Oil Core and Silica Shell Nanocapsules: Toward Controlling the Size and the Ability To Sequester Hydrophobic Compounds

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Nanocapsules were synthesized using the droplets of an oil-in-water microemulsion as a template. Ethyl butyrate was solubilized in normal saline using Tween-80, lecithin, and *n*-octadecyltrimethoxysilane as surfactants. A polysiloxane/silicate shell was formed at the surface of the mixed surfactant layer by cross-linking *n*-octadecyltrimethoxysilane and tetramethoxysilane. The shell stabilized the oil droplets against coalescence as seen by transmission electron microscopy (TEM) of the samples immediately following the synthesis and months afterward. The diameter of nanocapsules can be controlled by using different component ratios, as measured by quasi-elastic light scattering (QELS) and TEM. The efficacy of nanocapsules to sequester hydrophobic compounds made by using different formulations was studied by UV−visible spectrometry. The results showed that nanocapsules with smaller diameters are generally more efficient in the uptake process than larger ones.

Introduction

Nanosized particles have shown a great potential for encapsulation of guest molecules. Representative examples include solid lipid nanoparticles (SLNs),[1,2] nanoparticles,[3−5] microspheres,[6,7] liposomes,[8,9] polymer vesicles,[10] host−guest carriers,[11,12] and shell cross-linked knedel-like nanoparticles (SCKs).[13,14] A previous study reported that one possible strategy to prepare nanocapsules[15] is through the formation of microemulsions.[16] Oil-in-water (O/W) microemulsions are transparent, optically isotropic solutions, which are thermodynamically stable with oil droplet diameters < 250 nm, dispersed in a continuous domain of water.[17] Self-assembled block copolymers, surfactants, or microemulsion droplets are the most commonly used templates for the formation of mesostructured silica materials.[18] The morphology of templates is a function of surfactant geometry and concentration.[19] In this study we intentionally used surfactant with low cpp (critical packing parameter)[18a] at low concentration (<15 wt %) to obtain spherical microemulsion droplets. The creation of a spherical shell around the droplets suppresses coagulation and rupture. Exhibiting a robust character, nanocapsules avoid the morphological changes that can occur for their microemulsion precursors under environmental variations such as changes in ionic strength,[20] solvent system,[21] pH,[22] and temperature.[23,24] Core−shell systems of similar size to those investigated here exist in the literature and were able to encapsulate guest molecules. Examples of such systems include core−shell coarse emulsions,[25] onion-like layered particles,[26] SCKs,[27] poly(organosiloxane) nanospheres,[28] and polymersomes.[29]

Alkoxysilanes are well-known for their use in the formation of mesostructured materials. *n*-Octadecyltrimethoxysilane (compound **1**) forms a thin silicon oxide layer on an

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air/water interface. This layer can be cross-linked to form a stable floating 2D network material at an aqueous interface.[30] The cross-linking is achieved through condensation of the surface methoxysiloxane groups of **1**. As shown in a previous study, when the condensation of **1** occurs in the presence of hexadecane (oil) and Brij 97 (surfactant), it will form fortified oil-in-water (O/W) microemulsions.[16] The current study expands on this concept, forming nanocapsules from a more biocompatible oil phase, ethyl butyrate (compound **2**),[31] and surfactants such as Tween-80 (compound **3**)[32] and lecithin (compound **4**).[33,34]

The goal is to prove the generality of the templated microemulsion approach in the formation of nanosized capsules using ingredients that are approved by the Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition (CFSAN).[35] Controllability over particle size is demonstrated through the variation of the concentration of the formulation ingredients. Nanocapsules of different size show different sequestering ability toward a model hydrophobic compound.

In particular, we are interested in potential intravenous drug detoxification applications since overdoses pose a significant ongoing problem.[36] Many life-threatening drugs and insecticides do not have antidotes, and therapy is restricted to stabilizing the patient. One possible strategy, which involves the reduction in bioavailability of toxic compounds within the body, is relatively unexplored.[37] In addition to detoxification, the nanocapsules also may have applications as biosensors[38] through modification of their reactive silica surface.[39] Furthermore, they might serve as nanoreactors in catalysis[40,41] and extraction dots for removal of organic compounds in wastewater treatment.[42]

Experimental Section

General Synthesis of Nanocapsules. Octadecyltrimethoxysilane (**1**, Gelest Inc.) was distilled at 117 °C (0.1 mm Hg) prior to use. All other chemicals were used as-received. Tween-80 (**3**, 1.0 g, Sigma-Aldrich Chemical Co.), ethyl-butyrate (**2**, 0.1 g, Sigma-Aldrich Chemical Co., $\rho = 0.878$ g/mL), lecithin (**4**, 0.1 g, Alfa Aesar) were dissolved in 8.8 mL of normal saline (9 g/L NaCl, 3×10^2 mOsmol/L). Normal saline was chosen because it simulates human plasma and is the most commonly used medium for intravenous injections. The solution was heated with stirring to 70 °C for 24 h, which resulted in the formation of a microemulsion. Upon cooling of the mixture to room temperature (RT), compound **1** (0.03 g) was added and the mixture was heated for 24 h. The solution was cooled to RT and the pH was lowered to pH 2.5 using 0.5 M $HCl_{(aq)}$. The solution was stirred for 30 min at RT to hydrolyze **1**.[43] After 30 min, 1.4 mL of HEPES buffer (3-(2-hydroxy-ethyl)-piperazine-1-ethane-sulfonic acid, 0.1 M, Sigma-Aldrich Chemical Co.) was added to the solution, and the pH was increased to pH 7.4 using 0.5 M $NaOH_{(aq)}$. The HEPES buffer maintained the weakly basic pH to prevent flocculation of the nanocapsules.[44] Solutions at this point will be referred to as "oil cores" or "oil templates". The droplet size and morphology were analyzed by QELS and TEM. Tetramethoxysiloxane (**5**, 0.01 g, Sigma-Aldrich Chemical Co.) was added, and the solution was stirred for 24 h. A schematic of the synthesis is presented in Figure 1. Separate samples were prepared following the procedure described above, by systematically varying the amount of **3** between 3 and 15% w/w, the amount of **2** between 0.55 and 2.5% w/w, the amount of **4** between 0.17 and 2.2% w/w, the amount of **1** between 0.1 and 0.4% w/w, and the amount of **5** between 0.07 and 0.88% w/w. Solutions with higher **3** to **2** ratios were heated for shorter periods of time, while those with lower **3** to **2** ratios were heated longer. The purpose of creating these different samples was to investigate how each component affected the size and sequestering efficiency of the resulting nanocapsules.

