an aldehyde group and forming reversible imine bonds with the amino group of carboxymethyl cellulose. The main properties of hydrogels were also investigated.

2. Experimental

2.1 Materials

Sodium alginate (SA), sodium periodate (NaIO4) were bought from Aladdin Chemical Reagent Co., Ltd., Shanghai, China. Ethylene glycol, hydroxylamine hydrochloride, NaOH and carboxymethyl chitosan hydrogel were bought from Macklin Co. Ltd., Shanghai, China. All chemicals were analytical grade and were used without further purification.

2.2 Synthesis of Oxidized Alginate (OSA)

The oxidized alginate (OSA) was synthesized using the method previously described (Mu, Lu & Liu, 2011). 1.0 g of sodium alginate (SA) should be weighed into 100 mL of deionized water and magnetically stirred until fully dissolved to make a 1% (w/v) solution. Then 1.08 g NaIO4 was added and stirred for 5 hours in the dark at room temperature. To neutralize unreacted NaIO4, 1.5 mL of ethylene glycol was added and stirred for 1 hour. The product was separated through dialysis (MWCO of 3500) against water for 2 days and subsequently lyophilization for 48 hours.

2.3 Preparation of OSA-CMCS Hydrogel

The 0.04 g OSA and 0.04 g CMCS were dissolved in 2ml of deionized water each. Mixing and stirring the above two solutions at room temperature, the OSA/CMCS hydrogel was formed.

2.4 Characterizations

2.4.1 Fourier Transform Infrared Spectroscopy (FT-IR)

The chemical functional groups of the OSA were analyzed by a Bruker ALPHA II FTIR spectrometer (Bruker, Karlsruhe, Germany). All spectra were recorded in the transmission mode in the range of 4000–500 cm^{-1} with a resolution of 4 cm^{-1}.

2.4.2 Oxidation Degree Determination

The degree of oxidation was determined using the hydroxylamine hydrochloride titration method described by Zhao, et al. (Zhao, H., et al., 1991; Paiva D, et al., 2016). As excess hydroxylamine hydrochloride reacts with aldehyde groups in OSA, it produces HCl, which is then titrated with NaOH and the molar amount of aldehyde groups generated can be determined by calculation.

2.4.3 Rheological Measurements

The rheological properties of hydrogels were tested with an Anton Paar rheometer (MCR302, Austria).

The Oscillatory time sweeps: The hydrogel is placed on the rheometer, the test temperature is set to 37°C, the vibration frequency is 1HZ, the strain fixed at 1%, and the changes of storage modulus (G′) and loss modulus (G″) of the hydrogel are detected with the increase of time.

The oscillation frequency sweeps: The hydrogel is placed on a rheometer and set at 37°C. The vibration frequency is set at 1HZ, the strain fixed at 1%, and the angular frequency is set at 0.1 rad/s-10 rad/s. With the change of angular frequency, detect the change in storage modulus (G′) and loss modulus (G″) of the hydrogels.

Self-healing property: Amplitude oscillatory strains were switched from the small strain (γ = 1 %, scanning frequency 1 Hz) at the first 100s to the large strain (γ = 1000 %, scanning frequency 1 Hz) at the second 100s, and repeated five times.

3. Results

The hydrogels were synthesized in two steps. In the first step, OSA was oxidized with sodium periodate to produce the aldehyde-modified OSA, and in the second step, the aldehyde group of OSA was reacted with the amino group of CMCS by Shiff-base reaction to produce the hydrogel. The reaction route is shown in Figure 1.

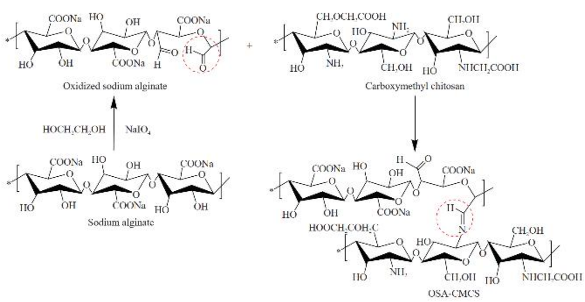


Figure 1. Synthetic route of OSA-CMCS hydrogels (Hou Bingna, et al., 2022)

3.1 Preparation and Characterization of OSA

The molecular structure and specific functional groups of the resultant OSA could be confirmed by FT-IR spectroscopy. Figure 2 illustrates that SA and OSA have broad absorption peaks between 4000 and 3000 cm^{-1}, which correspond to stretching vibration peaks of the hydroxyl groups.

