

Novel Hydrogels of Malic Acid and Zinc; Their Synthesis and Characterization

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Hydrogels of malic acid and zinc (Zn/MA hydrogels) were synthesized by controlling pH values with 1.00 mol/l of NaOH solution, in which 0.25, 0.40, 0.50 and 1.00 mol/l of zinc ion solutions were added to 0.50 mol/l of malic acid solution, and the mixtures were used as starting solutions. Glassy hydrogels with transmittance of 20.0 to 88.2% were obtained in a narrow pH range of 6.4-7.2 and at zinc concentrations of 0.40 and 0.50 mol/l. Rheological measurements indicated that the storage (G') moduli were higher than the loss (G'') moduli in all specimens, which indicates that the Zn/MA hydrogels have an elastic property rather than a viscous property. The maximum G' and G'' values were 9.42 ± 0.25 and 5.45 ± 0.11 kPa in the Zn-MA gel with a zinc concentration of 0.40 mol/l at pH 6.5, and 355 ± 18 and 136 ± 44 kPa in that of 0.50 mol/l at pH 6.8. The viscoelastic properties depended on the density of crosslinking (zinc concentrations) in the gel structure and the formation of zinc hydroxide in the process of gel formation. The red-shift of Raman lines assigned to (-COO)/(-OH) and (C-OH) was observed in comparison with spectra of pure MA and the hydrogels. It means that the zinc ions bonded to both carboxyl and hydroxyl groups and generated chelation/polymerization with MA molecules. Metal carboxylate gels with such a high transmittance based on the MA and zinc have not been described.

Key words: hydrogel, zinc, malic acid, viscoelasticity, FT-Raman

1. INTRODUCTION

Metal carboxylate gels have been widely investigated as precursors to produce metal oxides and ceramics with a perovskite-derived structure, such as titanate, chromate and cuprate [1-3]. They have an advantage that metal ions are homogeneously distributed in the gel network and metal oxide with a size of nanometers can be obtained [4]. The size of oxides obtained is very important for application to biosensor [5, 6] and the coating of biocompatible metal substrate [7].

In metal carboxylate gels, a key issue in synthesis is the information of metal-carboxyl complexes since metal-carboxyl complexes are basic structural units in the gels. In metal-EDTA gels, metal ions are bonded to all the functional groups of EDTA molecules, and form metal EDTA complexes [8]. In metal-citrate acid-ammonia gels, metal ions are bonded to carboxyl and α -hydroxyl groups of citric acid. [9]. Uncomplexed carboxyl groups in the metal-citrate complexes can form ionic bridges with ammonium and metal ions of other complexes. Ammonium and metal ions play a role of crosslinking between metal-citrate complexes [10, 11].

The viscoelastic properties of the hydrogels depended on the density of crosslinking in the gel structure. The Pechini process using ethylene glycol increased the viscoelasticity of metal-citrate gels to reduce diffusion distance of metal ions and inhibit phase separation [12]. In an ethylene glycol medium, ester bonds are formed between the free carboxyl groups of metal-citrate complexes and alcohol groups of ethylene glycol. The

formation of ester bonds and ionic metal carboxylate bonds increases the viscoelasticity of the gels.

The gels containing zinc ions have been widely used for biomaterials, such as ointment, since zinc has an anti-inflammation property [13]. The ointment containing zinc-amino complexes alleviates the pain caused by the inflammation of skin. Zinc-carboxylate hydrogels have not been described except for zinc-citrate-ammonium gel. Ammonium is not suitable for a skin ointment and other biomaterials.

Malic acid (MA) is one of carboxylate in the citric acid cycle of metabolic system. It has two carboxyl and α -hydroxyl groups, and forms a wide variety of complex species with metal ions, such as chromium, copper and vanadium. MA acts as a bidentate ligand, in which metal ions are bonded to the carboxyl and α -hydroxyl groups [14-16].

In this study, we established a method to produce zinc carboxylate hydrogels based on 0.50 mol/l MA solution containing zinc ions at a wide variety of concentrations by adding 1.0 mol/l NaOH solution. The viscoelastic properties and the gel network of Zn/MA hydrogels were elucidated by using rheological measurements and FT-Raman spectra against different zinc concentrations.

