Assembly of Thermo-Responsive Microcapsules

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Abstract:

Microcapsules are currently employed for a number of applications ranging from drug delivery vehicles to capsules contained in cosmetic products. In these applications, it is desirable that the microcapsules be able to control the timing of the release of their contents with external stimuli such as temperature changes or light illumination. The focus of this research was to design thermo-responsive microcapsules. Microcapsules were assembled as double emulsions using microfluidic polydimethylsiloxane (PDMS) devices. By varying the flow rates of the inner and middle phases, and by varying the composition of the middle phase that, after it has been polymerized, yielded the capsule shell, it was possible to control the thickness and thermo-response of the capsules.

Background:

Microcapsules having shells composed of polymers having a lower critical solution temperature (LCST) are well known [1]. Capsules, consisting of a shell that has a LCST, are shriveled at a temperature above the LCST of the polymer and are impermeable to hydrophilic molecules. When the capsules are brought to a temperature below the LCST, they swell, the shells become hydrated, and the capsules become permeable to hydrophilic molecules, thereby releasing their encapsulants.

Conversely, microcapsules having shells composed of polymers having an upper critical solution temperature (UCST) are much less researched. Contrary to polymers that have an LCST, capsules containing a polymer having a UCST would swell and release their encapsulants at temperatures above the UCST. These have numerous possible biomedical, cosmetic, and chemical applications not accessible using capsules with an LCST or no thermo-response.

In this research, we used microfluidic PDMS devices to fabricate double emulsion templates (Figure 1) for microcapsules containing a polymer (poly[2-(methacryloyloxy)ethyl dimethyl-(3-sulfopropyl)ammonium hydroxide]) (PMEDSAH) having a UCST [2]. Additionally, we studied the thermo-response of PMEDSAH in bulk as a function of the amount of triacrylate crosslinker added to the PMEDSAH hydrogel at different temperatures.

Experimental Procedure:

First, the solutions used for the inner, middle, and outer phases of the drops were prepared. The inner phase was 20% DEXTRAN with a molecular weight of 70 kDa, while the outer phase was HFE 7500 with 1% by weight of a fluorinated surfactant. Three different middle phases containing a solution of 2-(methacryloyloxy)ethyl dimethyl-(3-sulfopropyl)ammonium hydroxide (MEDSAH) and the photo initiator Irgacure 2959 with varied concentrations of cross linker were prepared. One-third parts ethanol was added to increase solubility of the triacrylate crosslinker.

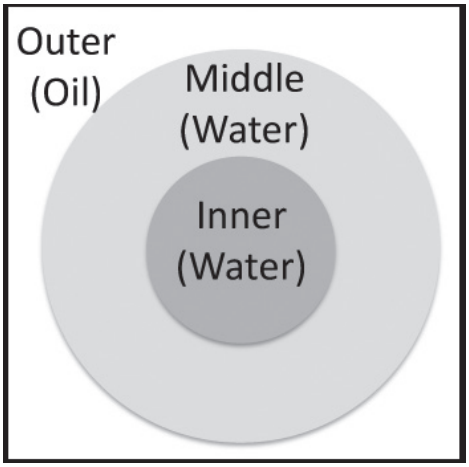

Figure 1: Water/water/oil double emulsion used as template for manufacture of microcapsules.

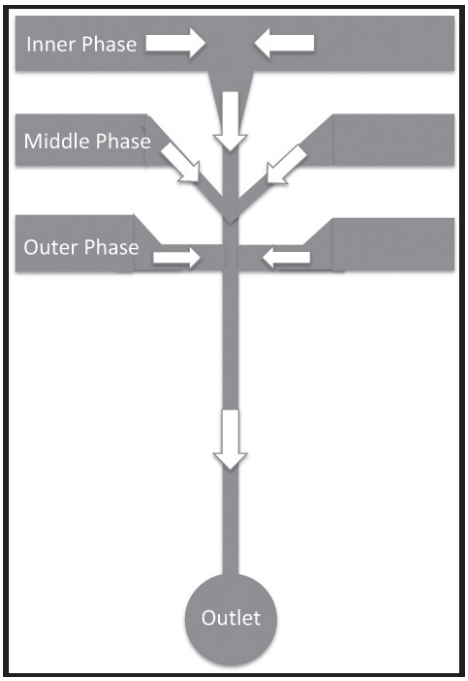

Figure 2: Diagram of microfluidic device used for manufacture of microcapsules.

The three solutions were then injected into a polydimethylsiloxane (PDMS) microfluidic device (Figure 2) with a channel width of 40 μm, using volume flow rate controlled pumps at flow rates varying between 0 and 100 μl/hr for the inner and middle phases, and 1000 μl/hr for the outer phase. The resulting emulsion containing monodisperse microcapsules was collected in vials and placed into a vacuum chamber for 12 hours to remove oxygen. After air bubbles were removed, the samples were irradiated with UV light for 15 minutes to initiate polymerization of the shell (creating pMEDSAH), and heated in an oven at 40°C for 24 hours in order to allow complete polymerization of the shell.

