Phase Transition Behaviors of Hydroxypropyl Methylcellulose Induced By Small Molecular Weak Acids

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Abstract

In this paper, phase change material hydroxypropyl methylcellulose (HPMC) was chosen to investigate the influence of small molecular weak acids on its phase transition temperature. The results showed that all of the chosen small molecular weak acids such as acrylic acid (AA), methacrylic acid (MAA), DL-lactic acid (LA), citric acid (CA) and acetic acid (AAc) can trigger the decrease of phase transition temperature of HPMC at different pH. With the increase of pH, AA, LA, CA and AAc can further lower the phase transition temperature, on the contrary, the phase transition temperature of HPMC increased with MAA. The change range of LCST was largest around pKa compared with other pH values because triggering effect changed gradually from hydrogen bonding effect to salt effect upon the increase of pH. Besides, phase transition temperature can also be reduced by the increase of acid concentration. This is attributed to smaller distance between molecules caused by higher concentration leading to stronger hydrogen bonding effect or salt effect. This paper provided a new perspective to modulate the LCST of phase change material by small molecular weak acids at different pH.

Introduction

Recently, phase transition behavior of thermosensitive natural polymers such as methyl cellulose (MC), hydroxypropyl cellulose (HPC), hydroxypropyl methylcellulose (HPMC) have attracted wide research interest because of their wide applications in personal care products, foods, pharmaceuticals and construction materials (Barros & Silva, 2018; Bashir et al., 2013; Fagundes et al., 2014; Jain et al., 2014; Ji et al., 2020; Jing & Wu, 2013; Karaca et al., 2014; Li et al., 2021; Park et al., 2013; Walter et al., 2012). Especially, HPMC is an important cellulose ether which has been widely investigated (Espert, Salvador, & Sanz, 2020; Tundisi et al., 2021). Its aqueous solution has a phase transition temperature, also called lower critical solution temperature (LCST) at which the polymer solution will cloud or precipitate, so how to lower phase transition temperature has a great significance especially when it is used as dispersant, emulsifier, thickener and so on (Zhong et al., 2020). Ji et al. (Ji et al., 2020) found that pH has a significant effect on the phase separation and gel behavior of gelatin (GA) and HPMC in binary solutions and gels. The morphology and rheological properties of GA/HPMC blends are affected by the competition of molecular chain coalescence and gelation (curing) rates. It can provide new ideas for the design of functional foods and edible packaging materials. Researchers have tried to modulate the phase transition temperature of HPMC aqueous solution by various external stimuli such as salts and additives. Almeida et al. (Almeida, Rakesh, & Zhao, 2014) examined the effects of salt solution (NaCl and CaCl₂) on HPMC solutions and manifested phase transition temperature shifted to lower temperature with increasing NaCl and CaCl₂ concentration. Liu et al. (Liu, Joshi, & Lam, 2008) also demonstrated that LCST of HPMC shifted to a lower temperature as increasing NaCl concentration as well. Xu et al. (Xu et al., 2006) found that as the ionic strength increased, the phase transition temperature of HPMC decreased with a negative linear correlation. Besides, Joshi et al. (Joshi & Chen, 2009) investigated how surfactants affected sol-gel transformation temperature in aqueous HPMC/surfactant mixtures and discovered that they can either increase or suppress the LCST of HPMC aqueous solution. The influence of substituted phenols on

HPMC phase transition was examined by Banks et al. (Banks et al., 2014), it is observed that phase transition temperature was suppressed concentration dependently. Richardson et al. (Richardson et al., 2006) investigated the influence of L-amino acid molecular structure on phase transition temperature of HPMC and manifested that small hydrophilic amino acids lowered the transition temperature, whereas large hydrophobic aromatic amino acids increased this temperature.