The nanocapsules were purified by dialysis. Dialysis was performed using Spectra/Por molecular porous membrane tubing with a molecular weight cutoff of 6000−8000 Daltons. The nanocapsule solution was poured into wetted tubing and placed in 1000 mL of Millipore ultrapure water (18 $M\Omega cm^{-1}$). The external water was replaced every hour for the first 4 h and then left overnight. The following day, the external water was changed every 8 h for a total of 48 h of dialysis. When dialysis was complete, the solution was stored in a sealed container for later use. The size of the oil templates and nanocapsules was determined by QELS and TEM.

Transmission Electron Microscopy. Contrast for transmission electron microscopy (TEM) was achieved by adding 1-dodecene (**6**, Sigma-Aldrich Chemical Co.) as a dopant to the nanocapsule oil core. A 10-fold diluted stock solution of nanocapsules was placed dropwise onto a carbon-coated nickel grid and left overnight to allow water to evaporate. The grid was placed in a sealed container, where OsO_4 vapor diffused through the polysiloxane/silicate to stain **6** in the core of the nanocapsules. The grids were stained for not less than 4 h. TEM images were obtained using an Hitachi H-7000 microscope at 75 kV. The size analysis was performed using Analysis software by averaging the size of a minimum of 20 nanocapsules per image and minimum of 10 when the concentration of **5** was >0.5 wt % (the solutions had to be dilute to prevent aggregation upon drying). Data were compared with images of three independently made formulations. Spherical oil cores were observed for the vast majority of samples (along with occasional unswollen

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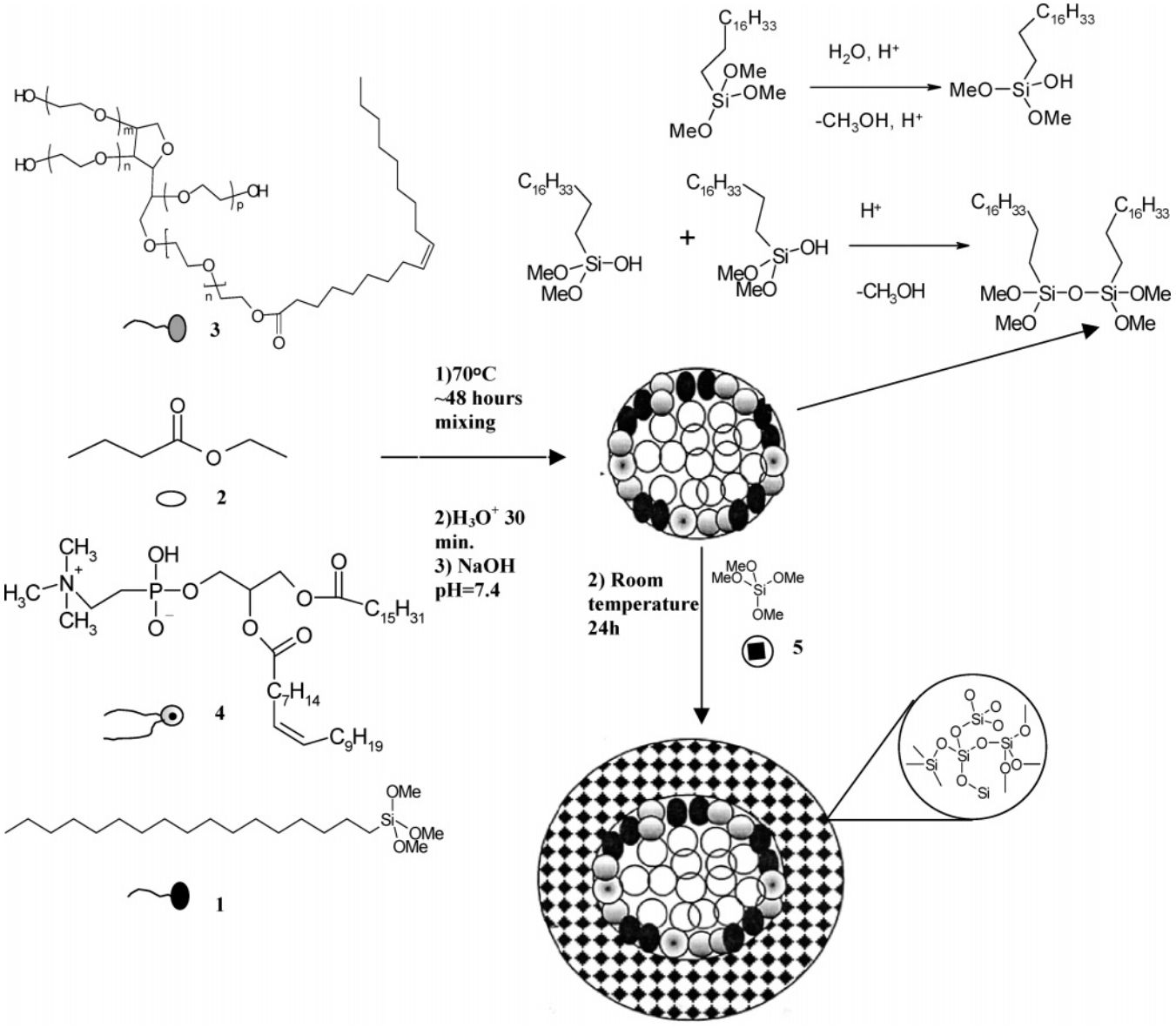

