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Synthesis and Characterization of New Polymer Nanocontainers

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Summary: New type of reactive, water-soluble and filled polymer nanocontainers that can be covalently attached to surfaces were synthesized. The encapsulation of a dye inside the nanocontainers allows their rapid detection. The model systems are based on crosslinked polystyrene (PS) and polymethylmethacrylate (PMMA). The synthesis of nanocontainers by two-step emulsion polymerization and characterization by NMR, IR, Dynamic Light Scattering, TEM and Confocal Laser Scanning Microscopy (CLSM) is presented.

Keywords: core-shell polymer; hollow sphere; nanoparticle

Introduction

In recent years, considerable progress has been made in the development of synthetic methods allowing the preparation of materials with precise control over size and morphology at the nanometer level. The principal example is the formulation of hollow nanoparticles. These hollow particles are particularly interesting for applications as confined reaction vessels, drug carriers or protective shells for dyes used as labels for enzymes or catalyst.[1-2] Similar nanometer-sized containers, e.g., micelles or vesicles are used by nature in biological system. However, their limited mechanical stability prevents many possible applications (e.g., in drug delivery).[3] Mechanically stable polymer nanocapsules can be prepared by using multiple techniques (see, e.g. [4-9]). Among others, water soluble and filled polymer nanocontainers can be synthesized by two-step emulsion polymerization via core-shell latexes. Here, our final objective was to develop a new technology that allows a specific and selective immobilization of labelled nanocontainers at surfaces. We first synthesized a new type of reactive, water-soluble and filled polymer nanocontainers that can be further covalently attached to surfaces. The encapsulation of a fluorescent dye (carboxyfluorescein) inside the nanocontainers allows quick detection of the particles. The core-shell particles presented in this report contain a liquid polydimethylsiloxane (PDMS) core and a shell of poly(styrene-methylmethacrylate-

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divinylbenzene), Poly(St-MMA-DVB). This system allows convenient separation and purification of the shell forming polymer.[10] Furthermore, the preparation method is suited for scaling up the production of different container systems and allows the optimization of the particles by variation of particle size, shell thickness and crosslinking density.

Synthesis of polymer nanocontainers

As a model system, we used crosslinked PS and PMMA nanocontainers by using DVB as crosslinking agent. The particles were synthesized by two-step emulsion polymerization via core-shell particles (Figure 1).[11] In the last step, the PDMS core can be removed by ultrafiltration in toluene.

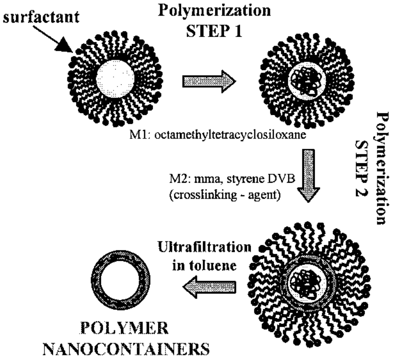


Figure 1. Schematic representation of the polymer nanocontainer preparation via core-shell latexes.

In the first step, the PDMS core is prepared by ring opening cationic polymerization of octamethyltetracyclosiloxane (M1) in water with dodecylbenzenesulfonic acid (DBSA) as both catalyst and surfactant. The synthesis of PDMS via the ring-opening polymerization of cyclic siloxane monomers has been described previously.[12-13] In general, this procedure yields polymers of low molecular weight. Concerning the alternative preparation route for this polymer, by emulsion polymerization, Bey *et al.* obtained PDMS latexes using DBSA as both surfactant and catalyst; the reported particle sizes varied between 50 and 500 nm with 1.5-4 g of DBSA for 100 g of siloxane monomer.[14-15] For that reason, the polymerization of PDMS was conducted using 20 g of water, 5 g of M1 and an appropriate amount of DBSA (between 0.5-5.0 wt% with respect to M1). Distilled water and the surfactant were added into a three-neck flask. The reaction mixture was magnetically stirred at ca. 400 rpm at room temperature and oxygen was removed by bubbling argon for 30 minutes. Next, the monomer was added dropwise. After the polymerization proceeded, the reaction was quenched with 1N NaOH.