However, pH effects on HPMC phase transition behaviors haven't been systematically reported. Small molecular weak acids can be easily mixed with HPMC and have obvious advantages in manipulating pH of solution, and were chosen as additives to investigate its influence on HPMC phase transition behaviors. Herein, based on the significance of HPMC in practical application, phase transition behaviors of HPMC aqueous solution triggered by five different small molecular weak acids, acrylic acid (AA), methacrylic acid (MAA), DL-lactic acid (LA), citric acid (CA), and acetic acid (AAc) were investigated. To achieve better insight into the interplay between HPMC and small molecular weak acids, the effects of pH and concentrations of acids have been investigated. All of the added weak acids triggered the LCST to a lower temperature, which may be explained by the hydrogen bonding interaction between HPMC polymers and -COOH of small molecular weak acids shown in Fig. 1.

Experimental Section

Materials

Hydroxypropyl methylcellulose (Mn=120,000), acrylic acid (AA), methacrylic acid (MAA), DL-lactic acid (LA) were provided by the Sigma-Aldrich Chemical Company. Citric acid (CA) and sodium hydroxide (NaOH) were from Sinopharm Chemical Reagent Co. Ltd. Acetic acid (AAc) was from Kunshan Jingke Microelectronic Materials Co. Ltd.

Preparation of HPMC and small molecular weak acid mixtures with different pH and concentrations.

Firstly, 2 wt. % HPMC aqueous solution was prepared by dissolving HPMC polymers in deionized water under constant stirring for 4 days at room temperature. 0.67 mol/L AA solution were prepared and its pH value was adjusted to be 3.0, 3.5, 4.0, 5.0, 6.0 using NaOH solution. 2 wt.% HPMC solution was added to the above solutions, respectively, then the mixture was stirred for another 20 minutes, thus mixed solutions with different pH were prepared. HPMC solution adjusted by other weak acids with different pH values was also prepared as above mentioned, as was shown in Table 1.

Table 1
Ingredients for Mixed Solution of HPMC polymer and Small
Molecular Weak Acids

Acids	AA	MAA	LA	CA	AAc	
mol/L	0.5 0.7	0.4 0.6	0.4 0.6	0.1 0.3	0.7 0.9	
pH	3.0	3.0	3.0	3.0	3.0	3.0
	3.5	4.0	3.5	4.0	4.0	3.5
	4.0	4.5	4.0	5.0	4.5	4.0
	5.0	5.0	5.0	6.0	5.0	4.5
	6.0	6.0	6.0	7.0	6.0	5.0
	/	/	/	/	7.0	6.0
The concentration of HPMC polymers was 0.5 wt. %.						

UV-Vis spectrophotometer characterization of solution phase transition behavior

0.5 wt.% HPMC aqueous solutions with different pH and concentrations adjusted by small molecular weak acids were measured at the wavelength of 500nm with a heating rate of 0.5°C/min by means of UV-visible spectrophotometer (Perkin Elmer, USA), respectively.

Results And Discussion

Hydrogen bonding effect of small molecular weak acids.

The phase change behaviour of HPMC solution was characterized through the transmittance of the solution by UV-Vis spectrophotometer. 0.5 wt.% HPMC aqueous solution was heated from 55°C to 80°C at a heating rate of 0.5°C/min. Upon heating, the transmittance decreased dramatically at a critical temperature, then transmittance-temperature curves were made. The phase transition of 0.5wt.% HPMC aqueous solution occurs at 69.6°C, it may be due to the delicate hydrophilic-hydrophobic balance of HPMC polymers structure (Yao et al., 2011). At low temperature in polar solvents, HPMC polymers are soluble in pure aqueous solution due to its relatively large dipole moment with a gauche orientation for C-C bonds and a trans conformation for C-O bonds in the hydroxypropyl group, while the temperature is increased, the solvent water becomes weak polar and dipole moment of hydroxypropyl group reduces to such an extent that phase transition occurs (Lu, Hu, & Schwartz, 2002). So it was possible to further lower the phase transition temperature of HPMC by adding small molecules containing carboxyl group (-COOH) due to the hydrogen bonding between -COOH and HPMC polymer chains were stronger than that between HPMC polymer and water, then five different small molecular weak acids that all had -COOH were selected to study whether they can affect the phase transition temperature of HPMC aqueous solution or

not, which were acrylic acid (AA), methacrylic acid (MAA), DL-lactic acid (LA), citric acid (CA), and acetic acid (AAc). Based on 0.5 wt.% HPMC, the concentration of AA was set to be 0.5 mol/L, LA 0.4mol/L, CA 0.1mol/L, AAc 0.7mol/L and MAA 0.4mol/L.

