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FULL PAPER

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Self-Rupturing and Hollow Microcapsules Prepared from Bio-polyelectrolyte-Coated Microgels**

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This paper reports on microcapsules obtained by layer-by-layer deposition of bio-polyelectrolyte multilayers at the surface of biodegradable dextran microgels. The behavior of the layer-by-layer coating upon degradation of the microgel core strongly depends on the bio-polyelectrolytes used. Two types of microcapsules, "self-rupturing" microcapsules and "hollow" microcapsules, are presented. Self-rupturing microcapsules are obtained when the swelling pressure of the degrading microgel core is strong enough to rupture the surrounding bio-polyelectrolyte membrane. Self-rupturing microcapsules could be of interest as a pulsed drug delivery system. Hollow microcapsules are obtained after applying multiple layers of bio-polyelectrolyte that can withstand the swelling pressure of the degrading microgel core. Biomacromolecules (such as albumin and dextran) spontaneously accumulate in the hollow microcapsules prepared from dex-HEMA microgels, which could be of interest for drug-encapsulation purposes.

1. Introduction

The advent of new biotechnological therapeutics has evoked novel challenges in drug delivery.[1] For several therapeutics, such as vaccines[2] and hormones,[3–5] a pulsatile release pattern could be beneficial. For example, a vaccine delivery system able to release the antigen in multiple pulses after a single injection[6–8] could replace the multiple injections that are currently required to generate sufficient immunity. Also, for drugs that develop biological tolerance when they are constantly present in the bloodstream, pulsed drug release instead of sustained drug release could be attractive. A way to achieve pulsed drug delivery could be the encapsulation of the drug in micro- or nanoparticles that release their contents at preprogrammed times after injection.

Recently, we introduced microcapsules that are able to explode, and thus release their contents, without the use of an external trigger.[9] As Figure 1A schematically represents, the so-called "self-rupturing" microcapsules consist of a biodegradable microgel surrounded by a semipermeable membrane. The microgels are based on dextran-hydroxyethyl methacrylate (dex-HEMA, Figure 1B). Dex-HEMA microgels are biodegradable through the hydrolysis of the carbonate esters in the crosslinks that connect the dextran chains.[10,11] Upon cleavage of the crosslinks, the swelling pressure of the dex-HEMA microgels increases.[12,13] This swelling pressure may rupture the surrounding membrane, depending on the properties of the membrane and the pH of the environment. In a previous paper, we reported that self-rupturing microcapsules could be obtained when the dex-HEMA microgels were coated with

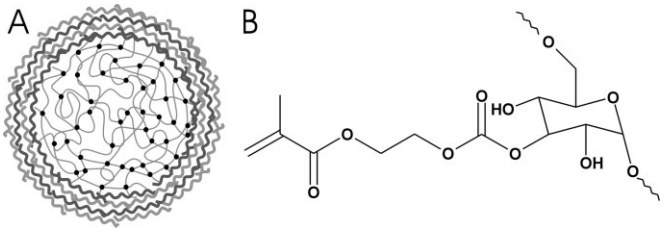

Figure 1. A) Schematic representation of a microcapsule. The inner core of the microcapsule is a microgel composed of dextran chains, which have been crosslinked (black dots). The microgel core has been coated with several polyelectrolyte bilayers of opposite charge (grey curves) using the layer-by-layer (LbL) technique. B) Molecular structure of dex-HEMA. Dex-HEMA are dextran molecules that have been derivatized with methacrylate groups connected to the dextran backbone by hydrolyzable carbonate esters. The dextran chains can be crosslinked by radical polymerization of the methacrylate groups, forming a 3D network. Hydrolysis of the carbonate esters in the crosslinks leads to the formation of the original dextran chains and polyHEMA fragments as degradation products. HEMA: hydroxyethyl methacrylate.

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poly(styrene sulfonate)/(poly(allylamine hydrochloride))$_3$, (PSS/PAH)$_3$, i.e., a membrane consisting of three polyelectrolyte bilayers, each bilayer composed of a sodium PSS layer and a PAH layer. The (PSS/PAH)$_3$ layer was applied by the layer-by-layer (LbL) technique.[14–17] LbL coating is the sequential adsorption of charged species, for example, polyelectrolytes,[16] nanoparticles,[18–20] nanotubes,[21] lipids,[22] or viruses,[23] on an oppositely charged planar or colloidal substrate. An important observation was that the (PSS/PAH)$_3$ coated dex-HEMA microgels only exploded when they were incubated at pH 9. Rupturing of the (PSS/PAH)$_3$ coating did not occur when the microcapsules were dispersed in buffer at a physiological pH value (pH 7.4). This was attributed to the pH-dependent permeability of the (PSS/PAH)$_3$ membrane; at pH 7, the (PSS/PAH)$_3$ membrane was permeable to the degradation products of the dex-HEMA microgels (mainly dextran chains of 19 kDa), whereas the membrane was impermeable at pH 9.[24] Consequently, at pH 9 the degradation products remained inside the microcapsules during the degradation process of the microgels, and thus increased the osmotic/swelling pressure of the core of the capsules, finally rupturing the (PSS/PAH)$_3$ membrane.