Additionally, samples of the middle phase were synthesized in bulk so as to measure the thermo-response of the PMEDSAH. Cylindrical molds were created by cutting the top off of ½-inch Falcon© tubes and affixing them to Petri® dishes using vacuum grease as an adhesive. Solutions of the middle phase containing no triacrylate crosslinker, 25 mg/mL crosslinker, and 250 mg/mL crosslinker were pipetted into the molds. As above, these samples were placed in a vacuum for a minimum of 30 minutes in order to remove oxygen, and then exposed to ultraviolet radiation to initiate polymerization. The samples were again rested for at least 24 hours in order to ensure that polymerization had completed.

The samples were removed from their molds, their dimensions measured, and placed into individual Petri dishes. Each dish was filled with water and sealed with strips of Parafilm to prevent evaporation. Samples of each crosslinker concentration were placed at 24, 40, and 65°C and their dimensions measured every hour.

Results and Conclusions:

Microcapsules were successfully assembled using water/water/oil double emulsions as templates. The 100% encapsulation efficiency and high degree of monodispersity make assembly of capsules using microfluidic devices advantageous.

The results of the thermo-response of the bulk samples of the middle phase are shown in Figure 3. One conclusion of this experiment is that crosslinker is necessary to create a thermo-responsive polymer in water, as all samples containing no crosslinker dissolved within two hours of placement in water. However, while some crosslinker is necessary, lower concentrations of crosslinker seem to yield a greater thermo-response. Additionally, the samples stored at 65°C seem to exhibit a greater thermo-response than those stored at lower temperatures. These results matched the expected outcome.

Future Work:

The microcapsules need to be quantitatively analyzed to determine if varying the rates of infusion for the inner and middle phases during assembly can control the shell thickness. More data needs to be collected for the middle phase in bulk to confirm a correlation between concentrations of cross linker, temperatures, and thermo-response.

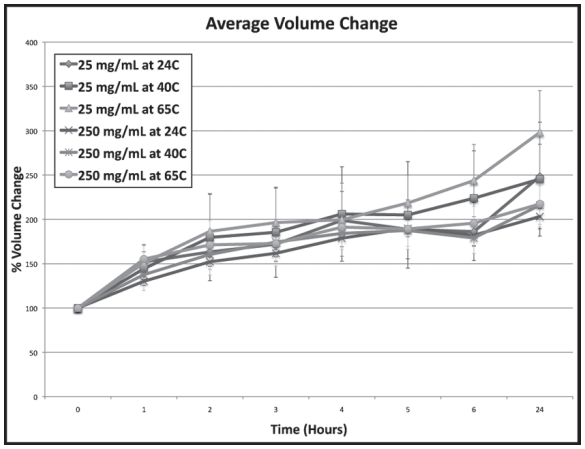

Figure 3: Average volume change of middle phase over time at varying cross linker concentrations and temperature.

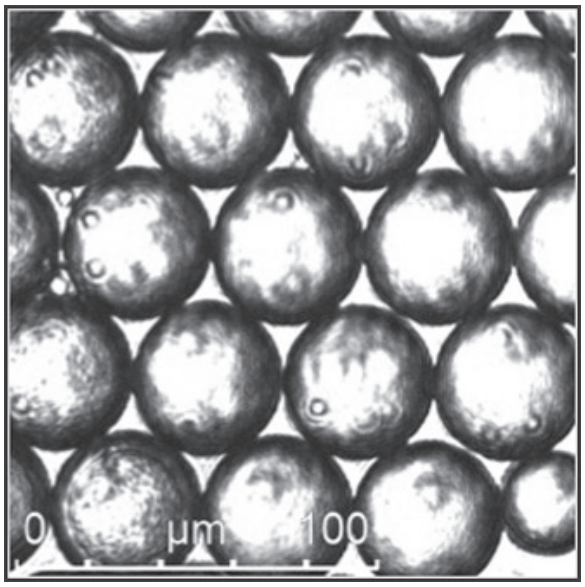

Figure 4: Confocal image of microcapsules assembled at inner and middle flow rates of 50 µl/hr.

Acknowledgments:

I wish to acknowledge my P.I. David A. Weitz and my mentor Esther Amstad, Kathryn Hollar, Jorge Pozo, Anna Hurlimann, and Tom Kodger for their contributions as well as the National Nanotechnology Infrastructure Network Research Experience for Undergraduates Program and the National Science Foundation for funding.

References:

[1] Seiffert, S.; Thiele, J.; Abate, A. R.; Weitz, D. A. J. Am. Chem. Soc. 2010, 132, 6606-6609.

[2] Xia, Y. N. and Whitesides, G. M. "Soft Lithography." Angewandte Chemie-International Edition 1998, 37(5), 551-575.