An Effective Method for Preparing Polymer Nanocapsules with Hydrophobic Acrylic Shell and Hydrophilic Interior by Inverse Emulsion Radical Polymerization

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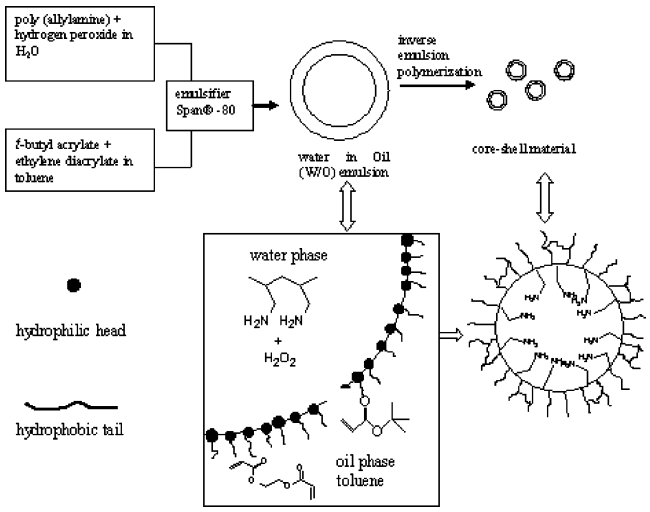
Polymer nanocapsules have attracted a great deal of interest in the development of new intracellular delivery systems such as biomedical imaging,[1] drug targeting,[2] and gene therapy.[3] Polymer materials exhibit a range of supramolecular structures and functionalities, which potentially allow for chemical tailoring of the materials properties for target-specific applications.[4] Kopelman and co-workers have developed an emulsion polymerization method for producing nanosized polymer hydrogels with fluorescence molecules entrapped in the polymer matrices, i.e., "probes encapsulated by biologically localized embedding" (PEBBLE).[5] Well-structured and functionalized polymer capsules, "shell cross-linked Knedel" (SCK),[6] have also been produced by Wooley and co-workers from chemical modifications of functional block copolymer micelles.[7] While the synthetic technique used in the PEBBLE method is simple and scalable, it is difficult to control the detailed functionalities of the polymer capsules at the level that the SCK method allows.

We report a new interfacial radical polymerization method for synthesizing novel polymer capsules with a hydrophobic poly(*tert*-butyl acrylate) shell and a hydrophilic poly(allylamine) interior. This method allowed the productions of narrowly dispersed polymer capsules with the nominal diameters of the capsules variable from 50 to 1000 nm by controlling the polymerization conditions. Our approach is based on the generation of the initiating polyradical on a water-soluble amine polymer in the aqueous phase (of the inverse emulsion) by hydrogen peroxide and subsequent grafting of a hydrophobic vinyl monomer to the polyradical from the water/oil interface (Scheme 1).[8] The macroradicals generated in situ act as emulsifier molecules and stay at the water/oil interface of the inverse emulsion which is further stabilized by a water-in-oil emulsifier such as Span 80.[9] The acrylate monomers are grafted to the macroradicals from the radical sites at the interface of the inverse emulsion and propagate in the oil phase. In the presence of a difunctional cross-linker in the oil phase, narrowly dispersed polymer nanocapsules can be produced. We have found that a fluorescence dye can be postsynthetically encapsulated into the polymer as a model for optical sensing or drug delivery. We also show that the *tert*-butyl group can be hydrolyzed under mild conditions to form an amphiphilic shell surface,

Scheme 1. Synthesis of Core−Shell Material



indicating that the shell surface can readily be further chemically modified. From a synthetic point of view, the combination of a water-soluble polyamine and H_2O_2 appears to be a general waterborne radical initiation method that allows well-controlled radical polymerization initiating only in the aqueous phase and propagating at the oil−water interface. The use of H_2O_2 as the coinitiator is critical. Other water-soluble oxidants such as persulfates led to the precipitation of poly(allylamine) in the reaction. In addition, H_2O_2 at a low concentration is a mild oxidant, considered safe to be used in bulk polymerization. From the materials functionality point of view, the interfacial polymerization method represents a combination of the synthetic simplicity of the PEBBLE method and the structural complexity of the SCK method. The acrylic shell and the amine interior should allow for various encapsulation applications.