As self-rupturing microcapsules may have great potential as a pulsed drug delivery system,[6–8] we aimed to design self-rupturing microcapsules that (i) solely consist of bio-polymers instead of synthetic polymers, such as PSS and PAH; and (ii) rupture upon incubation at a physiological pH. Herein, we show that this is possible by carefully choosing the appropriate bio-polyelectrolytes for building the LbL membrane. Furthermore, we demonstrate that, depending on the composition of the bio-polyelectrolyte membrane, self-rupturing microcapsules as well as "hollow" microcapsules can be fabricated by using the degradable dex-HEMA microgels as sacrificial templates. Hollow bio-polyelectrolyte microcapsules, prepared by LbL coating of melamine formaldehyde,[25] poly(lactic acid)-*co*-poly(glycolic acid),[26] and calcium carbonate microparticles[27] as a sacrificial template, have been reported before. However, the use of organic solvents to dissolve the core material may be disadvantageous, especially where the encapsulation of drug molecules is concerned.[25,26] Also, remnants of toxic melamine formaldehyde oligomers may remain in the walls of the capsules after dissolving the core.[28–30] Severe aggregation of the hollow microcapsules has also been reported.[27] In this study, we show that dex-HEMA microgels can be dissolved under mild conditions yielding nonaggregated hollow microcapsules.

2. Results and Discussion

2.1. Preparation of dex-HEMA Microgels

Biodegradable dex-HEMA microgels were fabricated according to the method of Franssen and co-workers, by a completely aqueous water-in-water emulsion technique based on the immiscibility of an aqueous polyethylene glycol phase and an aqueous dextran phase.[31,32] Radical polymerization of the pending HEMA groups led to the formation of a 3D network. Positively charged microgels (as evidenced from electrophoretic mobility measurements) with an average diameter of 7 μm were obtained by copolymerizing dex-HEMA with dimethyl aminoethyl methacrylate (DMAEMA), which is positively charged at neutral pH.[33] Figure 2A shows the size distribution of the microgels, as determined by laser diffraction; Figure 2B is a confocal image of dex-HEMA microgels homogenously loaded with fluorescein isothiocyanate (FITC) dextran. FITC-dextran stays encapsulated inside the dex-HEMA microgels, and is slowly released during the degradation of the microgel core over a period of seven days.

2.2. LbL Coating of dex-HEMA Microgels with Bio-polyelectrolytes

In the next step, we tried to coat the dex-HEMA microgels with four bio-polyelectrolyte bilayers by using the LbL technique.[34] The bio-polyelectrolyte-coated dex-HEMA microgels will be termed "microcapsules" in the rest of this paper. Initially, we attempted to coat the dex-HEMA microgels with a number of different bio-polyelectrolytes. Chitosan, poly-L-lysine, poly-L-ornithine, alginic acid, and hyaluronic acid were unsuitable bio-polyelectrolytes because severe aggregation of the microgels took place; in most cases the dex-HEMA