Figure 1. Schematic of the formation of nanocapsules. Step 1: Formation of a microemulsion using Tween-80 (3), ethyl butyrate (2), lecithin (4), and octadecyltrimethoxysilane (1). (**1** is added 24 h after **2**, **3**, and **4**, see Experimental Section.) Step 2: Stabilization of a microemulsion by condensing tetramethoxysilane (**5**) on the surface of a mixed surfactant layer.

micelles of **3**), except for the samples with high concentration of compound **4**, where large emulsion droplets and ellipsoids were observed. (See Supporting Information, pg 5.) Although this method revealed limited parts of the overall sample, the results obtained were in agreement with light scattering measurements.

Particle Size Analysis. All particle size analyses were achieved by quasi-elastic light scattering (QELS) using a self-calibrating Precision Detectors, Inc. (PDI) Particle Sizing Instrument. Sample cells were cleaned using a pressurized air duster and rinsed three times with Millipore ultrapure water (18 $M\Omega cm^{-1}$). The data were analyzed using PDI Software. A silica particle standard (100 ± 3 nm diameter, Duke Scientific Corporation) was used for a single-point check of the calibration, which yielded 103 ± 2 nm. Figure 2 shows the most frequently observed pattern included two peaks, a smaller one (6−10 nm) attributed to unswollen micelles of **3** and larger one attributed to microemulsion droplets ("oil cores") or nanocapsules. Dialysis removed the majority of unswollen micelles and we analyzed just larger oil cores or nanocapsule peaks. Data presented are derived from the average of four independently made formulations (data in Figures 4, 5, 7, and 8 refer to oil core/nanocapsule peaks).

Quinoline Uptake. Quinoline (**7**, Sigma-Aldrich Chemical Co.), a hydrophobic drug mimic $P_{o/w} = 115$ (oil/water partition coefficient) was monitored by its absorption peak at 299 nm. The stock solution of oil templates/nanocapsules (200 μL) was diluted with saline (buffered at pH 7.4) (1.8 mL); 10 μL (0.085 mmol) of **7** was added to the solution. Resulting solutions were stirred for 1 h and then filtered through 0.025 μm pore filters (Millipore Corporation) to remove free **7** and the spectrum was obtained. A 10 μL aliquot of the resulting solution was taken and diluted with 3.6 mL of normal saline in a cuvette. Note that the final concentration of oil templates/nanocapsules in a cuvette was lower (e.g., 0.055 w%) and concentration of **7** higher (~130 μmol) than in a method we already reported.[16] The decrease in absorption at 299 nm between control and respective solutions was measured. The UV−visible spectra were obtained using a Varian Cary UV−Visible−NIR instrument. Results are shown as rel.% = 100% − $(A_x/A_{tot}) \times 100$, where A_{tot} and A_x are absorbencies of the control sample and the sample of interest, respectively. The detection limit for 7 was 2 μmol and absorption in the concentration range used to asses the uptake ability of oil cores/nanocapsules obeyed the Beer−Lambert law. All spectra were scanned in a double-beam mode with normal

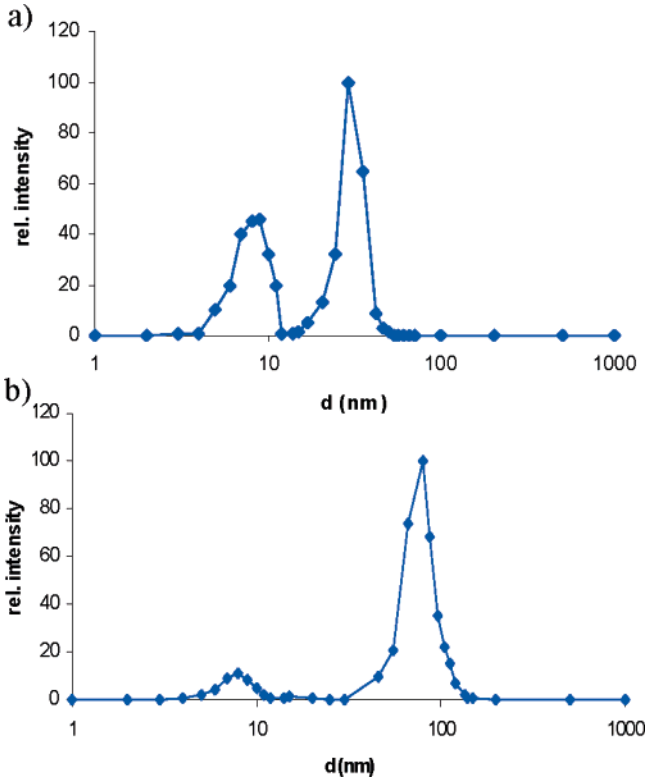

Figure 2. Size distribution of microemulsion (a) before adding compound **5** and (b) after adding compound **5** and subsequent dialysis. (Peak at 7−10 nm is due to unswollen micelles of **3**.[16])

saline as the reference. Each point presented here is the average with respective standard deviations (STD) of three independently made formulations.

