Smart Membranes for Flavor Delivery

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Abstract

This work focuses on the use of temperature-responsive gels (TRGs, polymeric hydrogels with a large temperature-dependent change in volume) for flavor retention at cooking temperatures. Specifically, we study a system with a lower critical solution temperature (LCST) that exhibits a two-phase region at elevated temperatures. A gel featuring a LCST swells at low temperatures and collapses at high temperatures. In the collapsed state the polymer acts as a transport barrier, retarding loss of volatile flavors. We have successfully modified a cellulose polymer to exhibit this volume change and have encapsulated an oil phase inside the gel.

Introduction

Hydrogels are hydrophilic polymer networks that can imbibe many times their weight in water yet (due to chemical or physical crosslinks, entanglements, or crystallinity) do not dissolve. Hydrogels have been utilized extensively in different industry applications such as super absorbent diapers, soft-tissue engineering, and drug delivery.

One interesting class of hydrogels change their volume in response to some environmental stimuli such as temperature,[1-3] PH,[4-7] solvent composition or electric field; among these, temperature responsive gels (TRGs) have attracted considerable interest in recent years. A TRG can alternate between a swollen state (absorbing water) and a shrunken state (expelling water) near the transition temperature. The response is commonly realized as a change in volume as well as a change in other characteristics such as opacity and mechanical properties. The critical temperature of volume transition is called the critical gel transition temperature (CGTT). Specifically, this paper focuses on TRGs with inverted phase transition behavior. In other words, as the temperature increases above the CGTT, the gel shrinks with the concomitant expulsion of water. On the contrary, when the temperature decreases below the CGTT, the gel reversibly swells absorbing the aqueous solution. This type of transition occurs for polymers that exhibit a LCST.

Because of this unique volume change behavior, such gels have been proposed as smart carriers that can store and release drugs triggered by body temperature (controlled drug release). This paper demonstrates a TRG membrane for encapsulation of a core material consisting of an oil phase loaded with flavor. At high temperature, the wall is collapsed, forming a dense film with low permeability to flavor in the oil core. At low temperature, the wall is swollen in presence of water, forming a loose film with relatively high permeability to flavor. If the critical temperature is appropriate, flavor is retained at high temperature during cooking or baking; while the flavor is released at body temperature or through mechanical disruption in the mouth.

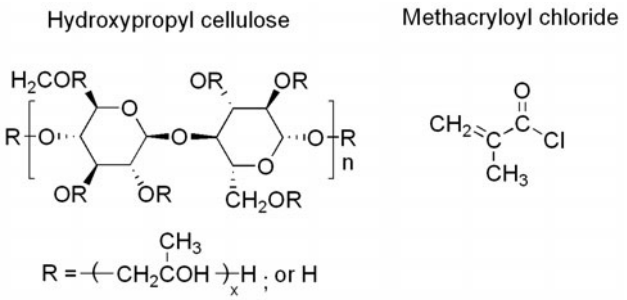

Figure 1: Chemical structures of HPC and MAC. Cellullose is functionalized with hydroxypropyl groups, where "x" is an integer 1-3, or hydrogen to form HPC.

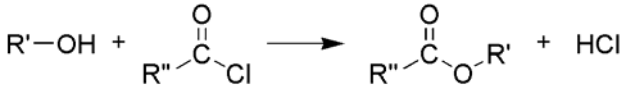

Figure 2: Reaction schematic between HPC and MAC. R' represents the HPC minus the reactive hydroxyl groups and R'' represents the vinyl group on the MAC. The reaction takes place between the hydroxyl group on the HPC and the carbonyl group on the MAC while forming HCl as the byproduct.

The goal of the project is to produce a TRG that is a good candidate for FDA approval. This goal has proven elusive since a responsive system has to meet many criteria to be suitable. One way to avoid toxic crosslinkers is to modify HPC by introducing double bonds to the polymer chain and allowing the crosslinking reaction to occur through unsaturation points with initiation by ultraviolet (UV) light.[8-9]

The modification reaction is esterification of the HPC with the acid chloride methacryloyl chloride (MAC) (Figure 1). The vinyl group on the MAC provides the unsaturation points for crosslinking. The reaction occurs between a hydroxyl group in the HPC and the carbonyl group in the MAC. The chloride and the hydrogen ions are abstracted to form hydrochloric acid and the carbonyl group is restored. The chemical formula of HPC is illustrated in Figure 1 where the functional group R represents a hydroxypropyl group and hydrogen or just hydrogen. The reaction scheme is simplified in Figure 2 where the HPC, except for the hydroxyl groups, is replaced with the functional group R' and the vinyl group in the MAC is replaced with R''.

