

RHEOLOGICAL PROPERTIES OF HYDROGELS PRODUCED BY CELLULOSE DERIVATIVES CROSSLINKED WITH CITRIC ACID, SUCCINIC ACID AND SEBACIC ACID

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Cellulose is the most abundant biopolymer in our world, and a natural, biodegradable and inexpensive resource for biomaterials. This work prepared cellulose-based hydrogels by cross-linking cellulose derivatives using citric acid, succinic acid, and sebacic acid, and explored the rheological properties of the three cellulose-based hydrogels. We found that the viscoelastic properties of this kind of cellulose-based biodegradable hydrogels can be manipulated by hydrogel concentration and using the three different cross-linkers. The cellulose-based hydrogels cross-linked with citric acid (CHCCA) and the cellulose-based hydrogels cross-linked with succinic acid (CHCSUA) exhibited nearly identical rheological behaviors (both linear and non-linear), due to the similar structure of the citric acid and succinic acid. Both CHCCA and CHCSUA showed similar viscoelastic solid gel-like behaviors, and the viscoelastic properties were stronger when hydrogel concentrations were increased. The CHCCA and CHCSUA also displayed nearly identical shear thinning behaviors, among all measured shearing rates. The cellulose-based hydrogels cross-linked with sebacic acid (CHCSEA) exhibited viscoelastic liquid or fluid-like behaviors, which are clearly different from those for the CHCCA and CHCSUA. The CHCSEA showed shear thinning characteristics during high shearing rates, but a Newtonian region at low shearing rates. This work paves the way for developing various inexpensive biodegradable cellulose-based hydrogels with desired rheological properties specific to applications such as cosmetic gels and wound-healing materials.

Keywords: cellulose, hydrogels, rheology, viscoelastic properties

INTRODUCTION

A hydrogel is a three-dimensional polymer network that can absorb a large amount of water. Hydrogels research and development have attracted much attention within the recent decades for applications of interest in drug delivery,¹ tissue engineering,² soil conditioners,³ and many other non-hygienic utilizations.⁴ The most commonly used hydrogels are based on polyacrylates and copolymers with polyacrylates.⁵ In addition, scientists seek more environmentally sustainable and inexpensive materials, such as carbohydrates, including cellulose and its

derivatives, for developing hydrogels.⁶

Cellulose is the most abundant natural polymer. It can be acquired from many sources, such as crop residues, cotton, wood, agricultural wastes, and non-plant resources.⁷ Due to its abundance, low cost, and renewable nature, cellulose can become a major chemical feedstock resource.⁶ Given that cellulose is insoluble in water, cellulose hydrogels are mostly prepared from its derivatives.⁵ A cellulose-based hydrogel is normally made by cross-linking cellulose filaments into a three-dimensional network. The many hydroxyl groups of cellulose allow for the

relatively easy preparation of hydrogels. Demitri *et al.*⁸ prepared a cellulose-based hydrogel by heating cellulose derivatives with citric acid at 80 °C. Pandey *et al.*⁹ developed cellulose-based hydrogels by microwave irradiation induced cross-linking with *N,N'*-methylenebis(acrylamide). However, although the rheological properties of cellulose-based hydrogels could limit their usage, they have been rarely reported.

Recently, we prepared cellulose derivative hydrogels of sodium carboxymethyl cellulose (CMCNa) and hydroxyethyl cellulose (HEC) with three cross-linkers – citric acid, succinic acid and sebacic acid. The mixture of CMCNa and HEC is much easier to dissolve in water and to react with the cross-linkers. The citric acid, succinic acid, and sebacic acid are all naturally occurring acids. Therefore, the prepared cellulose-based hydrogels are biodegradable.¹⁰⁻¹³ We found that the water absorption capacities of these cellulose-based hydrogels were dependent on the type of the cross-linker used, the cross-linker amount, and the cross-linking reaction temperatures. In this work, we evaluated the rheological properties of these cellulose-based hydrogels in order to identify their potential applications. Both linear and non-linear viscoelastic properties of these biopolymers were investigated.