Results and Discussion

General Synthesis of Nanocapsules. Various trials were conducted using compounds **1**−**4** to form a stable microemulsion. The trials revealed that **1** and **4** do not form microemulsions with **2** in the absence of **3**. Neither **1** nor **4** alone self-assemble in saline to form microemulsions. Optical microscopy revealed that all attempted solutions containing **1**, **2**, **3**, and **4** without heating were turbid due to formation of micrometer-sized coarse emulsion droplets, or other phases, instead of microemulsions. Furthermore, all of the aforementioned samples were thermodynamically unstable and phase separation occurred within hours, and such samples were not further studied.

In the approximate composition window of (3−15):(0.5−2.5):(0.3−2.5):(0.1−0.4)(% w/w ratios of **3:2:4:1**), most of the resulting solutions became clear upon heating, with the appearance of a bluish color indicating the formation of a microemulsion.[45] Formulations having relatively high concentrations of **4** (i.e., 2−2.5 w%) were turbid and phase-separated to a microemulsion phase and unidentified milky dispersion[52] after 24 h. On subsequent cooling, the O/W microemulsion was stable at RT for at least 72 h after which

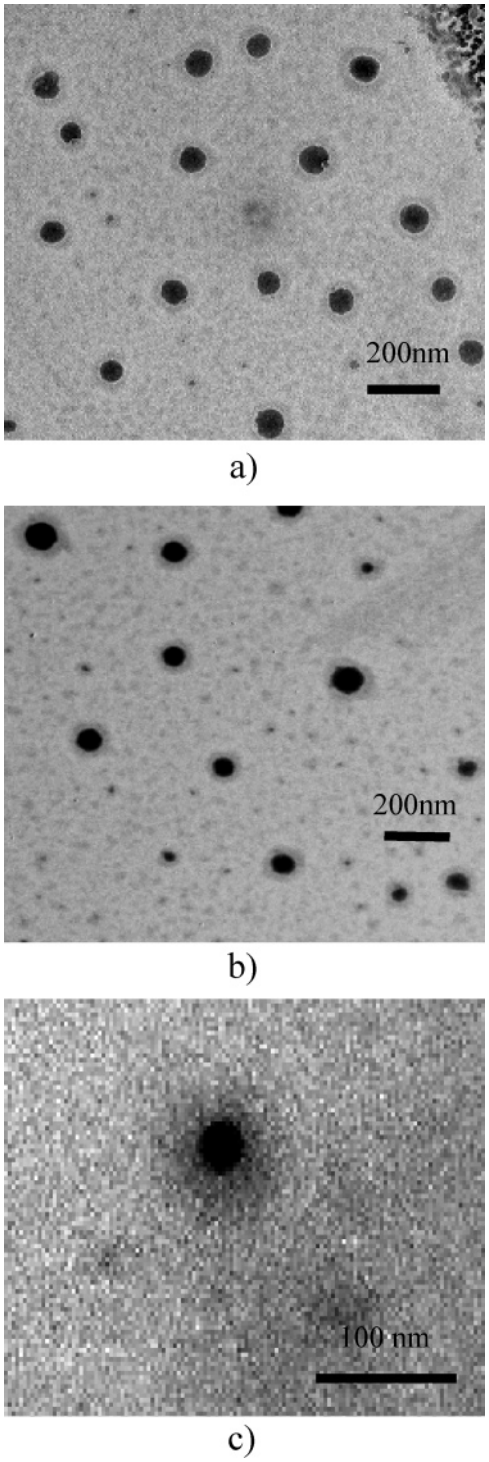

Figure 3. TEM images of nanocapsules with dark areas representing the cores stained with $OsO_{4(g)}$ surrounded by a lighter, unstained silicate shell: (a) immediately after synthesis, (b) 10 months after synthesis, and (c) an image of a single nanocapsule taken at high magnification.

coagulation occurred and the sample became cloudy. It should also be noted that while a large and rich literature exists of the phase behavior of a diverse range of assemblies

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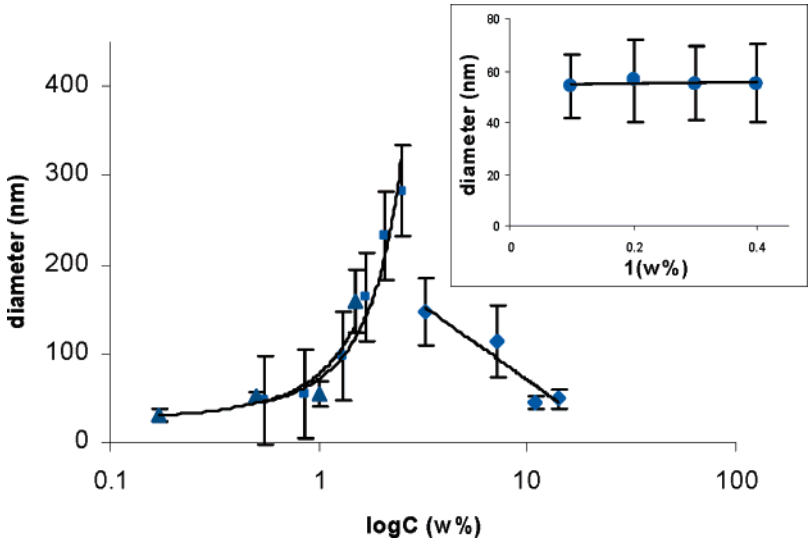

Figure 4. Effect of various components on the oil core size: (a) octadecyltrimethoxysilane (**1** inset), ethylbutyrate (**2** ■), Tween-80 (**3** ◆), and lecithin (**4** ▲).