In a typical synthesis, a solution of poly(allylamine) (PAA, 0.2 g) in water (5 mL) was mixed with *tert*-butyl acrylate monomer (4.5 mL) and the difunctional cross-linker ethylenediacrylate (ED, 0.7 mL) in a three-necked round-bottomed flask equipped with a thermometer, condenser, argon inlet, and magnetic stirrer. To the above mixture was added toluene (5 mL), Span 80 (10.0 mg), and H_2O_2 (1.0 mL). Inverse emulsion could be observed after sonicating the mixture at room temperature in an ultrasonic cleaner (Fisher FS6) for 20 min. The round-bottomed flask containing the emulsion was placed in an oil bath at 65 ± 2 °C for 4 h under argon while stirring (Corning magnetic stirrer). After the reaction, the milky white reaction mixture was poured into distilled water (150 mL) while stirring, and a white powder was precipitated. The polymer powder was washed with methylene chloride several times and dried by removing the solvent under vacuum to produce 0.7 g of final product for characterization. Initial spectroscopic and thermoanalysis characterizations allowed us to conclude the nature of the product to be a PAA-*graft*-tBAA copolymer.

Transmission electron microscopy (TEM) analysis of the above polymer sample provided conclusive evidence for the formation of nanosized polymer capsules. The TEM images of a dip-coated sample on a carbon-coated

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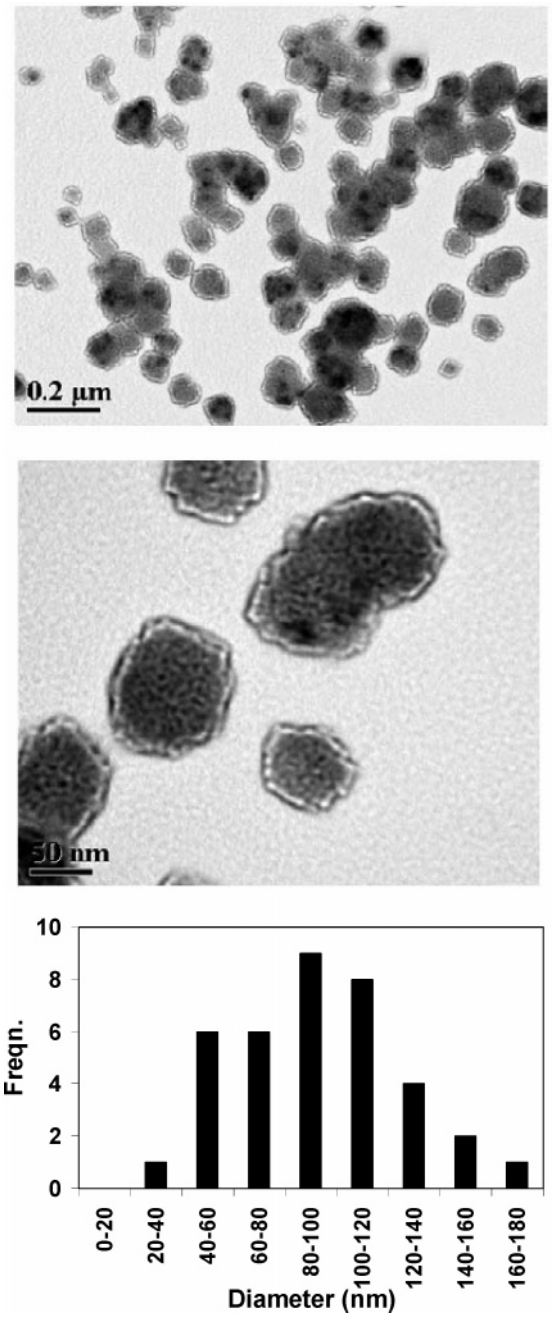

Figure 1. TEM images of the polymer nanocapsules in different magnifications, the histogram showed the size and size distribution of the polymer nanocapsules.

TEM grid from ~0.5 g/L suspension of the polymer nanocapsules in water are shown in Figure 1. In the image, the nanocapsules displayed a spherical morphology, consistent with interfacial polymerization conditions. The capsules are narrowly dispersed with an average diameter about 80 nm. The thin lighter lines surrounding the polymer capsules are most likely due to the deformation of the polymer shell on the TEM grid formed by the receding solvent when it evaporated.