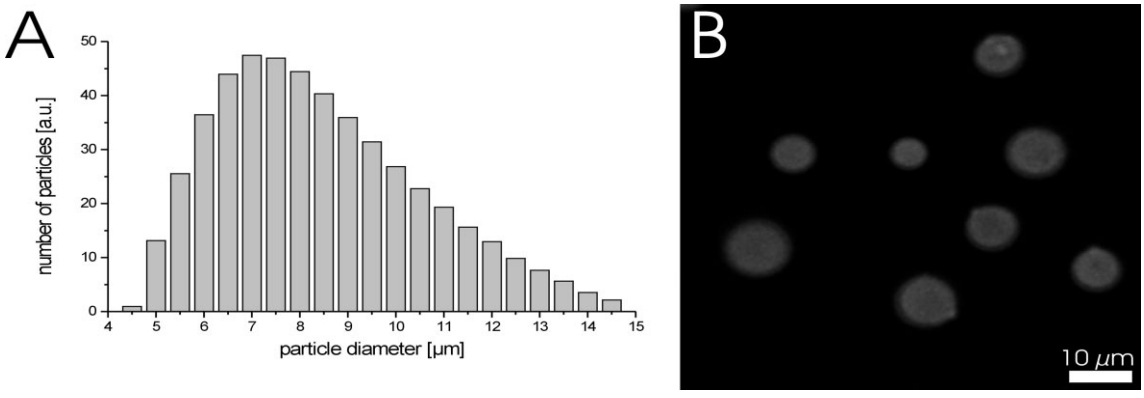

Figure 2. A) Size distribution of the dex-HEMA microgels, as measured by laser diffraction. B) Confocal microscopy image of dex-HEMA microgels fluorescently labeled with 150 kDa FITC-dextran. FITC: fluorescein isothiocyanate.

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microgels aggregated instantaneously upon dispersal in the bio-polyelectrolyte solution. The low charge density and relatively high viscosity (especially in case of chitosan, alginic acid, and hyaluronic acid) of the bio-polyelectrolytes may explain their failure. The only bio-polycation that coated the dex-HEMA microgels without aggregation was poly-L-arginine (pARG). pARG is the only polypeptide with side groups that are charged at almost every pH (the pKa of the side groups is 12.5), and is therefore a strong polyelectrolyte. Using pARG as the polycation, chondroitin sulfate (CHON), poly-L-aspartic acid (pASP), low-molecular-weight poly-L-glutamic acid (pGLUlow), high-molecular-weight poly-L-glutamic acid (pGLUhigh), and dextran sulfate (DEXS) seemed to be suitable polyanions for LbL coating of the dex-HEMA microgels. Figure 3 shows confocal microscopy images of dex-HEMA microgels coated with different combinations of bio-polyelectrolytes. A clear ring of red fluorescence (originating from the labeled pARG) surrounding the microgels can be observed, indicating a successful LbL coating of the dex-HEMA microgels.

2.3. Behavior of the Microcapsules upon Degradation of the Gel Core

To investigate how the degradation of the dex-HEMA microgel core influences the bio-polyelectrolyte coating, the microcapsules were incubated in a 0.1 M phosphate buffer (pH 7.4) at 37 °C. After five days (the time it takes to fully degrade the dex-HEMA microgel core at pH 7.4 and 37 °C), the microcapsules were investigated under a confocal microscope (Fig. 4). The result was clearly dependent on the composition of the LbL membrane. Figure 4A shows that all microcapsules were ruptured, and thus that self-rupturing capsules were successfully obtained. Figure 4B shows that some microcapsules were ruptured, while others remained intact and filled with FITC-dextran. Figure 4C shows that hollow microcapsules were obtained, i.e., the microcapsules did not rupture, but released the 150 kDa FITC-dextran, as no significant fluorescence was detected within the microcapsules.

Table 1 shows which LbL membrane compositions resulted in either self-rupturing and/or hollow microcapsules. The behavior of the LbL membrane during degradation of the microgel core most likely depends on its mechanical strength and its permeability to the degradation products (i.e., 19 kDa dextran chains) of the microgel. $(DEXS/pARG)_4$ membranes remained

Table 1. Index of the observed effect of the dex-HEMA microgel core degradation according to the composition of the coating membrane.

Self-rupturing microcapsules	Hollow and self-rupturing microcapsules	Hollow microcapsules
$(pASP/pARG)_4$	$(pGLU_{high}/pARG)_4$	$(DEXS/pARG)_4$
$(CHON/pARG)_4$		
$(pGLU_{low}/pARG)_4$		

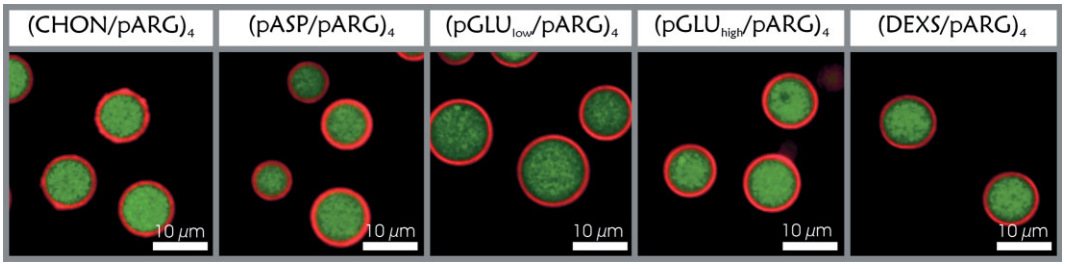

Figure 3. Confocal microscopy images of the microcapsules obtained after LbL coating of the dex-HEMA microgels with four bio-polyelectrolyte bilayers. The microgels were fluorescently labeled with 150 kDa FITC-dextran (green color), whereas the pARG in the LbL coating was fluorescently labeled with rhodamine B isothiocyanate (RITC; red color).