in lipid-based aqueous systems,[54] this study centered on compositions where spherical microemulsion particles were reproducibly attained and any other phases were not extensively characterized. To avoid coagulation, the microemulsions were stirred at low pH to hydrolyze the methoxy headgroups of **1** and induce polymerization. This process not only formed a thin silicate layer around the droplet, thus increasing the stability of droplets, but also provided some unreacted Si−OH groups to serve as anchor points for further cross-linking of the surface. Compound **5** readily hydrolyzes in water to give tetrahydroxysilane, which reacts with the hydroxyl groups on the microemulsion droplet surface forming a polysiloxane/silicate shell around the droplet (Figure 1). Formation of the shell is supported by the observed increase in the hydrodynamic radius of the droplets by QELS measurements (Figure 2). Furthermore, the silicate shell formed around the microemulsion droplets can be seen in TEM images (Figure 3). Figure 3 also demonstrates the shape persistence of the particles over extended periods of time.

Synthetic Control. Our first interest was in controlling the size of the nanocapsules obtained from this system. The fate of nano-objects in vivo is related to their size.[46] For application in drug detoxification, nanocapsules should be smaller than 5000 nm to be transported through the smallest human capillaries.[47] Furthermore, nanocapsules of different sizes may have different sequestering efficiencies. To create oil templates of various sizes without the "shell" (compound **5)**, a series of samples systematically varying ingredients **1**−**4** were made. The results are summarized in Figure 4.

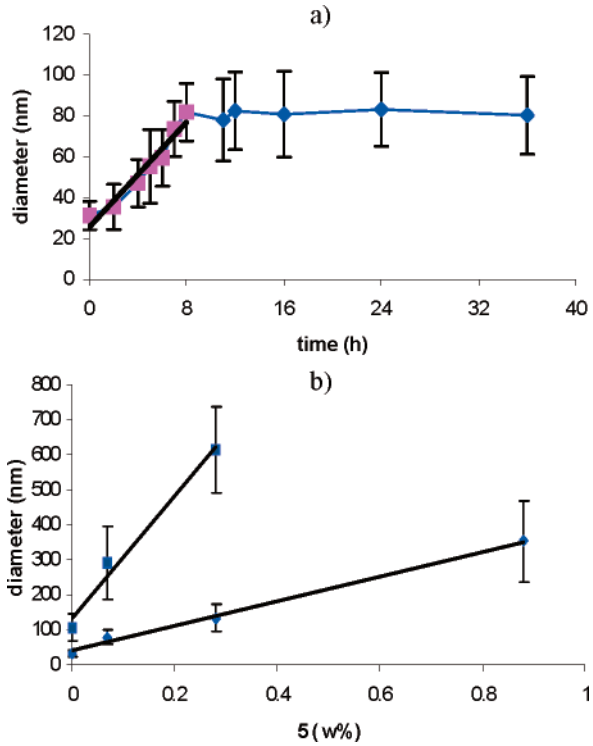

Figure 5. (a) The kinetics of shell formation under a fixed (0.07 wt %) concentration of tetramethoxysilane (**5**) (diameter refers to nanocapsule, not shell thickness); (b) nanocapsule diameter as a function of concentration of **5** for "small" core (◆) and "large" core (■).

The major component of the three surfactants used is Tween-80 (**3**). Compound **3** is soluble in water with a hydrophilic lipophilic balance (HLB) value of 15.4. As the amount of **3** was increased, the diameters of the resulting microemulsion droplets become smaller (Figure 4). When no compound **3** is present, a coarse emulsion is formed. Although exact particle size was not determined, they were large enough to be seen with minimum magnification under a light microscope, indicating that the droplets were micrometers in size. The decrease in size as the amount of **3** was increased can be attributed to the surfactant adsorbing at the O/W interface and lowering the interfacial tension.[48] The lower interfacial tension allows larger microemulsion

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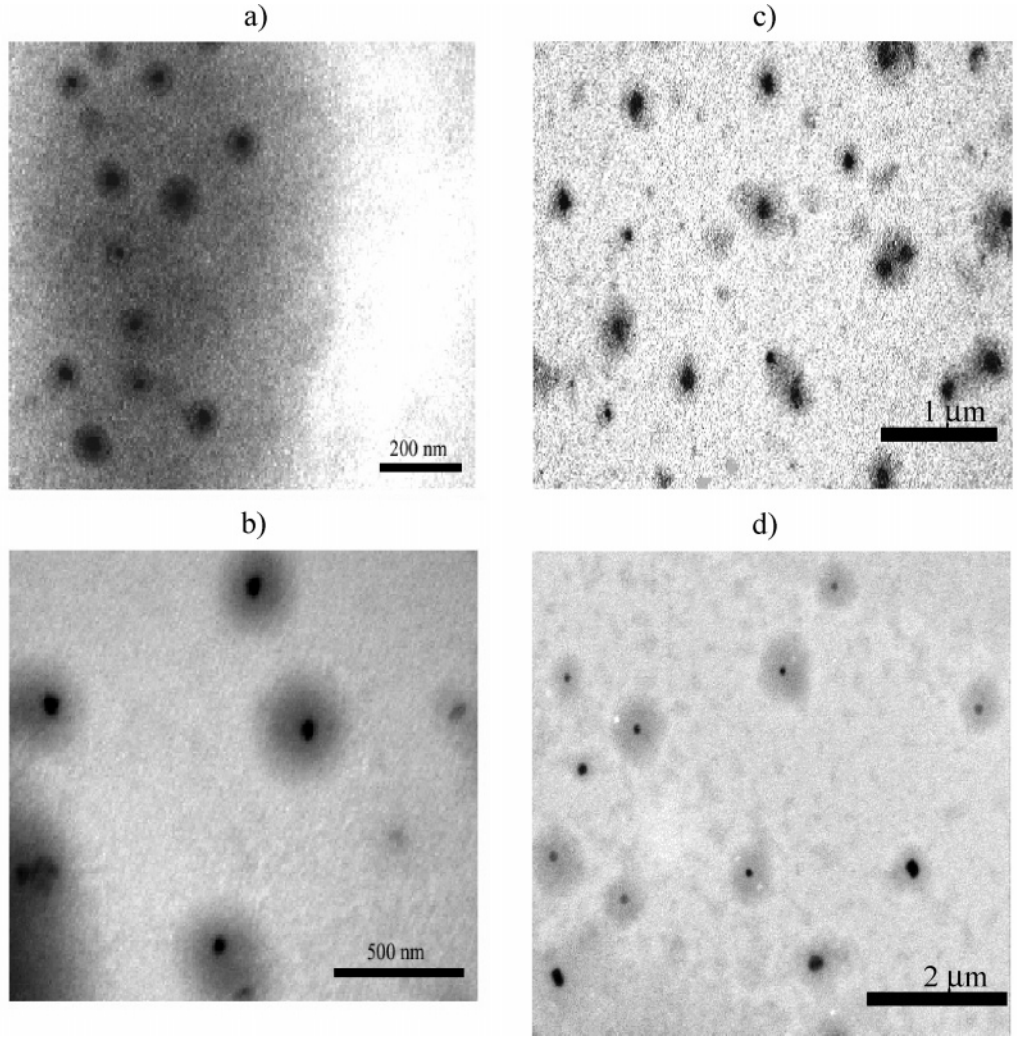