EXPERIMENTAL

Materials

Sodium carboxymethyl cellulose (CMCNa) (Product No. 419338, average $M_w \sim 700,000$), hydroxyethyl cellulose (HEC) (Product No. 54290, medium viscosity), citric acid (Product No. 251275), succinic acid (Product No. 398055), and sebacic acid (Product No. 283258) were all purchased from Sigma-Aldrich (St. Louis, MO, USA). The chemical structures of citric acid, succinic acid and sebacic acid used as cross-linkers are shown in Scheme 1.

Hydrogels preparation

Hydrogels were prepared by cross-linking cellulose derivatives⁸ with three organic acids (citric acid, succinic acid, and sebacic acid). Briefly, CMCNa and HEC were combined in a 3:1 weight ratio to make up a 2% (wt%) solution using nano-pure water at room temperature. The solution was kept stirred using a magnetic stir bar until it became clear (about 30

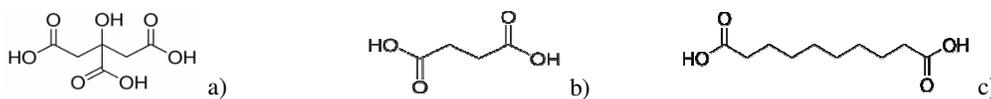
minutes), and then 1.75% (wt%) of the cross-linker (citric acid, succinic acid, or sebacic acid) was added. The sample solution was dried in an oven at 55 °C overnight to remove the water and then oven-heated again for 24 hours at 90 °C for the cross-linking reaction. The dry sample was then cooled down to room temperature and ground into powder using a food blender. The powdered samples were re-dissolved in water to prepare three concentrations (0.5%, 1.0%, and 1.5%) (wt%) at room temperature for at least 24 hours to become hydrogels. The prepared hydrogels were then kept in a refrigerator (4 °C) and used for rheology measurements within two days.

Rheological properties measurements

The rheological properties measurements were taken by a strain-controlled Rheometric ARES rheometer (TA Instruments, New Castle, DE, USA) using a 5-cm diameter parallel-plate geometry.¹⁴ The hydrogel sample for testing was put in between the top and bottom plates. The geometry chamber was maintained at 25 °C \pm 0.1 °C by a water circulation system. The edges of the plates were sealed with mineral oil to retain the moisture. For linear rheological property measurements, a strain sweep test was firstly carried out to evaluate the sample's viscoelasticity linear range. The strain linear range was less than 1% for all measured samples in this work. For the other linear rheological property experiments, a strain in the linear range was adopted for the same material; new samples were used for each test.

Stress relaxation tests were also conducted in the linear viscoelastic range, which measured the stress relaxation with the time after the sample is subjected to a step strain increase. Dynamic oscillatory experiments were conducted over a frequency (ω) range of 0.1-100 rad/s within linear strain, which generated the elastic or storage (G') and loss or viscous (G'') moduli. The elastic or storage modulus (G') and viscous or loss modulus (G'') represent the non-dissipative component and the dissipative component of the viscoelastic properties, respectively. The G' is characteristic of the material's elasticity, while the G'' is characteristic of the material's viscous flow. The non-linear shearing viscoelastic property measurements were performed within the shear rate range of 0.1-300 s⁻¹ after the linear rheological property experiments. The non-linear shearing properties show the material's viscosity versus shear rate.

Every experiment was repeated at least three times using different samples. The relative errors were all within the range of $\pm 7\%$.