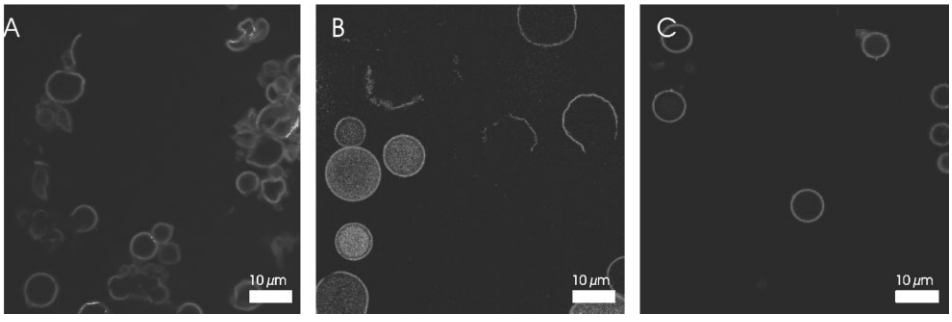

Figure 4. Confocal images of dex-HEMA microgels (fluorescently labeled with 150 kDa FITC-dextran) coated with A) $(CHON/pARG)_4$, B) $(pGLU_{high}/pARG)_4$, and C) $(DEXS/pARG)_4$ after degradation of the microgel core. In (A), all microcapsules were broken and released their contents. In (B), both broken as well as intact (still filled with 150 kDa FITC-dextran) microcapsules were observed. The capsules in (C) remained intact, but had released their contents by diffusion through the bio-polyelectrolyte coating. In all cases, the pARG was fluorescently labeled with RITC.

intact, probably because of the fact that they are not only permeable to the 150 kDa FITC-dextran, but also to the degradation products of the microgels, which hampers the build-up of a significant osmotic pressure. The other bio-polyelectrolyte coatings were apparently less permeable to the degradation products of the microgels, allowing the osmotic pressure to build up and rupture the membrane. It is also interesting to note that an increase in molecular weight of the pGLU clearly influenced the (mechanical and/or permeability) behavior of the microcapsules. Microcapsules fabricated with $pGLU_{low}$/pARG all ruptured, while those fabricated with $pGLU_{high}$/pARG did not all explode: a percentage of them remained intact, keeping the FITC-dextran encapsulated. This indicates that the increase in molecular weight of the pGLU changes the interplay between the mechanical properties and the permeability of the bio-polyelectrolyte coating.

2.4. Self-Rupturing Microcapsules

We took a closer look at the behavior of the (pGLUlow/pARG)$_4$ microcapsules during degradation of the microgel core (Fig. 5). The degradation was accelerated by increasing the pH of the dispersion (which accelerates the hydrolysis of the esters in dex-HEMA). Because pARG is a strong polyelectrolyte, its cationic groups are positively charged over a wide pH range. Therefore, we could expect that the alkaline pH does not influence the properties of the polyelectrolyte membrane. This is crucial, as it has been reported that the properties of polyelectrolyte membranes containing one or more weak polyelectrolytes may change significantly as a function of pH.[35–38] Figure 5 shows confocal images taken at 20 s time intervals after the addition of 5 μL of 0.5 M NaOH to 5 μL of the (pGLUlow/pARG)$_4$ microcapsule suspension. The microcapsules started to swell (Fig. 5A–D), and after a certain time (Fig. 5F) all microcapsules ruptured, most likely when the swelling pressure of the degrading microgels exceeded the tensile strength of the bio-polyelectrolyte membrane. After rupturing, only remnants of broken microcapsules were observed (Fig. 5F). The encapsulated FITC-dextran was completely released.