Experimental

Hydroxypropyl cellulose was obtained from Sigma Aldrich (Mw ~80,000 Mn ~10,000) along with n,n-dimethylacetamide (DMAc) and methacryloyl chloride. Food grade oil, miglyol 812 was obtained from Givaudan Flavors in Cincinnati, OH.

Vinylization is accomplished by dissolving 10-wt% HPC in DMAc at 60°C with nitrogen purge. Under nitrogen purge, 10-vol% MAC is mixed with DMAc in a separate flask and then added dropwise to the HPC solution at 60°C. The solution is left to react for 24 hours and then removed from heat. The vinylized HPC is precipitated in ether and purified by dissolving the modified polymer in methanol and then precipitating with ether for several cycles. After final precipitation the modified HPC is placed in a vacuum oven to remove residual solvent.

The encapsulation process utilized is an oil/water/oil (O/W/O) emulsion method. An oil-in-water emulsion is created by dissolving 10-wt% vinylized HPC in water and adding miglyol to the HPC solution in a ratio of 1 part miglyol to 3 parts HPC solution. The mixture is emulsified utilizing a sonicator for several minutes until a milky homogeneous solution is obtained. The HPC is crosslinked by utilizing ultraviolet light. In UV crosslinking the emulsion is added to a Teflon bowl containing approximately 3 times as much miglyol as emulsion. The solution is placed under (approximately 1 inch from the bulbs) a UVP XX-15S 254-nm UV lamp and is stirred at 500 rpm to break down the emulsion into small spherical droplets. After several minutes of stirring the UV lamp initiates the crosslinking reaction. After crosslinking for several

hours, the microcapsules are removed by filtration, thoroughly rinsed with water, and dried at ambient temperature.

Thin HPC films are formed by casting polymer solutions into glass molds in order to study the diffusion properties. The films are prepared by either crosslinking the polymer in solution or in bulk after allowing the film to dry in the mold. All films are crosslinked for one hour utilizing the UV lamp described previously and all films are placed approximately 1-2 inches from the UV bulb.

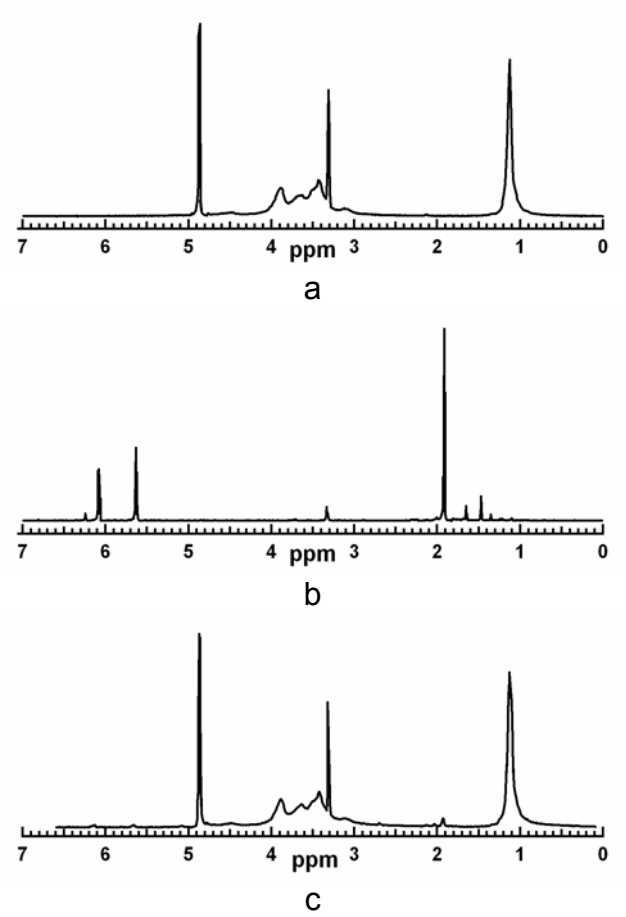

Figure 3: NMR spectra of (a) unmodified HPC, (b) methacryloyl chloride, (c) modified HPC. Carbon-carbon double bonds appear in the methacryloyl chloride spectrum near 5.6 and 6.1 ppm. These peaks also appear in the modified HPC spectrum indicating the HPC has been successfully modified.