Scheme 1: Chemical structures of (a) citric acid, (b) succinic acid, and (c) sebacic acid

RESULTS AND DISCUSSION

Three concentrations (0.5%, 1.0%, and 1.5%) (wt%) of hydrogels were prepared. The linear dynamic viscoelastic properties for the three different cellulose-based hydrogels are shown in Figures 1, 2 and 3. All measured cellulose-based hydrogels cross-linked with citric acid (CHCCA) exhibited viscoelastic solid gel-like behaviors;¹⁵ all measured G' were greater than G'' (Fig. 1). Both G' and G'' increased with CHCCA concentration, indicating that the viscoelasticity strengthened with increasing hydrogel concentration (Fig. 1). The curve of G' demonstrated nearly frequency independent within the middle range of measured frequencies (Fig. 1). The frequency independent G' at 1 rad/s for 0.5%, 1.0%, and 1.5% CHCCA were 66.7 Pa, 406.8 Pa, and 1125.7 Pa, respectively (Fig. 1). The phase shifts ($\delta = \tan^{-1}(G''/G')$) for the 0.5%, 1.0%, and 1.5% CHCCA were in the range of 8.5°-22.9°, 8.4°-22.5°, and 6.9°-20.8°, respectively. The phase shift characterized the material as solid ($\delta = 0^\circ$), liquid ($\delta = 90^\circ$), or viscoelastic ($0^\circ < \delta < 90^\circ$). For instance, the phase shift of steel is 0° , the phase shift of water is 90° , while the phase shift of rubber is about 11° .¹⁵ Because the phase shifts of CHCCA decreased as the hydrogel concentration increased, the phase shift results for CHCCA indicated that it became a little more solid-like as the hydrogel concentration increased.

Figure 2 displays the linear dynamic viscoelastic behaviors for the cellulose-based hydrogels cross-linked with succinic acid (CHCSUA). The measured linear rheological properties for CHCSUA (Fig. 2) were very similar to those for CHCCA (Fig. 1). The moduli for CHCSUA were enhanced as the hydrogel concentration increased. However, the viscoelastic properties for CHCSUA were slightly weaker than those for CHCCA (Fig. 2). The G' curve for CHCSUA also demonstrated a frequency independence within the middle range of measured frequencies (Fig. 2). The frequency independent G' at 1 rad/s for 0.5%, 1.0%, and 1.5% CHCSUA were 60.7 Pa, 386.7 Pa, and 1050.4 Pa, respectively (Fig. 2). The phase shifts for the 0.5%, 1.0%, and 1.5% CHCSUA were in the range of 10.8°-29.1°, 10.3°-25.9°, and 9.1°-24.5°, respectively, which is also evidenced by the CHCCA becoming more solid-like as the hydrogel concentration increased. Our other study on CHCCA and CHCSUA showed that they had similar water absorption behavior, suggesting that they had similar hydrogel network structures (data

not shown). The possible cross-linking reaction may have occurred between the carboxyl group of the citric acid/succinic acid and the hydroxyl group of the cellulose. From the citric acid and succinic acid structures, citric acid shows three possible reaction sites, while succinic acid has two sites. The distance between two carboxyl groups for the succinic acid and the citric acid is similar (see Scheme 1). Therefore, the similarity of the water absorption for the hydrogels cross-linked with citric acid and succinic acid should be due to the occurrence of similar cross-linking reactions. In addition, with the citric acid having three cross-linking reaction sites, but only two sites in succinic acid, the network of CHCCA might be a little more rigid than the network of CHCSUA. This is why the CHCCA network exhibited slightly stronger linear viscoelastic properties than the CHCSUA network (Figs. 1 and 2).

The linear dynamic rheological properties for the three concentrations of the cellulose-based hydrogels cross-linked with sebacic acid (CHCSEA) are displayed in Figure 3. All measured CHCSEA exhibited viscoelastic liquid or fluid-like behaviors based on all measured G' being lower than G'' (Fig. 3). The curves of G' and G'' for CHCSEA are presented as straight lines, almost parallel to each other, and they were very dependent on frequency (Fig. 3). The phase shifts for 0.5% and 1.0% of CHCSEA were in the ranges of 61.6°-85.4° and 55.3°-79.5°, respectively. This denoted that 0.5% CHCSEA showed very fluid-like behavior. When the concentration increased, 1.0% CHCSEA exhibited a slightly solid-like trend, as evidenced by the decreased phase shifts. When the concentration was further increased, the phase shifts for 1.5% CHCSEA were in the range of 52.5°-60.2°, showing a little more solid-like tendency, even though all measured CHCSEA displayed viscoelastic fluid characteristics. Comparing the structure of sebacic acid (see Scheme 1) and that of succinic acid, sebacic acid has a longer 'chain' or 'arm' than succinic acid. Therefore, sebacic acid plays the role of not only a cross-linker, but also as a part of the chain in the network due to its long 'chain' or 'arm', which resulted in a relatively 'loose' network of the CHCSEA, so that it could not form a firm gel-like viscoelastic solid network.