The OSA spectrum, in contrast to the SA spectrum, exhibited a new characteristic peak at 1735 cm^{-1}, which was the telescopic vibration of the aldehyde group, indicating successful preparation of the aldehyde group.

The degree of oxidation is defined as the fraction of substance of oxidized glyoxylate units to the overall SA glyoxylate units. Based on the hydroxylamine hydrochloride method, the degree of oxidation of OSA is 82.3%, and this result indirectly proved that SA has been oxidized.

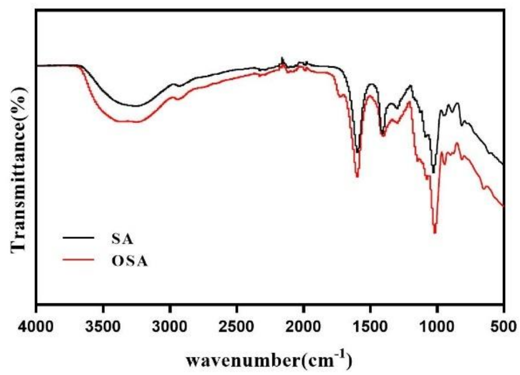
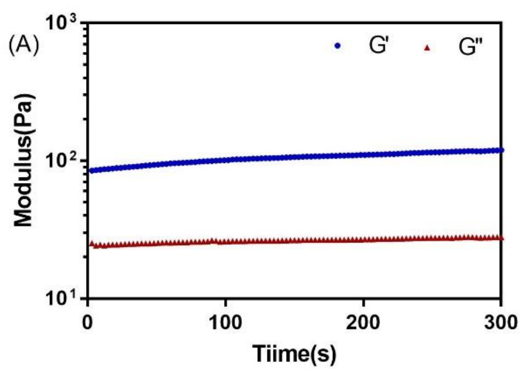


Figure 2. FTIR spectra of SA and OSA.

3.2 Preparation and Rheological Characterization of Hydrogels

The properties of self-healing OSA-CMCS hydrogels can be investigated by rheological experiments. Figure 3(A) shows the storage modulus (G′) and loss modulus (G′′) of OSA-CMCS hydrogels over time. Throughout the range of time, G′ and G′′ settings were almost constant, and G′ values of OSA-CMCS hydrogels were much higher than G′′, exhibiting typical gel characteristics. As the angular frequency increases from 0.1 to 10, the G′ of the gel remains parallel to G″, indicating that the solution has formed a gel and the state is stable, as shown in Figure 3(B).



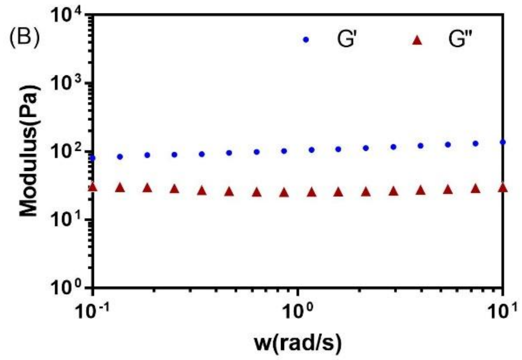


Figure 3. (A)Oscillatory time sweeps of OSA-CMCS hydrogels (B) Oscillation frequency sweep test of OSA-CMCS hydrogels

The aldehyde group of OSA and the amino group of CMCS can react to form dynamic imine bonds. An external force may break the imine bonds of the hydrogel, and the aldehyde group and amino group will react spontaneously to regenerate a new imine bond, thereby enabling the hydrogel to self-repair.

