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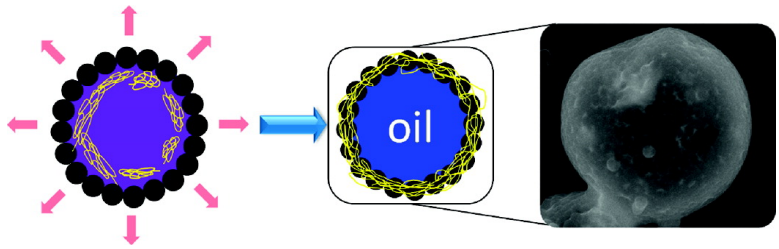

Emulsion-Templated Liquid Core−Polymer Shell Microcapsule Formation

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The fabrication of hollow microspheres to encapsulate functional molecules, such as drugs, insecticides, and proteins, is of ever-increasing importance. Many chemical and physicochemical methods have been tested for various specific encapsulations, but most of them have not been developed into an industrial process. In this work, we present a straightforward method to prepare liquid core−polymer shell microcapsules by first templating an oil-in-water emulsion stabilized by an interfacial monolayer of polystyrene latex particles (often referred to as "Pickering emulsion"), and subsequently locking the assembled particles into a robust polymeric shell through the precipitation of a biodegradable polymer poly(lactic-*co*-glycolic acid) (PLGA) at the interface. The resultant microcapsules that have a solid polymeric enveloped around the oil droplets are stable and retain their integrity during the drying in air. Therefore, they should have great potential to serve as vehicles for encapsulating functional molecules especially hydrophobic in nature.

The manufacture of polymer shell microcapsules with liquid cores is of ever-increasing importance to many industries because of their potential applications, which range from food, agriculture, to pharmaceutics.[1,2] As the liquid core is completely separated from its surroundings, it can be applied to protect products from deteriorating effects such as oxidation and moisture, especially in the food and beverage industry, as well as in the pharmaceutical industry, where drugs, proteins, and vitamins are the sensitive ingredients.[3] In recent years, considerable effort has been devoted to the design and preparation of polymer shell microcapsules with defined size, permeability, mechanical strength, and biocompatibility. The microcapsules are readily constructed by controlled gelation of polymer at the surface of droplets,[3] by emulsion polymerization,[4] by polymer precipitation by phase separation,[5] and by layer-by-layer electrostatic deposition of polyelectrolytes onto sacrificial templates.[6]

Recently, there has been growing interest in the use of particle-stabilized emulsion (often referred to as Pickering emulsion) as templates for the preparation of liquid core−polymer shell microcapsules.[2,7] This approach arises from using droplets as sacrificial templates on which colloidal particles are assembled at the oil−water interface. The permeable or semipermeable membranes and microcapsules are made by "locking" the interfacial particles to result in a solid elastic shell or film encapsulating the droplets. The first example of these microcapsules was made by Velev and Nagayama[8] by templating *n*-octanol-in-water emulsions stabilized by polystyrene latex particles and subsequently removing the *n*-octanol core by dissolution in ethanol. Dinsmore et al.[9] have modified the process and produced what they term as "colloidosomes" by the assembly of colloidal particles into shells around water-in-oil emulsion drops, followed by thermal fusion of the particles in the shell. In recent studies, advances have been made in developing temperature-responsive colloidosomes based on polymer microgels or polymer−silica composite microgel particles.[10,11]

For the route to fabricate microcapsules based on particle-stabilized emulsion, the locking or cross-linking of the interfacial particles to make a rigid shell is typically the most challenging step. Locking is essential to ensure that the final structure of microcapsule remains intact when the liquid−liquid interface is removed. Methods of locking involve van der Waals forces (i.e., simply letting the particle aggregate at the interface) or some active measures such as addition of a polyelectrolyte with opposite charge to the particles.[12] Besides, the addition of a polymer that can be subsequently covalently cross-linked onto the particles,[13] or simply sintering the colloidal particles (i.e., by heating slightly the dispersion above the glass transition temperature of the particles)[9] is also applied. Recently, Cayre et al.[14] have developed a gel trapping technique for fixing particle monolayers at droplet surfaces by gradually gelling the liquid core. Despite the enormous progress in cross-linking the interfacial particles, these methods are mostly confined by their applicability (e.g., a relatively high sintering temperature is required for colloid particles), the range of materials that can be used (e.g., the gelling techniques), or the ease of synthesis and fabrication (e.g., covalently cross-linking across the particles).