The results showed that all the small molecular weak acids can depress the LCST of HPMC aqueous solution at different pH values. **Fig. 2** summarized the variation of LCST after adding acids into HPMC aqueous solution. In an acidic solution of pH=3.0 where $\text{pH} < \text{pK}_a$, MAA and AA showed a relatively stronger hydrogen bonding effect compared to another three acids. Especially, the largest depression of LCST was triggered by MAA, which was about 21.4°C, followed by AA, which was about 8.5°C. For another three acids, it was relatively smaller, which was about 2.7°C induced by LA, 2.1°C by CA, and 0.4°C by AAc. In general, acids existed in molecules state when $\text{pH} < \text{pK}_a$. When acids and HPMC were mixed, the hydrogen bonding between HPMC and acids formed as shown in **Fig. 1**, acids acted as a proton donor and HPMC acted as a proton acceptor (Yao et al., 2011). The decrease of phase transition temperature was attributed to the formulation of hydrogen bonding between the -COOH of acids and the hydroxyl group (-OH) of HPMC polymer chains which screened the access of water molecules to HPMC polymer chains and decreased the solubility of HPMC in water, thus resulting in the increase of hydrophobic association of HPMC polymer chains (Liao et al., 2012). Here, MAA and AA demonstrated a stronger depression effect than the other three acids, it may due to conjugated bonds in their structure, which results in the hydrogen bonds between HPMC and the two acids being more stable than those between other three acids.

PH effect of small molecular weak acids.

As shown in **Fig. 2**, with the increase of pH, acids became dissociated and present an ionic state step by step, so the triggering effect changes from hydrogen bonding effect to salt effect. For AA, LA, MAA and AAc, their pK_a was 4.35, 3.85, 5.5, and 4.75, at meanwhile, CA has three pK_a values, which is 3.15, 4.77 and 6.40 respectively. When $\text{pH} \approx \text{pK}_a$, hydrogen bonding effect took the leading role. however, the salt effect was gradually dominant with the increase of pH value. For AA, it manifests hydrogen bonding effect in the molecular state at $\text{pH} < 4.35$ and salt effect at $\text{pH} > 4.35$. As we can see from **Fig. 2**, LCST had a slight depression upon the increase of pH, which meant that salt effect was slightly dominated than hydrogen bonding effect, which led to the small change in LCST. For LA, its suppression effect on LCST improved with increasing pH, which indicated that salt effect triggered by LA was superior to hydrogen bonding effect. Relatively sharper trend was observed around 3.85, pK_a of LA, which is virtue of acids existing in a comparatively single state, either molecules or ions, but in a changing state around pK_a . For CA, three pK_a values contributed to a little alter of shifty trend, slightly change can be caught as $\text{pK}_a > 6.40$, the third pK_a of CA. For AAc, an apparent reducing tendency can be observed upon the increase of pH, especially around 4.75, pK_a of AAc, though it makes little difference to LCST in $\text{pH}=3.0$. Distinct from others, hydrogen bonding effect takes the leading role in contrast with salt effect for MAA. **Fig. 2** shows that MAA has a most powerful hydrogen bonding effect in $\text{pH}=3.0$ and a sharp tendency change around $\text{pH}=5.5$, pK_a of MAA. However, the highest LCST of HPMC aqueous solution. For AA, LA, CA and AAc, LCST decreased upon the increase of pH was due to more salt ions attracting more

hydration water molecules around them and disrupting the structured water around the hydrophobic side groups on the HPMC chains to form water cages (Liu et al., 2008). But to MAA, LCST increased with increasing pH may be attributed to the hydrogen bonding between HPMC and MAA being stronger than the attraction of salt ions to hydration water molecules or it may be related to steric effect, polarity effect or pKa.