2. EXPERIMENTS

2.1. Synthesis and characterization of Zn/MA gels

L(-)-MA powder (Wako Pure Chem. Co., Japan) was dissolved to 0.50 mol/l in distilled water. $ZnCl_2$ powder (Wako Pure Chem. Co., Japan) was

added into the solution up to zinc concentrations of 0.25, 0.40, 0.50 and 1.00 mol/l at room temperature. The Zn/MA solutions had lower pH values than 1.0. A NaOH solution (1.00 mol/l) was dropped into 10.0 ml of Zn/MA solutions to increase the pH to 5.5-7.5 while stirring.

The Zn/MA solutions were further stirred for 5 minutes and then stood for 24 hours at room temperature to form glassy hydrogels.

The optical transmittance of Zn/MA hydrogels was measured using HITACHI U-2000 double beam spectroscope at 500 nm. The Zn/MA gels were put into PMMA cells with the path length of 10 mm. Distilled water was used as a reference sample. The measurement was conducted 3 times at room temperature. Furthermore, the samples were put into quartz cells with the path length of 10 mm. FT-Raman spectra were measured with Perkin Elmer NIR FT-Raman GX spectrometer under a laser power of 1.1 kW, an accumulation time of 256 and the resolution at 4 cm^{-1} . Raman spectra were obtained at a region of 400 to 2000 cm^{-1} at room temperature.

2.2 Rheological measurement

Viscoelastic properties were investigated with the viscoelastic meter RheoStressRS1 (HAAKE, Germany), equipped with plate-plate tools of 20 mm in diameter with the gap length of 1 mm. After adding of a NaOH solution to Zn/MA solutions while stirring for 5 minutes, the solutions were run into a silicone sheet bored through 20 mm in diameter and 1.5 mm in depth. The samples were carefully pinched with polypropylene and glass boards, extra samples were flew out, and then the samples were held in a constant humidity vessel until measurement was done. All measurements were conducted at room temperature (298±0.5K). Before starting any measurement, the Zn/MA hydrogels were rested for 1 minute, allowing the stress induced during sample loading to be released.

The extent of a linear viscoelastic region was determined by performing a stress sweep measurement under the conditions that the shear stress was changed from 0.1 to 1000 Pa and the frequency was fixed at 1.0 Hz. In the low strain region, the values of G' and G'' , and tangent delta values were evaluated at various pH values. The dynamic frequency sweep was conducted by applying a constant shear stress of 1.0 Pa within the linear region over a frequency range between 0.1 and 10 Hz.

2.2 Theory of Rheology

Rheological parameters used were the storage (G' in Pa) and loss (G'' in Pa) moduli, and the tangent phase angle (tangent delta) and the complex shear (G^* in Pa) moduli. The G' modulus provides information about the elasticity or the energy stored in the material during deformation, whereas the G'' modulus indicates the viscous character or the energy dissipate as heat. The ratio between the viscous and elastic moduli is expressed by the following loss tangent:

$$\tan\delta = G''/G' \quad (1)$$

where δ is the phase angle.

The combined viscous and elastic behavior is given by the absolute value of the complex shear module G^* as a function of the frequency ω in Hz:

$$G^*(\omega) = (G'(\omega)^2 + G''(\omega)^2)^{1/2} \quad (2)$$

The experimental data of all frequency sweep tests are correlated by the following power law:

$$G^*(\omega) = (G'(\omega)^2 + G''(\omega)^2)^{1/2} = A\omega^{1/z} \quad (3)$$

The correlation between G^* and ω is obtained by the following linear regression analysis:

$$\log G^* = z^{-1} \log \omega + \log A \quad (4)$$

The slope is the reciprocal of z and the intercept at $\omega = 1.0$ Hz is $\log A$

The parameter A is the gel strength in the power law relaxation at the gel point modulus of gel:

$$G(t) = A t^{-n} \quad (0 < n < 1) \quad (5)$$

The n is the relaxation exponent. The A provides the information of the gel for the cross-linking density [17-22].

3. RESULTS

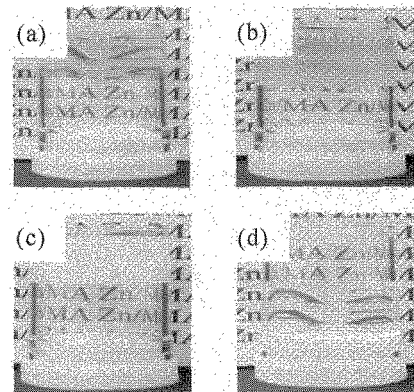


Photo 1. The resultant compounds of Zn/MA. (a) Glassy hydrogel, (b) hydrogel, (c) opaque gel, (d) no gelation.