2.5. Hollow Microcapsules

Figure 6 shows confocal microscopy images of (DEXS/pARG)$_4$ microcapsules both before (Fig. 6A) and after (Fig. 6B) degradation of the microgel core. After degradation,

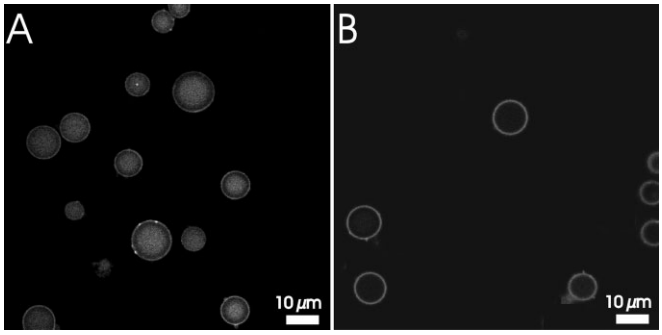

Figure 6. Confocal microscopy images of (DEXS/pARG)$_4$-coated dex-HEMA microgels before (A) and after (B) degradation of the microgel core. The pARG was red fluorescently labeled with RITC. The microgels were initially loaded with 150 kDa FITC-dextran.

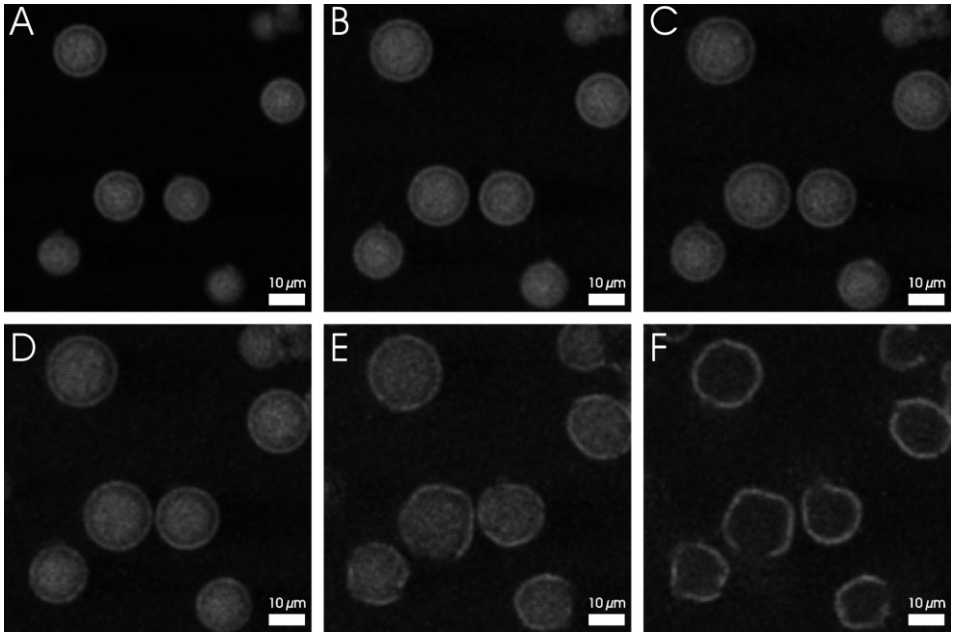

Figure 5. Confocal snapshots of (pGLUlow/pARG)$_4$-coated microcapsules during degradation of the microgel core at alkaline pH. The microgels contained 150 kDa FITC-dextran, and the pARG was fluorescent labeled with RITC. The time interval between the successive snapshots (A–F) is 20 s.

the interior of the microcapsules was no longer (green) fluorescent, which indicates the outward diffusion of the FITC-dextran during the degradation process of the microcapsules. Figure 7 shows scanning electron microscopy (SEM) images of the microcapsules before (Fig. 7A), and after (Fig. 7B) degradation of the microgel core. The rough surface in Figure 7A is probably a result of the differential drying between the dex-HEMA microgel core and the $(DEXS/pARG)_4$-coating upon sample preparation. In Figure 7B, one can see a collapsed microcapsule, which confirms that the microgel core has indeed been degraded, yielding a hollow microcapsule. By using atomic force microscopy (AFM), the thickness of the bio-polyelectrolyte membrane could be estimated (Fig. 7C and D) according to the method reported by Leporatti et al.[39] Taking into account the fact that the measured height is twice the thickness of a single microcapsule wall, the thickness was estimated to be (45 ± 4) nm (as obtained from measurements on three different microcapsules). Compared to other LbL membranes, the $(DEXS/pARG)_4$ coating seems to be rather thick. Déjugnat and Sukhorukov[35] reported a bilayer thickness of 3.5 nm for PSS/PAH; we measured 11 nm per DEXS/pARG bilayer. Bio-polyelectrolyte multilayers deposited on flat substrates have been studied by Picart et al.[40,41] They reported that the thickness of the membranes increased exponentially as a function of the number of adsorbed layers. Also, LbL multilayer films from polysaccharides and polypeptides seemed to show an exponential growth, in contrast to PSS/PAH multilayers, which showed a linear growth step as a function of layer number.[40,41] It could also be possible that, in Figure 4C, not all of the degradation products of the microgel (i.e., 19 kDa dextran chains) were expelled from the interiors of the microcapsules (see section 2.6). These residual dextran molecules could result in a higher estimation of the shell thickness from AFM measurements.