Postsynthetic uploading of a guest molecule into the capsules was examined by mixing an aqueous suspension of the polymer nanocapsules with Eosin Y (0.5% in water). As shown in Figure 2, the white polymer (Figure 2a) turned red (Figure 2c) after the orange colored dye (Figure 2b) was extracted from the solution into the polymer nanocapsules. Because the interior of the nanocapsules is most likely cationic due to the protonation of the amine functionalities, the extraction of the Eosin Y is plausibly attributed to the ionic attraction between the anionic group of the Eosin Y and the protonated amino groups at neutral pH in water. This acid−base reaction is evident from the changes in the color of the dye before and after encapsulation. The high loading of the encapsulation is evident from the almost complete extraction of the dye in the solution into the polymer (Figure 2c). From the nature of inverse emulsion polymerization, the TEM images, and the above colorimetric observations, it can be concluded that the inner space of the polymer nanocapsules is packed with water with polyamine at the interface. The acrylic thin shell allows for easy diffusion of small molecules into the center of the capsule which can be loaded using concentration gradients and solubility differences between the inside and outside of the nanocapsules.

Figure 2d shows the fluorescence microscopy image of polymer nanocapsules which were loaded with Eosin Y. When the sample is excited with a green laser, the red fluorescence emission shows an intensity profile that is typical of a spherical structure, with highest emission intensity from the center of the particles, which fades away gradually toward the shell of the particles. Again, this indicates that the core of the polymer particle is loaded with the dye molecule due to the interaction between the amine groups of PAA backbone inside the core and the carboxylic group of the dye molecule. The absence of the fluorescence in the shell demonstrated that the shell of the polymer particles is composed of *t*-BA polymer chains that are grafted from the backbone of PAA. From the loading of the dye it can be concluded that the core of the polymeric particle is functionalized

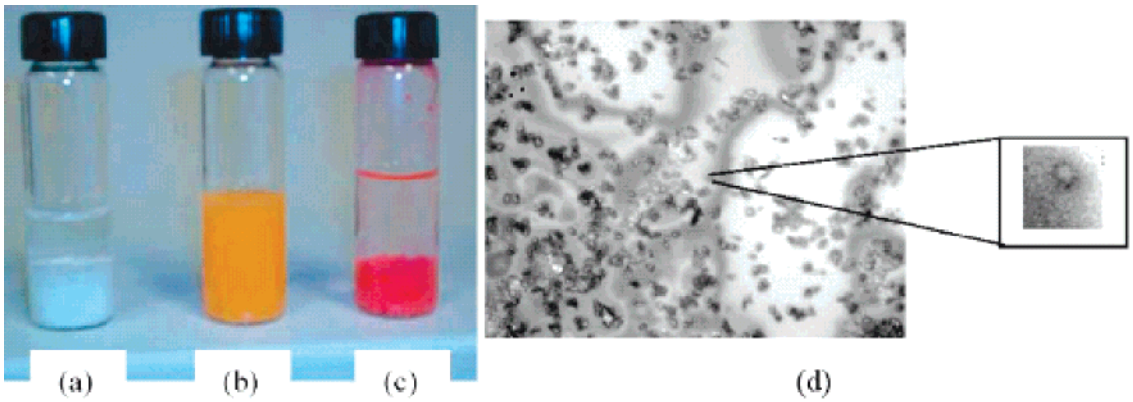

Figure 2. (a) Aqueous suspension of polymeric core shell material (b) Aqueous solution of Eosin(Free Acid) (c) Polymeric core shell material after the addition of the Eosin solution (d) Fluorescent microscopic images of the core shell material.

with the pendant amine groups in a hollow aqueous core as we hypothesized. The aggregation of the polymeric particles is also evident from fluorescent microscopic images, but the presence of cores within a continuum matrix can be seen.

In conclusion, we developed a new method for producing nanoscopic polymer capsules of 50−1000 nm with well-defined nanostructures and surface functionalities. In particular, with biomedical applications as one of the primary goals of this research, polymer capsules with a hydrophobic acrylic shell and a poly(allylamine) interior were effectively produced. The radical initiation method uses a combination of polyamine and hydrogen peroxide which appears to be a new and general waterborne radical initiation system with commercial ingredients of minimum hazard. Our preliminary results show that the *tert*-butyl groups of the polymer capsule are readily removed. Further chemical modifications of the surfaces of the nanoparticles are underway.

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Supporting Information Available: FT-IR and thermal characterization of the core−shell material. This material is free of charge via the Internet at http://pubs.acs.org.

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