Figure 6. TEM images of "small" core at (a) 0.07 wt % of **5** and (b) 0.88 wt % of **5** and "large" core at (c) 0.07 wt % of **5** and (d) 0.28 wt % of **5**.

droplets to break apart to form smaller droplets. This process is limited by the amount of surfactant necessary to form a monolayer at the interface around the droplet. Each time a droplet breaks apart to form smaller ones, it creates more surface area. Once the surface area is large enough to utilize all the surfactant at the O/W interface, the droplets will not subdivide. The resulting smaller droplets would be unstable.[48]

The second surfactant used in this system is lecithin (**4**). Figure 4 shows that as the amount of **4** is increased, the diameter of the resulting microemulsion droplets actually increases from 30 nm to 160 nm. This is contrary to what was observed with compound **3**. With an HLB value of 9.2−9.5,[49] **4** is not soluble in saline, but is readily soluble in oil.[50] High concentrations of **4** caused a phase transititon from clear, isotropic liquid to a turbid, thermodynamically unstable phase which was not further characterized. We believe that compound **4** partitions preferentially into the interior of the oil droplets, leaving only a minimum amount at the interface. Furthermore, compound **4** may act to increase the interfacial tension when present in large enough quantity (Figure 4). Both of these effects would result in the observed increase of the oil core diameter.

The third surfactant in this system is *n*-octadecyltrimethoxysilane (**1**). Clear isotropic microemulsions were not formed when the concentration of **1** was higher than 0.6 wt %. The diameter of the oil template remains essentially constant within the concentration range that allowed the formation of a microemulsion (Figure 4 inset). As with compound **4**, compound **1** is not soluble in water but is soluble in oil. It is likely that, within the current concentration window, all molecules of **1** absorb at the O/W interface, without partitioning into the oil phase, **2**, thus keeping the diameter of the oil template constant. From these results it is obvious that the surfactant which plays the most important role in reducing the size of the oil templates is Tween-80.

Figure 4 shows the diameter of oil templates is increased with the increase of oil phase concentration as expected.[51] The surfactant(s) will disperse a finite amount of oil, limited by the amount of surfactant present. If the amount of oil is such that there is more surfactant present than is needed to saturate the O/W interface, then the excess surfactant remains molecularly dissolved in the oil phase or as unswollen micelles in the aqueous phase. Once the amount of oil is increased to the point where a majority of surfactant is attached to the O/W interface, then any additional oil will add to the droplets already present rather than create new droplets, thus maintaining the lowest possible surface area-to-volume ratio. The consequence of such action will result also in a decreased number of droplets due to unavailability of surfactant molecules. The combination of these effects is