Herein, we present a new and simple strategy to fabricate liquid core−polymer shell microcapsules by first templating an

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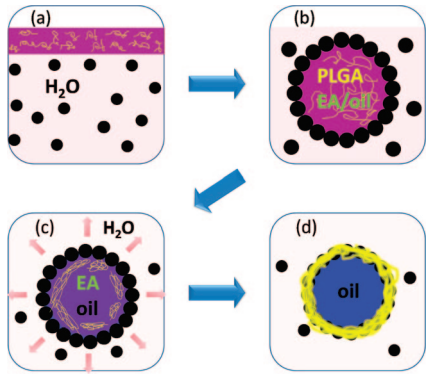

Figure 1. Schematic showing the liquid core−polymer shell microcapsule formation by templating a particle-stabilized oil-in-water emulsion.

oil-in-water emulsion stabilized by an interfacial monolayer of polystyrene latex particles, and subsequently locking the assembled particles into a robust polymeric shell through the precipitation of a biodegradable polymer at the interface. The formulated microcapsules are stable, and their final structures can be preserved even after drying in air. Therefore, they should have a great potential for encapsulation applications that are particularly attractive for use in the field of medicine, pharmaceutics, agriculture, and cosmetics.

Figure 1 schematically shows our approach. It consists of first emulsifying a mixture of *n*-octanol oil, ethyl acetate (EA), and EA-soluble, water-insoluble polymer such as poly(lactic-co-glycolic acid) (PLGA) in the aqueous outer phase which is saturated with EA and contains some polystyrene latex particles. The particle surfaces are coated with ionizable carboxylic acid groups so that the wettability (hydrophobicity) of the particle can be tuned by solution pH. The resultant oil-in-water emulsion has a microencapsulated oil phase consisting of PLGA and saturated water as the continuous phase and is stabilized by an interfacial monolayer of the polystyrene latex particles (Figure 1b). In a second step, a large amount of pure water is added to the continuous phase. Since EA is more miscible with water than *n*-octanol, we expect that EA molecules will diffuse from the inside of the oil droplets into the outer aqueous phase, probably through the interstices among the assembled latex particles (Figure 1c). As a consequence, the EA-soluble but *n*-octanol-insoluble PLGA in the oil core will undergo an outward transport and likely get entrained at the interface to lock the assembled particles, leaving a solid polymeric envelope around the octanol oil (Figure 1d). The formulated liquid core−solid shell microcapsules are well suited for encapsulating functional molecules, especially those that are hydrophobic in nature.

The polystyrene latex particles used to stabilize the oil-in-water emulsion were prepared by surfactant-free emulsion polymerization. Copolymerization with methacrylic acid (MAA) provides the carboxylic groups that allow varying the surface charge, that is, the wettability of the particles, by changing the solution pH. To prevent the polystyrene latex particles from dissolving in dispersed oils, the cross-linker divinyl benzene (DVB) was added during the polymerization. The resultant carboxylated polystyrene particles have an average hydrodynamic radius around 130 nm as determined both by dynamic laser light scattering and scanning electron microscopy (SEM) (see the Supporting Information). The inset SEM picture confirms that the prepared particles are spherical and monodispersed. Previously, we have shown that, under the condition of high pH solution, where the particles are fully ionized, stable oil-in-water (O/W) emulsions solely stabilized by those charged particles