A vertical diffusion cell from Hanson Research is utilized for the diffusion studies with the lower cell filled with water and the upper cell with 1000 ppm solution of benzaldehyde in miglyol. Samples are measured for benzaldehyde concentration utilizing UV visible spectrophotometry at a single wavelength of 280 nm. All samples are either performed at room temperature or at 60°C.

Results and Discussion

The modification of the HPC is characterized by 1H NMR. All samples are referenced to MeOH-d3 at 3.31 ppm. The NMR spectra of unmodified HPC as received from Aldrich (Figure 3a), methacryloyl chloride (Figure 3b), and vinylized HPC (Figure 3c) are compared. The NMR spectrum of methacryloyl chloride gives rise to three strong peaks with two peaks near 5.6 and 6.1 ppm indicating the carbon-carbon double bond. After modification, these peaks again show in the modified HPC NMR spectrum.

From the NMR spectra, it is clear the HPC has been successfully modified. Modification is also revealed by crosslinking since unmodified HPC does not crosslink. After vinylization, the critical temperature of the polymer is depressed by several degrees depending on the amount of modifier added (Figure 4). This result supports the idea that hydrophobicity lowers the LCST. In other words, by changing the ratio of hydrophilic and hydrophobic groups on the polymer, the LCST can be tailored to a desirable temperature.

Light scattering is utilized to characterize the gel microcapsules. A Micromeritics Saturn Digisizer™ particle size analyzer performed the measurements. Light scattering is a technique utilizing Mie scattering theory to resolve the morphology of particles within the range of 0.1-1000 μm. Light scattering illuminates a sample with laser light (658 nm according to Micromer-

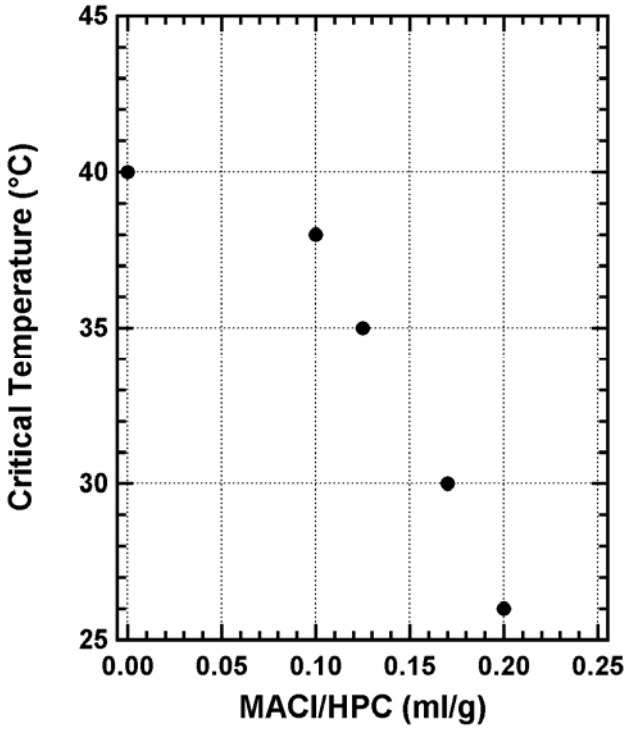

Figure 4: Depression of lower critical solution temperature as the amount of modification increases.