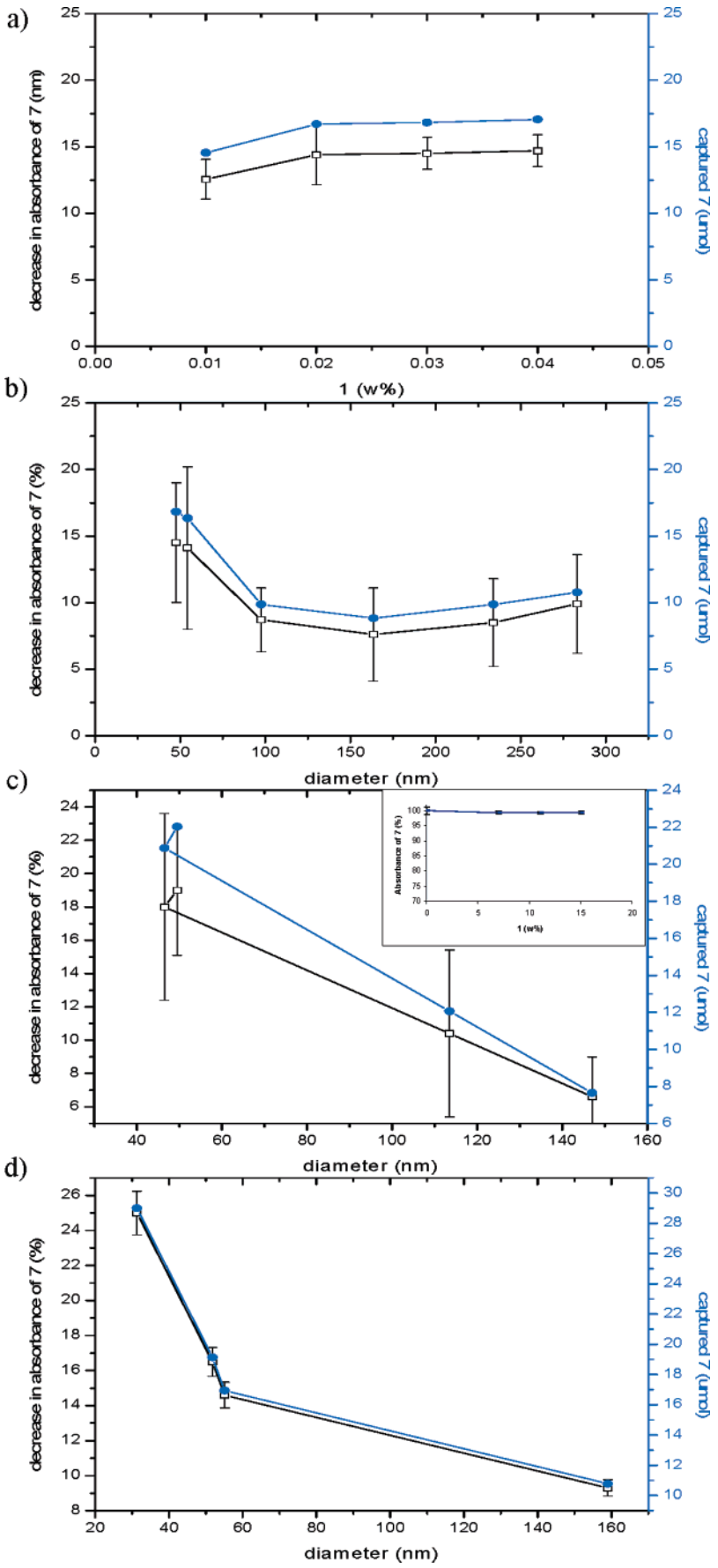

Figure 7. Uptake efficiency of oil templates formed by changing the concentration of (a) compound **1** (plotted as wt % of **1** vs decrease in absorbance for clarity), (b) compound **2**, (c) compound **3** (inset represents the decrease in absorbance for solutions containing just **3**), and (d) compound **4**.

likely to cause the increase of oil template size shown in the figure. The only morphology of samples with different concentration of oil (concentration of surfactants was kept constant) was spherical droplets as observed by TEM.

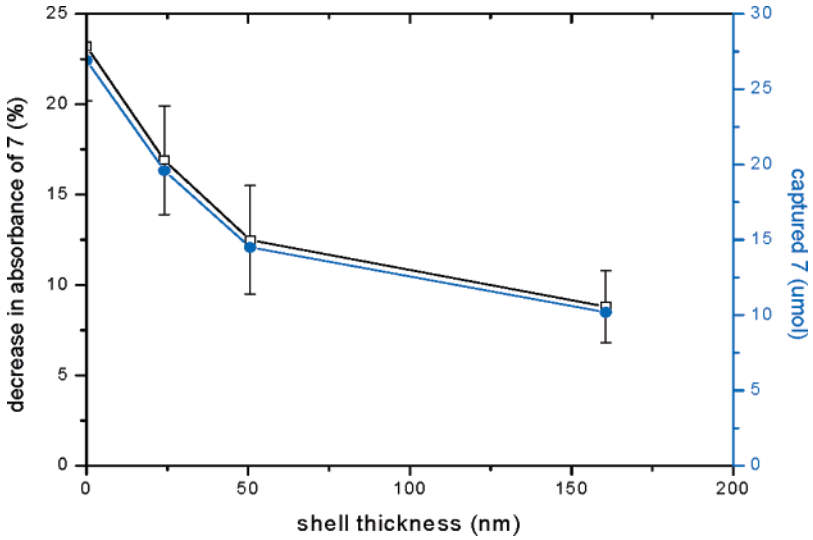

Figure 8. Uptake efficiency as a function of shell thickness according to eq 10 obtained by QELS (values for d_{tot} and d_0 are taken from Figure 5b).

The final component of the system is tetramethoxysiloxane (compound **5**), which forms the outer shell. Figure 5 shows that increasing the concentration of **5** reacting at the surface of the droplet increases the shell thickness and overall diameter of the resulting nanocapsules. The evolution of shell formation is shown in Figure 5a, where the initial concentration of **5** was 0.07 wt %. The diameter steadily increases during the first 8 h of reaction and afterward remains constant even for prolonged reaction times, indicating the end of the shell formation process. The difference in thickness of the formed shell between oil templates of different size (at the same concentration of **2**) is a function of the surface area (Figure 5b). The "large" core sample (oil core $d = 103 \pm 37$ nm) has less overall surface to be covered because there are fewer oil template particles, which leads to a larger shell thickness increase than the "small" core sample (oil core $d = 31.3 \pm 7$ nm).