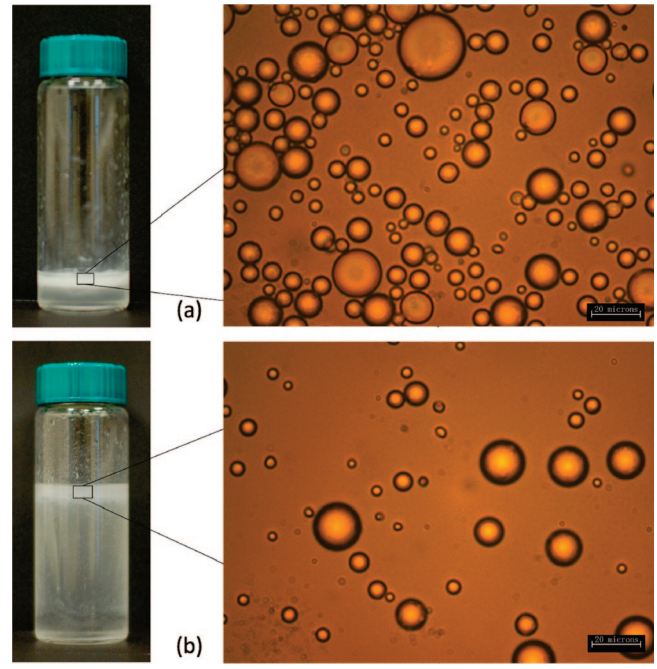

Figure 2. Appearance of the formed particle-stabilized emulsions and their corresponding optical micrographs: (a) The emulsion was prepared by homogenizing the octanol oil, EA, and PLGA in an aqueous solution which was saturated with EA and contained polystyrene latex particles at a solution pH of 11. The optical micrograph was obtained by dilution with EA-saturated water. (b) Obtained dilute emulsion and optical micrograph when 20 mL of pure water was added to the outer phase of the vial in (a).

could be successfully prepared. With the solution pH lower than 4, no stable O/W emulsions were formed.[15] In this way, only the emulsion prepared at high solution pH, that is, pH = 11, will be used here to test the locking mechanism.

An oil-in-water (O/W) emulsion of 1 mL of octanol/EA mixture (6:4 in volume) containing 1.1 mg of PLGA and 4 mL of EA-saturated water at a solution pH of 11 in the presence of 0.13 wt % polystyrene particles was prepared by using an Ultra Turrax T25 homogenizer (1 cm head) operating at 13 500 rpm for 1 min. The appearance of the resultant emulsion is shown in Figure 2a. The emulsion was completely stable to coalescence and ripening, as shown by the observation that no visible separation of dispersed phases occurs. Since the density of mixed oil is less than that of water, creaming of the O/W emulsion occurs over time. The microscope image demonstrates that the droplets remain spherical and stable after the emulsion is diluted with EA-saturated water. Our previous results showed that the stability of this emulsion comes from the dissociation of the polystyrene latex particle surface ionizable −COOH group, which ensures wettability of the latex particles.[15,16] It is revealed that, under ionizing conditions ($-COO^-$) in which polystyrene particles are highly charged, the oil droplets appear completely covered with a monolayer of particles to inhibit the coalescence of droplets. The dense packing of the particles at the interface occurs in a situation where the particles are highly charged, most likely involving charge-induced capillary attractive forces between the interfacial nanoparticles.[15,17] However, at that time, we had not yet found good ways to lock the particles at the oil−water interface into a robust shell that an intact liquid core−polymer shell microcapsule could not be obtained.

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In contrast to the optical image shown in Figure 2a which obtained after the emulsion was diluted with EA-saturated water, Figure 2b shows the optical images after 20 mL of pure water was added to the emulsion. As EA is much more miscible with water so we expect that EA molecules should diffuse from the inside of the oil droplets into the outer, water phase, probably through the interstices among the adsorbed particles. To confirm that, we have measured and taken an average of 300 oil droplets of different optical images of the emulsion diluted with both EA-saturated water and pure water. For the emulsion diluted with EA-saturated water, the average diameter of the oil droplet is ~7.5 μm. However, the size decreases to ~6.7 μm after dilution with pure water. As the oil volume contains 40% EA, based on the recipes of emulsion preparation, the volume of the oil droplet will shrink to 60%, which corresponds to the diameter of the droplet being reduced to 84%, that is, 6.3 μm, if all the EA molecules are released. The measured size resembles closely the calculated result and supports our hypothesis that the EA molecules can be extracted to the outer water phase. On the other hand, since PLGA is only EA-soluble, we conjecture that the extraction of EA by the addition of pure water likely will make the *n*-octanol insoluble PLGA in the oil core to have an outward transport and finally participate at the interface to lock the adsorbed latex particles, leaving a polymeric envelope around the oil droplet.