3.1 Characterization of Zn/MA hydrogels

Glassy hydrogels (Photos 1-a, -b) with the transmittance over 20.0% were obtained in narrow ranges of pH and zinc concentration. The pH range was 6.4 to 7.2 and the zinc concentrations were 0.40 and 0.50 mol/l. In the case of a zinc concentration of 0.40 mol/l, the polymerization reaction did not occur at lower pH values (ca. pH 6.0) and the specimens had high transmittance (ca. 98.0%). Opaque white gels (Photo 1-c) were obtained by adding 13.0 ml a NaOH solution. By increasing the volume of a NaOH solution, viscous solutions with precipitations of small fragments were obtained and then zinc hydroxide precipitations were formed. The adding of a NaOH solution probably induced the polymerization/chelation of zinc ions with the MA molecules and the formation of zinc hydroxide. The glassy

hydrogels were formed under the competition of the two reactions.

The polymerization reaction between zinc ions and MA was completed within 12 hours after adding of a NaOH solution due to the equilibrium of transmittance. The specimens obtained just after the addition were opaque because a drastic reaction occurred between acid and alkali. The pH value gradually increased with the reaction time. The transmittance of the hydrogel at a zinc concentration of 0.40 mol/l was 88.2 %. This indicates that zinc ions are uniformly distributed in the glassy hydrogel.

In FT-Raman spectra, pure MA solution without zinc ions at pH 2.0 had -C=O Raman lines at $1725/834\text{ cm}^{-1}$ and the double Raman line of -C=O that completely diminished with increasing pH values. Moreover, the $\nu_s(\text{COO})$ Raman line of pure MA in the solution at pH 7.0 appeared at 1341 cm^{-1} . Another $\nu_s(\text{COO})$ Raman line of pure MA in the solution at pH 2.0 was observed at 1409 cm^{-1} (free group), and those at pH 7.0 at 1418 cm^{-1} (dissociated group) and 1403 cm^{-1} (free group). The $\delta_s(\text{OH})$ and $\nu_{as}(\text{C-OH})$ Raman lines of pure MA in the solution at pH 7.0 were also detected at $1233/1087\text{ cm}^{-1}$ as same as reported previously [23,24].

The Zn/MA hydrogels with zinc concentrations of 0.40 and 0.50 mol/l also had the $\nu_s(\text{COO})$ Raman lines at 1327 and 1328 cm^{-1} , and these Raman lines showed a red shift compared with those of pure MA solution. Other $\nu_s(\text{COO})$ Raman lines of Zn/MA hydrogels with zinc concentrations of 0.40 and 0.50 mol/l appeared at around 1400 cm^{-1} were each split into 3 Raman lines at 1444 , 1421 and 1400 cm^{-1} , and 1448 , 1426 and 1403 cm^{-1} , respectively. This indicates that zinc ions were bonded to the carboxyl groups of MA in the polymerization process.

The $\delta_s(\text{OH})$ and $\nu_{as}(\text{C-OH})$ Raman lines of the Zn/MA hydrogels with zinc concentrations of 0.40 and 0.50 mol/l were detected at 1210 , 1097 and 1080 cm^{-1} , and 1211 , 1090 and 1077 cm^{-1} , respectively. These Raman lines shifted in a complex manner towards red and blue compared with those of pure MA in the solution at pH 7.0. Therefore, the α -hydroxyl groups of MA affected the formation of the Zn/MA hydrogels. The strong Raman line newly appeared at 881 cm^{-1} in the Zn/MA hydrogels is probably assigned to Zn-O-Zn vibration. This Raman line was not observed in the spectra of opaque white gels under any conditions.

3.2 Rheological properties

The G' and G'' values were highest at 11.5 ml of a NaOH solution. The highest G' and G'' values of the specimen at a zinc concentration of 0.40 mol/l were $9.42 \pm 0.25\text{ kPa}$ and $5.45 \pm 0.11\text{ kPa}$, respectively, which were lower than those at a zinc concentration of 0.50 mol/l (G' : $354 \pm 18\text{ kPa}$ and G'' : $136 \pm 44\text{ kPa}$). These results indicate that the amounts of zinc ions in the hydrogels are strongly correlated with the viscoelastic properties because the increase in the zinc content increased the polymerization among the zinc ions and the carboxyl or hydroxyl groups of MA. Furthermore, the G' moduli were higher than the G'' moduli in

all specimens, which indicates that the Zn/MA hydrogels have an elastic property rather than a viscous property.