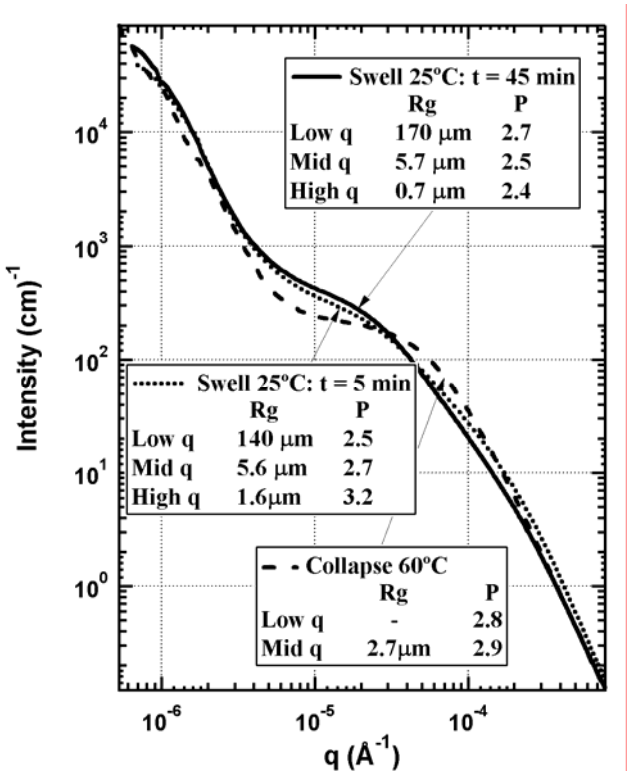

Figure 5: Light scattering data of gel microcapsules indicated three length scales large (low q), overall capsule size; intermediate (mid q), oil containing pores; and small (high q), polymer struts and voids.

itics) and a CCD camera collects the scattered intensity as a function of angle to the incident beam. Mie theory relates the scattered intensity as a function of wavelength, angle, particle size, and refractive index. Analysis of the scattered intensity leads to the prediction of the sample morphology

Light scattering was performed on gel capsules at room temperature and at 60°C (Figure 5). The radius of gyration (Rg) and the Porod exponent (P) are obtained for several size scales. These parameters are utilized to evaluate morphological features within the sample.

Morphological features at multiple size scales are seen in the data throughout the q range for the capsules at room temperature. For most of the data, three length scales are needed to fit the data (roughly 1 μm, 5 μm and 160 μm). The 160 μm corresponds to the over-

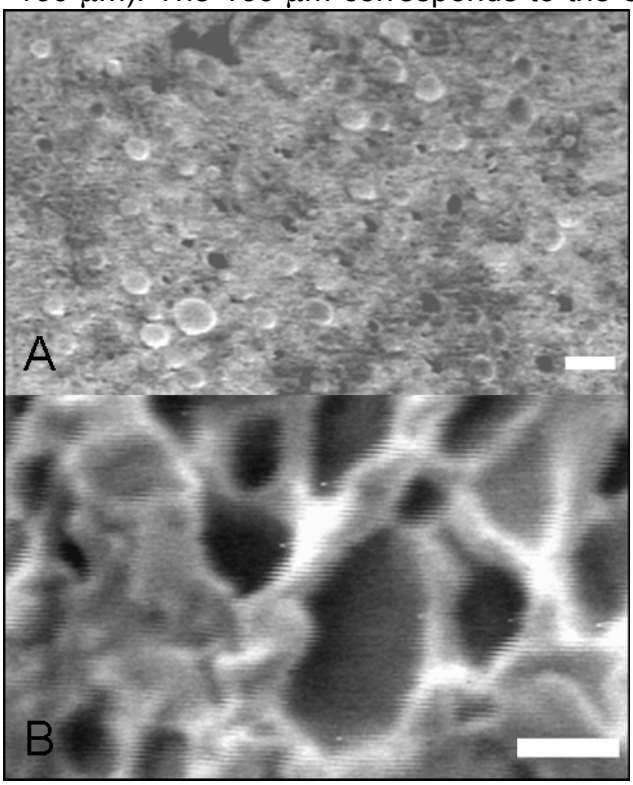

Figure 6: SEM images of a cross sectioned microcapsule. A: Low resolution image at 100x and a scale bar of 50 μm. B: High resolution image at 25,000x and a scale bar of 0.5 μm. Both images reveal porous morphology.

all size of the microcapsules. The domains at 5 μm are due to the secondary oil phase within the capsule, which can readily be seen as pores in the SEM images of the capsules (Figure 6). The domains near 1 μm are possibly due to voids or spaces between the polymer struts since the radius of gyration decreases during swelling.

During swelling the large-scale domains get larger while the small-scale domains get smaller. In the collapsed state (60°C) only the intermediate length-scale is observed (Radius of gyration, Rg = 2.7 μm). The large-scale domains are too large to be resolved by the instrument. That is the capsules appear larger in the "collapsed" state. This observation could be explained by aggregation of the capsules.