In the second step, the synthesis of the crosslinked shell was done via the seeded polymerization of St-MMA-DVB on the seed PDMS particles. Potassium persulfate (KPS) was used as initiator, without additional surfactant. A selected amount of PDMS latex (10 mL), water (10 mL) and KPS (2.5 wt% relative to St-MMA-DVB monomers) were first loaded into the flask, from which oxygen was removed by bubbling argon for 30 minutes. When the temperature reached 80°C, the monomer mixture was added dropwise at a low rate (ca. 10 ml/h) and the polymerization was proceeding for 4 hours. Then, in the third step, the PDMS core was removed by dissolving the core-shell particles in toluene and subsequent ultrafiltration (Millipore cellulose 100000). Finally, concerning the encapsulation of carboxyfluorescein, two strategies were used. In the first approach, the nanocontainers were dissolved in a good solvent (e.g dioxane), where they swell and become permeable so that the dye molecule can diffuse into their interior from the solution. Then, a subsequent change of solvent conditions (e.g addition of water) will contract the polymer shells and decreases their permeability, while the dye molecules will be entrapped in the container interiors. By the second, more convenient strategy, carboxyfluorescein is incorporated directly during the preparation of core-shell particles. This way, the dye has to be dissolved within the liquid PDMS core. The main advantage of this approach is that the particles can be used directly without the last purification step, where the PDMS core is removed.

Characterization of polymer nanocontainers

The resulting core-shell particles were first characterized by FTIR spectroscopy (Figure 2). The spectrum reveals strong adsorption at 2950 cm^{-1} and 1750 cm^{-1} that corresponds to aliphatic C-H and carbonyl C=0 stretches, respectively. A medium band at 1260 cm^{-1} was due to the siloxane stretching. Two strong bands in the 1100-1050 cm^{-1} region and at 801 cm^{-1} originate from siloxane vibration (Si-O-Si) and from the silicone adsorption, respectively. Finally, the strong band at 699 cm^{-1} corresponds to the phenyl ring of PS. The IR spectroscopy data shows clearly the presence of PDMS core and that of PS-PMMA shell.

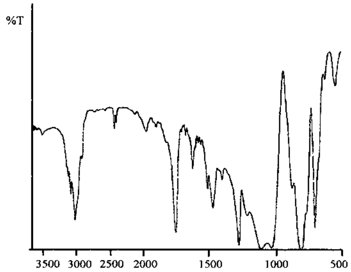


Figure 2. IR spectrum of the core-shell particles.

The size of the latex particles was determined by light scattering, which provided both the average diameter and the size polydispersity. Nanocontainers of different sizes were obtained by varying the monomer/surfactant (M1/DBSA) ratio in the first step of the synthesis (Table 1). A systematic variation of the particle size provides the information about the size dependence on the loading and detection of the nanocontainers containing a fluorescent dye. In fact, at the same concentration, larger particles will contain a higher number of dye molecules. However, concerning the immobilization and the distribution of labelled nanocontainers on surfaces, smaller particles allow a higher surface coverage and more homogeneous distribution.

Table 1. Particle size as a function of the dodecylbenzenesulfonic acid (DBSA) amount.

%weight of DBSA/M1	Dp[a] (nm)	Polydispersity at θ=90
0.5	470	0.24
1.5	336	0.08
2.5	246	0.22
3.5	110	0.19
5	86	0.13

[a] Particle diameters determined by dynamic light scattering after extrapolation to zero angle.