The first direct evidence of such an assumption is that the emulsion in Figure 2b after the dilution and diffusion of EA shows stability for more than 1 h even if the solution pH is dramatically decreased to 2 (see the Supporting Information). As we have mentioned before, it has been reported that, also included our previous work, no stable O/W emulsion can be formed for carboxylated−polystyrene latex particles with solution pH lower than 4.[15,18] To further confirm the role of PLGA, a dilute sample of emulsion in Figure 2b was dried in room temperature for 6 h and imaged by using a FEI Quanta 400 FEG scanning electron microscope operating at 10 kV. Figure 3a and b show the typical obtained microcapsules with a diameter around 3−4 μm. The surface of the microcapsule is completely coated with the polystyrene latex particles which are most likely locked together by the PLGA polymer into a polymeric shell so that they retain the integrity even after the emulsion is directly dried in air. A ruptured capsule (see the Supporting Information) shows that the interior of this capsule is hollow and it provides strong evidence that the adsorbed latex particle at the droplet surface forms a single monolayer, rather than multilayers. However, in a control experiment no PLGA polymer was added during the first emulsification of the oil mixture in the polystyrene particle dispersion. After diluting the emulsion with pure water to diffuse the EA molecules and then directly drying in air, Figure 3c and d shows that the resultant structures are spongelike, in which the primary polystyrene nanoparticles are fused into larger agglomerates.

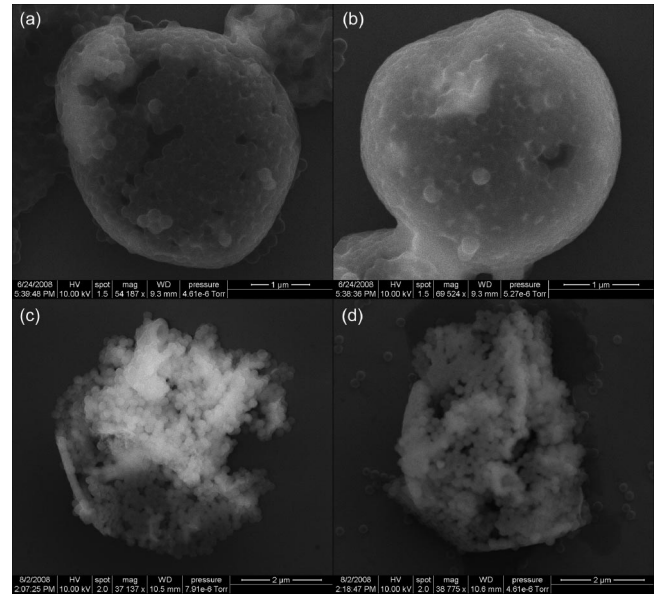

Figure 3. Typical SEM micrographs of the particle-stabilized emulsions after drying in air. (a,b) Emulsification containing PLGA; images show that they retain the structure integrity. (c,d) Controlled experiment where no PLGA is added during the first step of the emulsification; spongelike structures are observed.

In summary, we report a novel and efficient approach to fabricate liquid core−polymer shell microcapsules. This is achieved by templating oil-in-water emulsions and subsequently cross-linking the interfacial particles through the precipitation of a biodegradable polymer at the oil−water interface, leaving a polymeric envelope around the oil droplet. The formed microcapsules are well suited for encapsulating hydrophobic actives, which is especially attractive for many industrial uses because of the relative simplicity. More direct evidence about our proposed mechanism is being explored in order to apply this fabrication technique to other colloidal systems. Finally, as PLGA used to integrate latex particles is biodegradable, the release strategy and kinetics of the formed microcapsules is also an interesting issue under investigation.

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Supporting Information Available: Plot showing the typical hydrodynamic radius distribution $f(R_h)$ of the polystyrene latex particle prepared by surfactant-free emulsion polymerization; images showing the time dependence of the stability of the particle-stabilized emulsion at pH 2; and image showing a ruptured emulsion droplet. This material is available free of charge via the Internet at http://pubs.acs.org.

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