2.6. Loading of Hollow Microcapsules

Hollow $(DEXS/pARG)_4$ capsules, obtained after degradation of the dex-HEMA microgel cores, were incubated for 30 min in FITC-bovine serum albumin (FITC-BSA) or 40 kDa FITC-dextran solutions (0.5 mg mL^{-1}). Figure 8A and B shows the FITC-BSA and FITC-dextran strongly accumulated inside the hollow microcapsules. Nearly no fluorescence in the solution surrounding the microcapsules was observed. Similar results were obtained for FITC-dextran with a molecular weight ranging from 4 to 2000 kDa (data not shown). In contrast, hollow $(DEXS/pARG)_4$ capsules fabricated from $MnCO_3$ microparticles as a sacrificial template did not become filled with FITC-BSA (Fig. 8C), in agreement with earlier findings.[42,43]

Currently, it remains speculative why hollow $(DEXS/pARG)_4$ dex-HEMA microgel-templated microcapsules so strongly absorb FITC-BSA, whereas hollow $(DEXS/pARG)_4$ microcapsules templated on $MnCO_3$ exclude FITC-BSA. It is known that the permeability of polyelectrolyte membranes not only greatly depends on external conditions, such as pH and ionic strength, but also on the type of sacrificial template from which they are fabricated.[44–47] As 150 kDa FITC-dextran is able to diffuse through the $(DEXS/pARG)_4$ membrane during degradation of the dex-HEMA microgel core (Fig. 6), it is very likely that most of the 19 kDa dextran chains, from which the microgels were fabricated, are also able to permeate the $(DEXS/pARG)_4$ membrane. It remains possible, however, that not all the dextran chains left the microcapsules. Indeed, when the hollow $(DEXS/pARG)_4$ microcapsules were viewed with the confocal microscope at maximum laser intensity, traces of green fluorescence (due to remaining 150 kDa FITC-dextran) could still be observed inside the microcapsules (data not shown). It is known that many proteins show affinity for dextran,[48] therefore remnants of dextran in the hollow capsules might explain the accumulation of FITC-BSA.

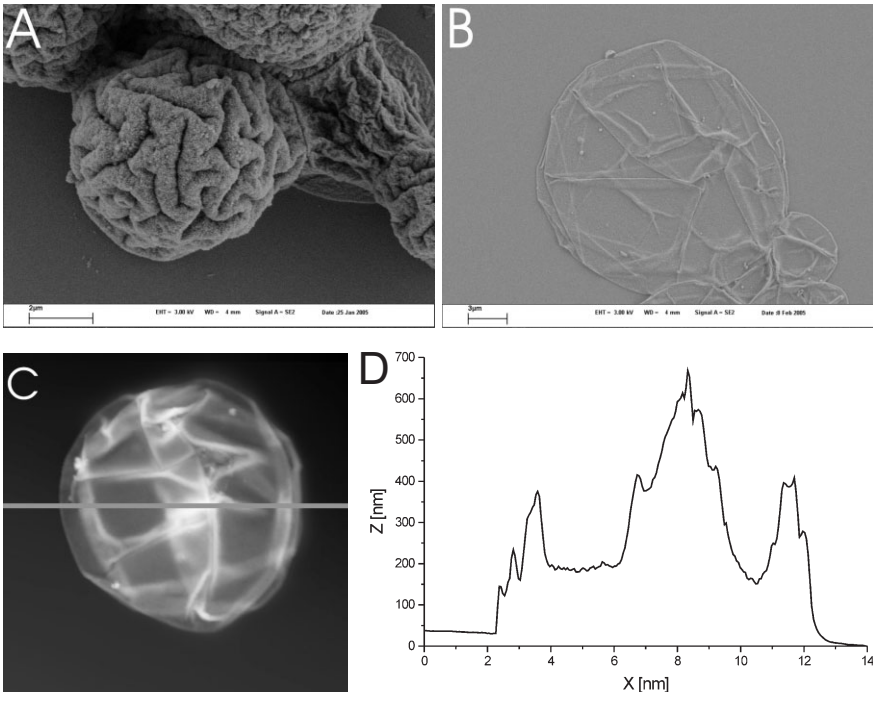

Figure 7. SEM images of $(DEXS/pARG)_4$ coated dex-HEMA microgels before (A) and after (B) degradation of the microgel core. C) AFM image of a hollow $(DEXS/pARG)_4$ microcapsule fabricated from a dex-HEMA microgel as sacrificial template. D) Height profile along the line indicated in (C).