It was also of interest to see if the size of the oil core remains constant throughout the shell formation process. We prepared solutions that contained compound **6** (20% w/w of the oil phase), which was subsequently stained with OsO_4 for better resolution of the oil core and shell by TEM. The results of these experiments are shown in Figure 6a−d. The analysis of "small" core 0.07 wt % of **5** image (Figure 6a) revealed oil core diameters 35 ± 6 nm and overall sizes of 77 ± 10 nm, which is in fair agreement with the results obtained with QELS (Figure 5b). Diameters of "small" cores with **5** at 0.88 wt % (Figure 6b) are 42 ± 14 nm and 237 ± 62 nm, for oil cores and overall nanocapsules, respectively. The difference between TEM (237 nm) and QELS data (352 nm) for "small" cores 0.88 wt % is likely a consequence of greater sensitivity of QELS and any scattering technique to larger particles; in addition, the presence of any aggregate (inevitable at high concentration of **5**) would overly bias QELS results to larger particles. Better agreement is also observed between TEM and QELS data for "large" core samples; for 0.07 wt % of **5** the diameters are 116 ± 23 nm for the core and 308 ± 98 nm for the overall nanocapsule, and for 0.28 wt % of **5**, 127 ± 36 nm core diameter and 646 ± 152 nm for the overall nanocapsule by TEM. These data suggest that the diameter of an oil core remains essentially unchanged during the shell formation process.

Partitioning Studies. The overall objective of this work was to formulate a system that would effectively remove lipophilic compounds from aqueous media. In our previous work, it was shown that a similar system was able to remove greater than 90% of quinoline (compound **7**) at a concentration of 8 μM from normal saline.[16] Here, the ability for nanocapsules of differing compositions to remove lipophilic compounds from normal saline was investigated. Controlling the size of the nanocapsules also provides insight into how the architecture influences the efficiency of the system to sequester lipophilic compounds.

Initially, several uptake experiments were performed on the microemulsions (oil templates) which were stabilized by cross-linking of **1**, but without subsequent templating and growth of the shell. Each value was obtained 1 h after the addition of compound **7**, when the equilibrium was reached.[16] A potential complication to these experiments was the fact that QELS measurements of all tested samples showed a small peak around 6−10 nm, which was attributed to unswollen micelles of compound **3**.[16] Compound **7** is soluble in a solution of **3**; therefore, there is a possibility that the decrease in absorbance of **7** is due to unswollen micelle absorption. Several experiments were performed to understand the influence of this process on the observed decrease in absorbance of **7**. Solutions containing just compound **3** at concentrations of 3, 7, 11, and 15 wt % and compound **7** were monitored by UV−Vis spectroscopy to monitor the change in absorbance of **7**. The results presented in the inset of Figure 7c, show no effect. Therefore, the observed decreases in absorbance can be accounted for by **7** being sequestered inside the oil cores or nanocapsules.

Compound **7** is readily soluble in the oil phase (**2**), and Figure 7a, c, d shows uptake trends for oil cores of different diameters made by changing the amount of **1**, **3**, and **4**, respectively, while the concentration of oil phase **2** is constant at 1 wt %. A general observation based on these graphs is that oil templates of smaller diameter have better uptake capabilities than larger ones. The ratio between total surface areas of two oil templates having different diameters is inversely proportional to their corresponding diameters. The smaller oil templates will have a larger interfacial area, which

accounts for more efficient partitioning in the sense that oil phase is more "available" to guest molecules. This interpretation is also in agreement with the results from the literature,[53] where solubilization or release from micellar systems is proportional to the size of the interface area (i.e., number of droplets). Interestingly, the Coulombic attraction between the negatively charged **4** (pI < 6.5) and positively charged **7** at pH 7.4 seems not to have significant impact on uptake, although this phenomenon was not further quantified in the current study.

It was surprising that the uptake remained fairly constant with the increase in the oil concentration (Figure 7b). An advantage of increasing the oil concentration is the resulting decrease in the number of droplets ("oil cores"). This effect minimizes the surface-to-volume ratio as expected since fewer surfactant molecules are available at higher concentrations of oil (Figure 4). Therefore, the drug partitioning in the oil cores is proportional to the interfacial area and is not a function of the oil phase concentration.

Figure 8 shows that the drug partitioning decreases as the shell thickness increases. Shell thickness is given by

$$St = \frac{(d_{tot} - d_0)}{2} \quad (1)$$

where d_{tot} and d_0 are respective diameters of the nanocapsule and oil core. This result is not surprising as increasing the concentration of **5** results in a thicker shell (as illustrated in Figures 5 and 6), thus diminishing the permeation of the drug. The effect is at least partly due to the effect of larger shell thickness increasing the denominator of $d\mu/dx$, where μ is the chemical potential driving force between the aqueous and the oil phase for these particles. The results also argue against significant absorption of **7** at interstices of the mesoporous silica shell itself.

Conclusions

Core−shell nanosized capsules have been synthesized using a microemulsion as a template by a method already reported in the literature. Changing the concentration of surfactants and oil phase can control the size of an oil core. It is found that depending on their concentration and nature, surfactant either reduces the size of the oil core (compound **3**), increases the size by partitioning inside the oil pool (compound **4**), or absorbs at the interface with no influence on oil core size (compound **1**). The diameter of oil template, once assembled, remains essentially constant throughout the shell formation process. A greater increase in shell thickness occurs in larger oil templates than in the smaller ones. Consequently, the shell thickness is more easily controlled for smaller oil templates. The uptake efficiency of the nanocapsules was evaluated at different formulations. Results showed that the amount of sequestered guest molecule is proportional to the size of oil/surfactant interface, independent of the oil phase concentration and inversely proportional to shell thickness. As for the aimed drug detoxification purposes, where the goal is to remove the maximum amount of a target drug, nanocapsules having small core and thin shell are highly desired. The functionalization of nanocapsules with poly(ethylene oxide) (PEO) and biological evaluation of these formulations, along with drug partitioning studies in real-life systems (human plasma and whole blood) are currently underway.

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Supporting Information Available: Additional data, table, and graphics (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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