The stress relaxation studies for the hydrogels are displayed in Figures 4 and 5. All three CHCCA did not fully relax after 1000 seconds,

instead of reaching plateaus (Fig. 4). The plateau was higher when CHCCA concentration was greater (Fig. 4). These results suggested that the measured CHCCA should be viscoelastic solid-like networks and gels. The relaxation behaviors for the CHCSUA were almost the same as those for the citric acid (CHCCA) hydrogels (data not shown), which supported that CHCSUA and CHCCA were composed of networks with very similar structures. The relaxation moduli ($G(t)$) for the lower concentrations (0.5% and 1.0%) of the cellulose-based hydrogels cross-linked with sebacic acid (CHCSEA) relaxed rapidly after the initial step of strain; and fully relaxed within a few seconds (Fig. 5). The 1.5% cellulose-based hydrogels cross-linked with sebacic acid (CHCSEA) relaxed slower than those with 0.5% and 1.0% CHCSEA, but the relaxation modulus

($G(t)$) did not reach a plateau and continuously relaxed after 200 seconds (Fig. 5). These results indicated that the CHCSEA hydrogels were viscoelastic fluid-like materials; the networks were extremely loose, even though the networks became slightly stronger with greater concentration of the CHCSEA. The strain sweep experiments for the studied CHCCA showed that the linear range of the viscoelasticity was 1% and less (Fig. 6). The linear viscoelasticity for the CHCSUA was also $\leq 1\%$ (data not shown). However, the linear viscoelasticity for the CHCSEA was about 25% and less (Fig. 6). These results also supported the preceding conclusions that CHCCA and CHCSUA had networks with very similar structure, while the CHCSEA possessed a different structure.

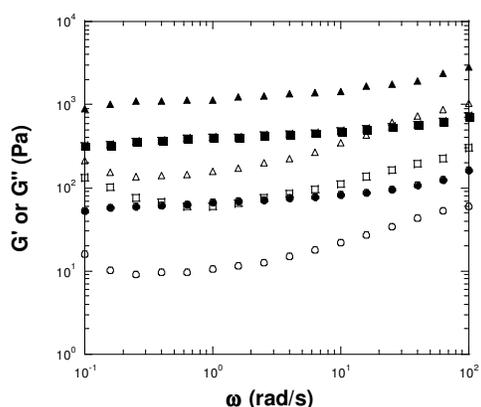


Figure 1: Linear viscoelastic properties of hydrogels containing 0.5%, 1.0% and 1.5% (wt%) CHCCA. Storage modulus (G') and loss modulus (G'') vs. frequency at 25 °C with 0.8% strain. G' – filled symbols, G'' – opened symbols; (●, ○): 0.5% (wt%) CHCCA; (■, □): 1.0% (wt%) CHCCA; (▲, △): 1.5% (wt%) CHCCA