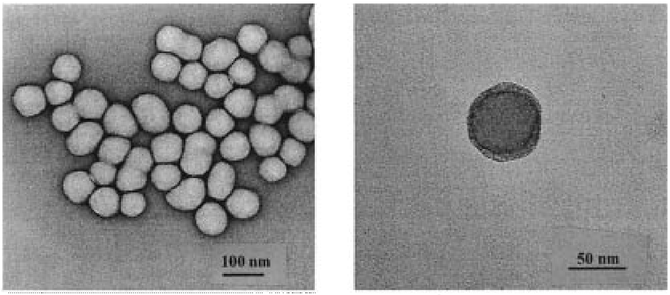
In the second step of the synthesis, we controlled the thickness of the container walls by varying the core-shell ratio in the reaction mixture (Table 2). In fact, a higher shell thickness leads to more stable and less permeable particles, but, at the same time, results in the more unfavourable encapsulation ratio.

Table 2. Shell thickness as a function of core-shell ratio in the second step of the emulsion polymerization.

Core/Shell molar ratio	%mol of crosslinking DVB/M2	Shell thickness[a] (nm)
1/1	10	20-25
1/0.5	10	5-7
1/0.25	10	-

[a] Shell thickness determined by dynamic light scattering.

The morphology of core-shell particles was studied by transmission electron microscopy (TEM). The PDMS/PS-PMMA-DVB core-shell particles were thinned with distilled water and sonicated. Uranyl acetate was used as the contrast enhancing stain. As can be seen in the TEM image (Figure 3 (a)), the synthesized particles were found spherical and very monodisperse in size. Their monodispersity is in good agreement with the dynamic light scattering data (Table 1). Furthermore, the image (Figure 3 (b)) shows clearly the formation of a core-shell particle, where it is possible to distinguish the core from the shell.



a b

Figure 3. TEM images of core-shell particles after the seeded polymerization of St-MMA-DVB on the seed latex particles.

In Figure 4, the electron micrograph shows clearly that the polymer particles are hollow, after the ultrafiltration step allowed to remove the PDMS core. The deformation of the spherical shape of these particles is also visible, and is possibly due to the sonication and subsequent drying on the TEM grid.

Finally, the polymer nanocontainers were labelled with the fluorescent dye, carboxyfluorescein. These dye-loaded nanoparticles were studied in the bulk and on surfaces with a Zeiss 510 upright confocal laser scanning microscope. A 488-nm line of the argon-ion laser was used for the excitation of carboxyfluorescein.

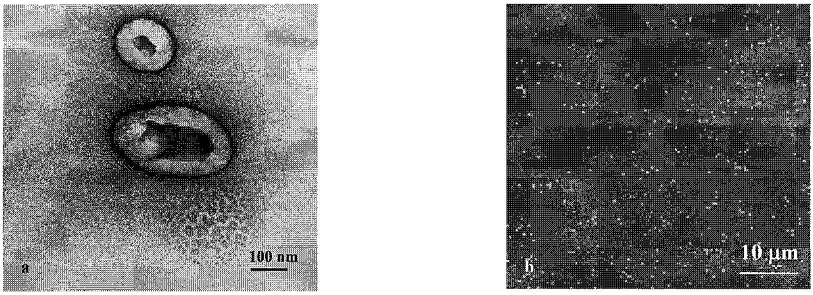


Figure 4. a/ TEM image of polymer nanocontainers after ultrafiltration in toluene. b/ Confocal image of the labelled nanocontainers.

Figure 4b shows the dye-loaded nanocontainers obtained after several washing cycles to remove the free dye: this result proves clearly the encapsulation of carboxyfluorescein inside the nanocontainers.

Conclusion

In conclusion, the polymer nanocontainers with two different shell thicknesses and various diameters have been synthesized. Next, the morphological study by TEM confirms the formation of spherical particles of a core-shell type. Furthermore, the ultrafiltration step is a well-suited method for removing the core to obtain the polymer nanocontainers. We have also demonstrated that the nanocontainers could be labelled with carboxyfluorescein dye. In the future, the outer surface of nanocontainers will be modified with functional groups that enhance the solubility in aqueous media and allow their covalent binding to surfaces.

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