3. Conclusions

This study reports the successful fabrication of microcapsules consisting of a biodegradable dextran microgel core surrounded by a bio-polyelectrolyte multilayer coating applied to the microgels by layer-by-layer technology. Upon degradation of the microgel core either self-rupturing or hollow microcapsules were ob-

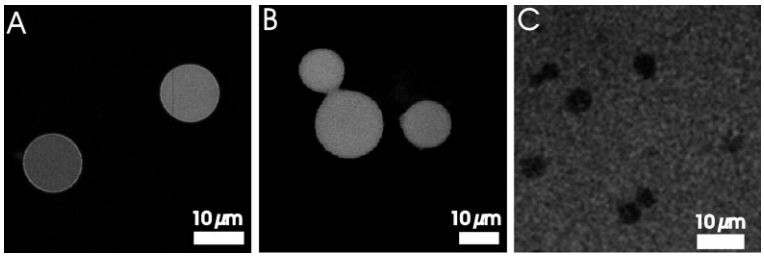

Figure 8. Confocal microscopy images of hollow $(DEXS/pARG)_4$ microcapsules, fabricated from dex-HEMA microgels as a sacrificial template, dispersed in A) FITC-BSA solution and B) 40 kDa FITC-dextran solution. C) Confocal microscopy image of hollow $(DEXS/pARG)_4$ microcapsules, fabricated from $MnCO_3$ microparticles as a sacrificial template, dispersed in a FITC-BSA solution.

tained, depending on the composition of the bio-polyelectrolyte coating.

Self-rupturing microcapsules—microcapsules that rupture as a result of the swelling pressure of the degrading microgel core—were obtained by LbL coating of dex-HEMA microgels with four bio-polyelectrolyte bilayers of CHON/pARG, $pGLU_{low}$/pARG, or pASP/pARG. The major difference between the self-rupturing microcapsules described herein and those previously reported by our group[9] is that the former burst at a physiological pH. Their exterior coating consists not of synthetic, but biological polyelectrolytes. Both the rupturing at a physiological pH and the use of bio-polyelectrolytes are promising features in the development of self-rupturing microcapsules for drug delivery purposes.

Hollow capsules could be obtained by degrading dex-HEMA microgels after they were coated with four bio-polyelectrolyte bilayers of DEXS/pARG. It was shown that FITC-BSA and FITC-dextran spontaneously accumulated in the hollow capsules, whereas they did not accumulate in $(DEXS/pARG)_4$ hollow microcapsules prepared from $MnCO_3$ microparticles as the sacrificial template. Previously reported procedures to load hollow polyelectrolyte microcapsules with macromolecules often required the inclusion of oppositely charged species,[49] or an additional step such as a change in pH,[50,51] ionic strength,[52] solvent polarity,[53] or crosslinking[54] to temporarily change the permeability of the microcapsule's membrane. The spontaneous deposition of biomacromolecules in hollow microcapsules prepared from dex-HEMA microgels as a sacrificial template could be of interest for drug encapsulation purposes.

4. Experimental

Materials: Dextran (weight-average molecular weight (M_w) ca. 19 kDa), *N,N,N′,N′*-tetramethylenediamine (TEMED), DEXS ($M_w \approx 10$ kDa), pARG ($M_w \approx 100$–200 kDa), CHON, pASP ($M_w \approx 15$–50 kDa), $pGLU_{low}$ ($M_w \approx 15$–50 kDa), $pGLU_{high}$ ($M_w \approx 50$–100 kDa), FITC-BSA, FITC-dextran ($M_w \approx 20$, 40, 70, 150, 500, and 2000 kDa), and rhodamine B isothiocyanate (RITC) were purchased from Sigma–Aldrich/Fluka. Potassium persulfate (KPS), dimethyl aminoethyl methacrylate (DMAEMA), poly(ethylene glycol) (PEG; $M_w \approx 20$ kDa), citric acid, sodium hydroxide, and hydrochloric acid were purchased from Merck. RITC-labeled pARG was synthesized by mixing RITC and poly-L-arginine in 0.1 M borate buffer at pH 8.5, followed by dialysis with pure water for several days.