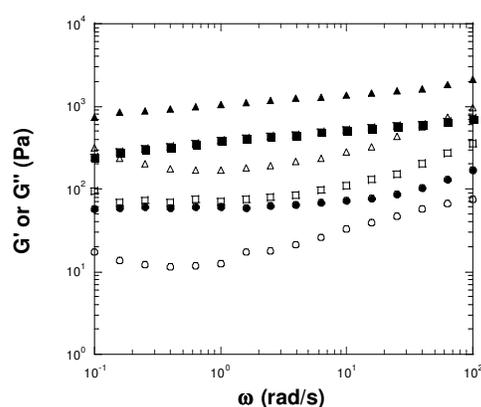


Figure 2: Linear viscoelastic properties of hydrogels containing 0.5%, 1.0% and 1.5% (wt%) CHCSUA. Storage modulus (G') and loss modulus (G'') vs. frequency at 25 °C with 0.8% strain. G' – filled symbols, G'' – opened symbols; (●, ○): 0.5% (wt%) CHCSUA; (■, □): 1.0% (wt%) CHCSUA; (▲, △): 1.5% (wt%) CHCSUA

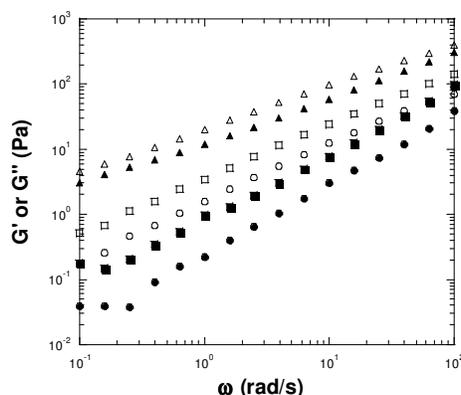


Figure 3: Linear viscoelastic properties of hydrogels containing 0.5%, 1.0% and 1.5% (wt%) CHCSEA. Storage modulus (G') or loss modulus (G'') vs. frequency at 25 °C with 5% strain. G' – filled symbols, G'' – opened symbols; (●, ○): 0.5% (wt%) CHCSEA; (■, □): 1.0% (wt%) CHCSEA; (▲, △): 1.5% (wt%) CHCSEA

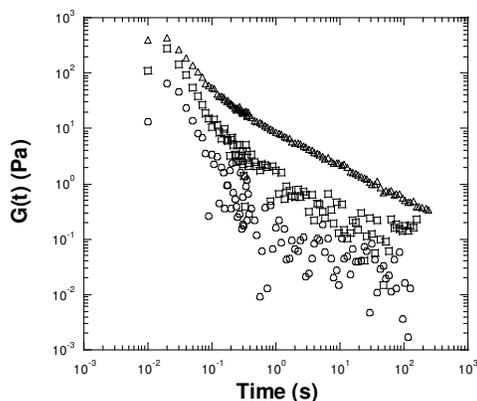


Figure 5: Stress relaxation measurements of hydrogels containing 0.5%, 1.0% and 1.5% (wt%) CHCSEA after being subjected to 5% strain at 25 °C; (○): 0.5% (wt%) CHCSEA; (□): 1.0% (wt%) CHCSEA; (△): 1.5% (wt%) CHCSEA

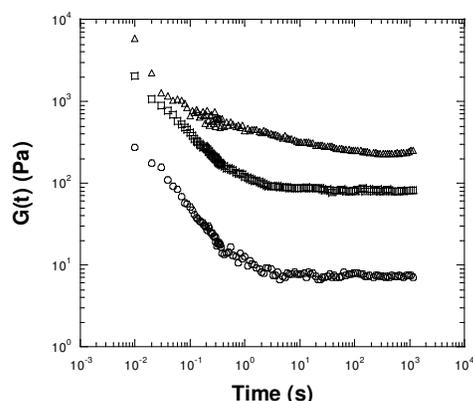


Figure 4: Stress relaxation measurements of hydrogels containing 0.5%, 1.0% and 1.5% (wt%) CHCCA after being subjected to 0.8% strain at 25 °C; (○): 0.5% (wt%) CHCCA; (□): 1.0% (wt%) CHCCA; (△): 1.5% (wt%) CHCCA