Figure 1 shows the gel strength (A) calculated by the equation (4) that is based on rheological theory. The gel strength of Zn/MA hydrogels with a zinc concentration of 0.50 mol/l was highest at an additional volume of 11.5 ml of a NaOH solution at $223 \pm 21\text{ kPa s}^{1/2}$, which was coincident with the changes of G' and G'' moduli.

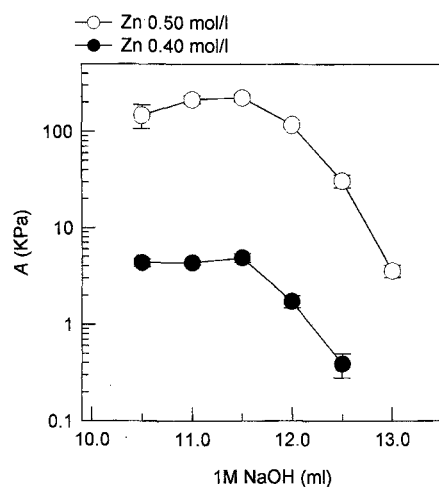


Figure 1. The gel strength (A) values of Zn/MA hydrogels with zinc concentrations of 0.40 and 0.50 mol/l due to the amounts of NaOH solution.

The increase of zinc concentrations caused an increase of crosslinking density and a drastic increase of gel network strength at about two orders of magnitude. The A values of the opaque white gels were smaller than those of the glassy hydrogels. These results indicate that an excess addition of NaOH to the Zn/MA solutions does not polymerize MA molecules with zinc ions but forms zinc hydroxide. The G' and G'' moduli increased with time. The formation of network structure was completed within 12 hours due to the equilibrium of G' and G'' moduli. The tangent delta values were lower than 1.0 in the polymerization process, which indicates that the hydrogels obtained forms a three-dimensional network structure within a 12 hours.

4. DISCUSSION

The Zn/MA hydrogels obtained are classified into metal carboxylate gel with a three-dimensional network formed through an inorganic polymerization process. We have succeeded the gel formation of Zn/MA without adding ammonium ions. FT-Raman spectra indicated that an interaction between zinc ions and the carboxyl/hydroxyl groups of MA resulted in a red shift as observed in the glassy hydrogels. In Zn/MA hydrogels, the crosslinks between zinc and MA complexes are ionic zinc-carboxylate and zinc-hydroxylate bonds. Further experiments concerned with the detailed structure of the Zn/MA complexes are needed, however, the

inorganic polymerization reaction was supported by the appearance of a new Raman line at 881cm^{-1} assigned to $\nu(\text{Zn-O-Zn})$ of the hydrogels and rheological measurements.

The glassy hydrogels were formed in a narrow pH range of 6.4 to 7.2. The dissociation of carboxyl groups of MA (the dissociation constant pK_2 of 5.05) was strongly correlated with the polymerization process since the hydrogels were obtained at the pH over 6.4. The three-dimensional gel network of glassy hydrogels was constructed in the existence of the complexes of zinc ions and MA molecules, and no precipitation of zinc hydroxide. The excess amount of NaOH resulted in the pH values over 7.2 and zinc hydroxide was precipitated. The opaque white gels obtained at the pH values over 7.2 contained zinc hydroxide and thus their rheological strength was lower than that of the glassy hydrogels.

5. CONCLUSION

Glassy Zn/MA hydrogels with high viscoelasticity were successfully synthesized by adding a NaOH solution to zinc and MA solutions. The gels were formed in a narrow pH range of 6.4 to 7.2 and zinc concentrations of 0.40 and 0.50 mol/l. The parameter A was introduced to provide the information of the gel for the cross-linking density. The A and G' moduli of glassy hydrogels showed the highest values when 11.5 ml of NaOH solution were added into the Zn/MA solutions. At this point, chelation and polymerization process was generated. The FT-Raman spectra demonstrated a new Raman line at 881cm^{-1} assigned to Zn-O-Zn and a red shift of the carboxyl and hydroxyl groups of MA. Zinc ions were bonded to carboxyl and hydroxyl groups of MA molecules.

6. REFERENCES

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