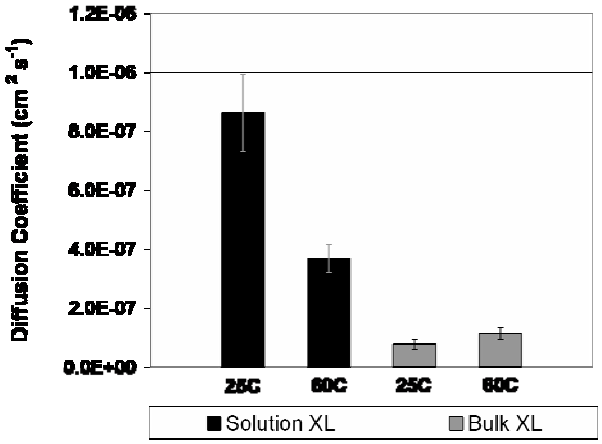

Figure 7: Diffusion coefficients for benzaldehye through hydrated solution crosslinked and bulk crosslinked HPC films at 25°C and 60°C

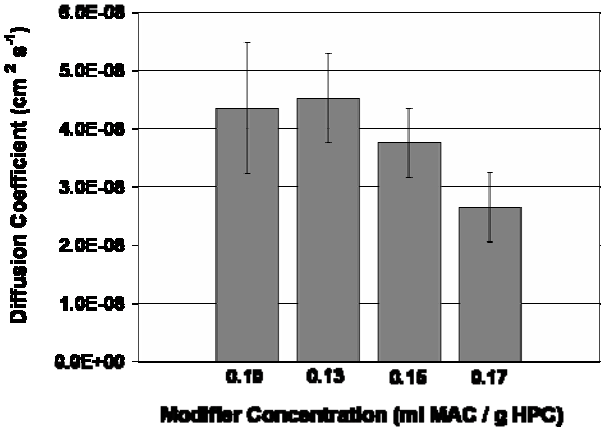

Figure 8: Diffusion coefficients for benzaldehyde through hydrated bulk crosslinked HPC films. The diffusion coefficient decreases as the modifier concentration increases.

Diffusion data are calibrated utilizing a benzaldehyde calibration curve of UV absorbance for known benzaldehyde concentrations in water. The diffusion coefficient is calculated by equations 1 and 2 according to Peppas.[10]

$$\ln(1-\frac{2C_t}{C_0}) = \frac{2A}{V}Pt \qquad (1)$$

$$D = \frac{Pl}{K_d} \qquad (2)$$

Here, C_t is the concentration of the diffusing species at time t, C_0 is the concentration of the chromophore in the donor cell, A is the area of permeation, V is the cell volume, P is the permeability coefficient, D is the diffusion coefficient, l is membrane thickness, and K_d is the partition coefficient. A linear plot of equation 1 versus time gives the slope P which is used to determine the diffusion coefficient utilizing equation 2.

The transport data show the diffusion coefficient for a solution crosslinked film is higher than the dry or bulk crosslinked film (Figure 7). Also, the change in diffusion coefficient above the LCST for the solution crosslinked film is lower and more pronounced than the bulk crosslinked film. The data also indicate (Figure 8) the greater the degree of modification (defined by the concentration of modifier added during modification), the lower the diffusion coefficient.

Conclusions

Hydroxypropyl cellulose methacrylate is synthesized by grafting vinyl groups to hydroxypropyl cellulose. The grafting reaction introduces hydrophobicity to the polymer chain. The increased hydrophobicity is indicated by the depression of the LCST for the hydroxypropyl cellulose methacrylate compared to that of the virgin hydroxypropyl cellulose. The LCST of the polymer becomes lower as the amount of modification increases.

Utilizing a multiple emulsion method, microcapsules of a temperature responsive gel containing oil droplets are produced. The temperature responsive gel is synthesized by crosslinking hydroxypropyl cellulose methacrylate through the double bonds. The microcapsules also respond to temperature.

Transport studies indicate a decrease in the diffusion coefficient for solution crosslinked films as the temperature increases above the LCST. This decrease is attributed to the collapsed (denser) morphology of the gel above the LCST. As the modifier concentration increases the diffusion coefficient decreases for the bulk crosslinked films.

Acknowledgement

This work was supported by the Membrane Applied Science and Technology (MAST) Center at the University of Cincinnati through funding by the National Science Foundation and Givaudan Flavors in Cincinnati, OH. The facilities of the Manuel Lujan Jr. Neutron Scattering Center are gratefully appreciated. This work was supported in part by the Office of Basic Energy Science, U.S. Department of Energy.

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