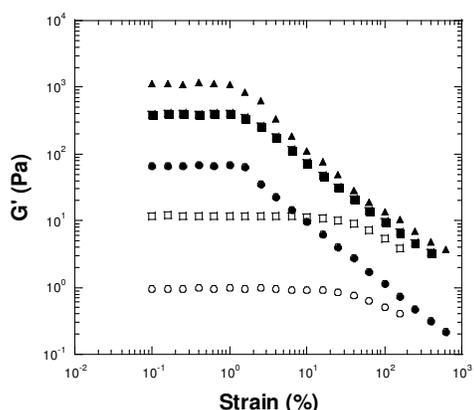


Figure 6: Strain sweep experiment of hydrogels containing CHCCA and CHCSEA with 1 rad/s frequency at 25 °C; (●): 0.5% (wt%) CHCCA; (■): 1.0% (wt%) CHCCA; (▲): 1.5% (wt%) CHCCA; (○): 0.5% (wt%) CHCSEA; (□): 1.5% (wt%) CHCSEA

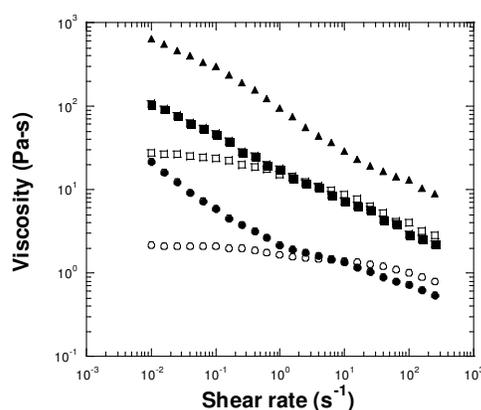


Figure 7: Non-linear viscoelastic properties of steady shear measurements of hydrogels containing CHCCA and CHCSEA at 25 °C; (●): 0.5% (wt%) CHCCA; (■): 1.0% (wt%) CHCCA; (▲): 1.5% (wt%) CHCCA; (○): 0.5% (wt%) CHCSEA; (□): 1.5% (wt%) CHCSEA

The non-linear viscoelastic properties for the CHCCA and the CHCSEA hydrogels are presented in Figure 7. The viscosities for the three concentrations of CHCCA exhibited similar shear thinning behaviors¹⁵ within the measured shear rates, that is, all three viscosity curves followed nearly the same power-law of about -0.35; and viscosity increased with the greater concentration of the CHCCA (Fig. 7). The viscosities for the CHCSUA exhibited nearly identical shear thinning behaviors to those of CHCCA (data not shown), which also supported that both CHCCA and CHCSUA hydrogels were composed of networks with similar structure. The non-linear viscoelastic properties for the CHCSEA hydrogel exhibited shear thinning during the relatively high shear rates, but the viscosity curves were not as

step as those for CHCCA. In addition, there were Newtonian regions¹⁵ of the viscosity curves for the CHCSEA, among relatively low shear rates (Fig. 7). These shearing experiment results also supported the above conclusions that the CHCCA and the CHCSUA hydrogel networks were very similar in structure, while the CHCSEA possessed a different structure.

The cellulose-based hydrogels crosslinked with citric acid, succinic acid, and sebacic acid in the current study are biodegradable. They can be used as materials for seed coating, paper pants/diapers, drug delivery, wound healing, and cosmetics. We previously found that the water absorption of this kind of biodegradable hydrogels can be adjusted by using different cross-linkers, and varying the concentrations of

the cross-linkers and cross-linking reaction temperatures (data not shown). The current work suggests that the properties of these cellulose-based hydrogels can be manipulated by altering the cross-linkers and hydrogel concentrations. Therefore, different hydrogels can be prepared according to their required properties for different applications.

CONCLUSION

In summary, we studied both linear and non-linear rheological properties of cellulose-based hydrogels cross-linked with citric acid, succinic acid, and sebacic acid. We found that the viscoelastic properties of this kind of biodegradable hydrogels can be manipulated with these three different cross-linkers and hydrogel concentrations. Therefore, we can prepare various inexpensive biodegradable cellulose-based hydrogels according to different applications, such as agricultural seed coating, paper pants/diaper materials, drug delivery, wound healing, and cosmetic materials.

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