Above all, all five acids at pH=3.0 triggered the phase transition of HPMC aqueous solution to occur at a lower temperature. The triggering effect of MAA was the strongest, followed by AA, LA and CA, while AAc made little difference. With the increase of pH values, AA, LA, CA and AAc can further lower the phase transition temperature and the trigger effect of AAc was strongest while AA was weakest as pH elevated from 3.0 to 6.0. In contrast to another four acids, MAA caused the phase transition to occur at the lowest temperature.

Concentration effect of small molecular weak acids.

To explore how acid concentrations affected the phase transition temperature of HPMC, concentration of acids was improved to be 0.2mol/L and the transmissivity data of solutions were collected, the pH of solution was fixed to be 3.0 and the LCST verse pH curves were shown in **Fig. 3**. The phase transition temperature of HPMC aqueous solution can be further reduced by increasing the acids' concentration. MAA had the largest reduction scope, followed by CA, AA, LA and AAc, pH was then varied to investigate the combined effect. As shown in **Fig. 4A**, the reduction range of LCST was improved by increasing CA concentration and pH values, and it reached 26.7°C as pH=6.0. In **Fig. 4B**, depression range of LCST by increasing AAc concentration was 5.1°C as pH=6.0 and LA was 4.2°C (**Fig. 4C**). However, the depression range of LCST triggered by increasing acid concentration was smaller for AA (**Fig. 4D**) and MAA (**Fig. 4E**), which was 2°C and 0.4°C, respectively. For AAc, CA, LA and AA, hydrogen bonding is weaker at pH<pKa than salt effect at pH>pKa, then the variation of LCST at pH<pKa is smaller than that of pH>pKa. For MAA, hydrogen bonding effect was superior to salt effect and LCST decreased in a large extent at pH<pKa than that at pH>pKa. To our best knowledge, the higher concentration, the smaller distance between molecules, thus the hydrogen bonding became stronger while increasing the concentration of acids at pH<pKa, and the decrease of phase transition temperature was attributed to a stronger hydrophobic association. Similarly, higher concentration accounted for stronger salt effect, which finally resulted in the further depression of LCST.

Conclusion

Phase transition temperature of hydroxypropyl methylcellulose induced by small molecular weak acids at different pH and concentrations was investigated. When pH=pKa, phase transition temperature of HPMC decreased sharply as it enhanced the hydrophobic association through formation of hydrogen bonding between carboxyl group of acids and oxhydryl of HPMC polymer chains, and screened the access to HPMC polymer chains for water molecules. With the increase of acids pH, LCST of HPMC can be further decreased by AA, LA, CA and AAc, except for MAA. Around pH=pKa, the tendency was sharpest. And

triggering effect changed from hydrogen bonding effect to salt effect upon the increase of pH. For all five small molecular acids, higher concentration of acids results in lower LCST of HPMC as higher concentration leads to stronger triggering effect.

Declarations

Conflict of interest

The authors declare that they have no conflicts of interests.

Consent for publication

All authors have read and approved this version of the article, and due care has been taken to ensure the integrity of the work. We declare that none of the work contained in this manuscript is published in any language or currently under consideration at any other journal. All authors agreed to submit manuscript to “Cellulose” for publication.

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Figures

Figure 1

Schematic illustration of hydrogen bonding between hydroxypropyl methylcellulose (HPMC) and small molecular weak acids.

Figure 2

LCST of HPMC in present of various small molecular weak acids

Figure 3

Depression of LCST induced by increasing acids concentration for 0.2 mol/L at pH=3.0

Figure 4

Effect of five acids concentration at different pH on LCST of HPMC: (A) CA, (B) AAc, (C) LA, (D) AA and (E) MAA.