Synthesis of dex-HEMA Microgels: Dex-HEMA was synthesized as previously reported [10,11]. The degree of substitution (DS; the number of HEMA groups per 100 glucopyranose units) was 2.5, as determined by ^{1}H NMR spectroscopy. Fluorescent dex-HEMA microgels were fabricated according to Franssen and co-workers [31,32] by dissolving dex-HEMA (71 mg), FITC-dextran solution (50 mg mL^{-1}, 20 μL), and DMAEMA (35 μL) in water (1.577 mL), and subsequently emulsifying this solution with an aqueous PEG solution (24 % (v/v), 3.35 mL). Radical polymerization of the aqueous dex-HEMA emulsion droplets was initiated by adding TEMED (100 μL, pH neutralized with 4 N HCl) and KPS (180 μL, 41 mM). The reaction was carried out at room temperature for 1 h. Afterwards, the obtained microgels were washed three times with pure water to remove PEG, KPS, and TEMED. Finally, the microgels were suspended in water (5 mL) and stored at –20 °C. The size distribution of the microgels was determined by laser diffraction (Malvern Mastersizer).

Polyelectrolyte Coating of the Microgels: The dex-HEMA microgels were coated by the consecutive adsorption of oppositely charged polyelectrolytes [55]. A dex-HEMA microgel dispersion (500 μL) was mixed with polyelectrolyte solution (1 mg mL^{-1} in 0.5 M NaCl, 1 mL). The polyelectrolytes were allowed to adsorb for 10 min under continuous shaking. The dispersion was then centrifuged at a speed of 300 g for 3 min. Subsequently, the supernatant was removed and the microgels were redispersed in Milli-Q water to remove the nonadsorbed polyelectrolytes. This washing was repeated twice before the second polyelectrolyte solution was added. As the microgels were positively charged, we started the LbL coating with the polyanion. In total, four polyelectrolyte bilayers were deposited.

Preparation of Hollow Microcapsules using dex-HEMA Microgels as the Template: To obtain hollow microcapsules, dex-HEMA microgels coated with four DEXS/pARG bilayers were dispersed for 30 min in 0.1 M NaOH (to degrade the dex-HEMA microgel cores), followed by three washing steps with pure water to remove the degradation products of the microgels and the NaOH. Finally, the hollow microcapsules were dispersed in 1 mL Milli-Q water.

Preparation of Hollow Microcapsules using $MnCO_3$ as the Template: $MnCO_3$ particles with an average diameter of 5 μm were prepared as reported by Zhu et al. [56]. LbL coating of the $MnCO_3$ particles occurred as described above for the LbL coating of dex-HEMA microgels. The MnCO3 cores were dissolved by adding citric acid (0.2 M, 1 mL) in HCl (0.1 M) to the coated MnCO3 particles, followed by several washing steps with pure water [35].

SEM Measurements: SEM measurements were conducted on a Gemini Leo instrument operated at an acceleration voltage of 3 kV. For sample preparation, a drop of microcapsule suspension was applied to a glass slide, dried overnight, and sputtered with gold.

AFM Measurements: AFM images were taken in tapping mode on a Nanoscope IIIa Multimode SFM (Digital Instruments Inc.) in air at room temperature. Samples were prepared by applying a drop of microcapsule suspension onto a freshly cleaved mica substrate, followed by drying under a gentle stream of nitrogen.

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FULL PAPERS

Drug Delivery

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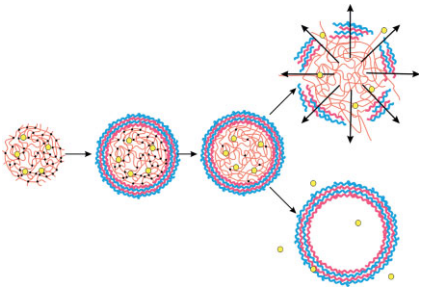
Self-Rupturing and Hollow Microcapsules Prepared from Bio-polyelectrolyte-Coated Microgels



Biodegradable microgels are coated with bio-polyelectrolytes by using the layer-by-layer (LbL) technique. Following the degradation of the microgel core, the LbL coating can rupture or stay intact, depending on the bio-polyelectrolytes used (see figure). Both self-rupturing and hollow capsules could be of interest for biomedical applications.