As shown in Figure 4, the initial application of 1% strain to the hydrogel, G′ > G′′, indicates gel formation. After 100s, the strain suddenly increased to 1000%, and the energy storage modulus and loss modulus then suddenly decreased, with the energy storage modulus being smaller than the loss modulus. This indicates that the gel's cross-linking network had been totally destroyed at this point. In contrast, when the strain is reduced to 1%, the value of the energy storage modulus is again greater than the loss modulus, and is slightly lower than the initial value, indicating that the gel has re-formed in a short period of time. In repeated strains from 1% to 1000%, similar results are obtained. The results of this experiment demonstrate that the hydrogel has a high degree of self-healing capacity.

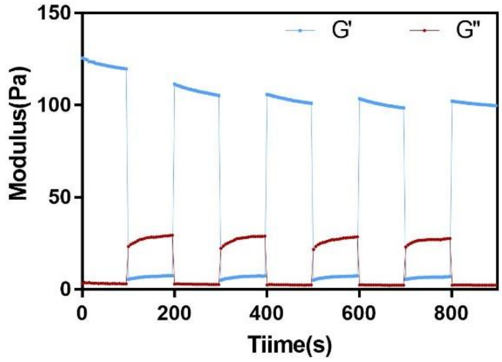


Figure 4. Dynamic cyclic strain sweep measurements of OSA-CMCS hydrogels

4. Reference Course Assignment

(1) Task 1: (preview before class) Can SA and CMCS be prepared into a hydrogel that is capable of self-healing? How to characterize self-healing hydrogels? In this assignment, students are required to search the literature to understand the concept of polymer modification, combine that concept with the fact that imine bonds can self-heal, and identify the modification option as SA oxidation. Additionally, this is an open-ended question, students are encouraged to modify two molecules simultaneously and come up with a variety of solutions.

(2) Task 2: After each class, targeted questions are asked. For example, how can gels with greater and lesser oxidation be obtained? Is there a way to improve the strength of the hydrogel? Students provide solutions based on a review of the literature.

(3) Task 3: Using sodium alginate and chitosan as raw materials, design temperature-sensitive hydrogels/pH-sensitive hydrogels. The assignment will be completed in small groups and will be followed by a program debriefing.

(4) Task 4: The experimental report should be written in the format of a scientific paper, including an introduction, the results of the experiments, a discussion, and a conclusion.

5. Teaching Thoughts and Suggestions

This comprehensive chemistry experiment includes the synthesis, characterization and performance testing of self-healing hydrogels, covering the titration analysis of basic chemical experiments, the use of FT-IR and the analyzers, as well as enhancing students' literature search and reading, spectral analysis, and the use of GraphPad and other software. Experimental content covers a wide range of knowledge, integrates the knowledge of different disciplines, and is relatively challenging compared with basic experiments, making it appropriate for undergraduate students majoring in chemistry or materials science. It is recommended to concentrate on the experimental teaching week and conduct the experiment in groups of 4-5 people. Class hours should be arranged between 16 and 20 hours, as shown in the table below.

Table 1. Course content and recommended number of hours

	Content of the course	Number of lesson hours
1	Synthesis of oxidized alginate (OSA)	2
2	Preparation of OSA-CMCS hydrogel	2
3	Fourier transform infrared spectroscopy (FT-IR)	4
4	Oxidation Degree Determination	4
5	Rheological measurements	4-6
6	Presentation	2-3

The experimental procedure is simple and does not involve toxic, hazardous or dangerous chemicals. However, safety precautions should still be taken especially when performing infrared and rheological tests. This experiment represents the entire process of topics, from the formulation of problems to the design of experiments, data analysis, and analysis summary. After completing the experiments, students gain an understanding of the scientific research process in chemistry. It may be possible for students to use the results of Task 3 as the topic of their graduation thesis. In addition, they may be able to publish the results of certain innovative experiments they have undertaken. Through the implementation of this experiment, students will cultivate their scientific research literacy and interest in chemistry, and expand their academic horizons. The objective of this experimental study is to establish a solid foundation for implementing scientific research training projects throughout the university and for future postgraduate research careers.

Fund Project

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