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Synthesis of Chitosan-Stabilized Polymer Dispersions, Capsules, and Chitosan Grafting Products via Miniemulsion

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The potential of chitosan as an emulsion stabilizer is combined with the miniemulsion technique to generate oil droplets, hollow capsules, and latex particles in the diameter range of 100−300 nm carrying a functional biopolymer surface. It turned out that chitosan alone, independent of its molecular weight, is just moderately efficient, which is speculatively attributed to its stiff polysaccharide structure. The addition of biocompatible costabilizers with higher flexibility either to the oil phase or to the water phase, such as Jeffamine or Gluadin (a peptide), eliminates these deficiencies, and very small nanocapsules made of biopolymer hybrids can be obtained. NMR analysis shows that the costabilizer is effectively grafted/cross-linked to the chitosan which makes the miniemulsion route also effective for the modification of hard-to-handle, amphiphilic biopolymers either from the water or from the oil phase.

Introduction

Chitosan, a biodegradable, nontoxic, and renewable resource commodity, is a naturally occurring polymer of β-(1−4)-2-amino-2-deoxy-D-glucopyranose, prepared by partial alkaline deacetylation of chitin, a main structural component of the cuticles of insects, mollusks, and crustacean.[1] Its copolymer structure is depicted in Figure 1.

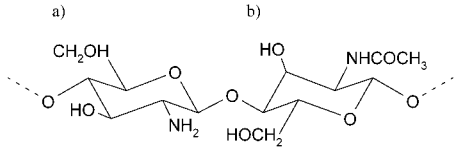

Figure 1. Chemical structure of chitosan consisting of (a) deacetylated and (b) actetylated units.

The biopolymer is insoluble in water at pH = 7 but becomes soluble and positively charged in acidic media and can therefore be used either as a flocculating agent[2,3] or as a biosurfactant.[4] This polyelectrolyte has been successfully used to stabilize polymer nanoparticles of poly(methyl methacrylate)[5] and of poly(butyl cyanoacrylate).[6] In these cases, the chitosan is thought to be grafted onto the particles by a hydrogen abstraction mechanism. These positively charged nanoparticles can be used as ideal candidates for the purification of proteins from a crude biological mixture.[7] If its pH is kept above 7, the proteins carry a net negative charge and can therefore develop electrostatic interactions with the particles. These nanoparticles are also well suited as site-specific drug carriers.[6] Indeed, the positively charged particles have an improved stability in the presence of biological cations and are gaining increasing importance for drug delivery following intravenous, oral, or ocular administration. Thus, as chitosan is a biocompatible[8] and biodegradable cationic polyelectrolyte, it has attracted great attention in pharmaceutical and biomedical fields[9] and was used to synthesize sustained release gels[9] and capsules.[10] The capsules can be prepared in different ways. The coacervation technique is a simple process, which uses the solubility properties of chitosan.[10,11] By blowing a solution of chitosan into a nonsolvent, e.g., a NaOH−methanol mixture, the polymer precipitates at the surface of the droplets thereby forming capsules. The product to be encapsulated has thus to be water soluble. On the contrary, in the coating process[10,12] the oil phase containing the product is blown in the chitosan solution, the polymer precipitating at the surface of the droplets. A more elegant process involves the self-assembling properties of complexes between chitosan and polyions in solution.[13,14] However, this process often leads to the formation of fibers rather than capsules. Finally, the surface properties of chitosan were used to produce capsules by cross-linking the chitosan at the interface.[15−17] The cross-linking agent is in most cases glutaraldehyde. However, the capsules are quite big (from 500 nm to several micrometers), and the size distribution is large.

In this contribution it is shown that chitosan is also a well-suited stabilizer for miniemulsion polymerization and can be used to produce a variety of latexes ranging from simple polystyrene particles to well-defined nanocapsules. The miniemulsion polymerization is a novel and powerful technique to produce these latexes.[18] The particles are preformed as oil droplets with a size of 50−500 nm already from the beginning of the reaction by shearing a system containing oil, water, a surfactant, and a highly water insoluble compound, the so-called hydrophobe.[19−21] The surfactant stabilizes the droplets against collisions, and mass exchange (Ostwald ripening) between the droplets is suppressed by the use of the hydrophobe.[22] Each droplet behaves like a nanoreactor, and the polymer particles produced have ideally the same size as the monomer droplets.[23] This makes the miniemulsion process suitable for many reactions. For the formulation of miniemulsions, a wide variation of ionic

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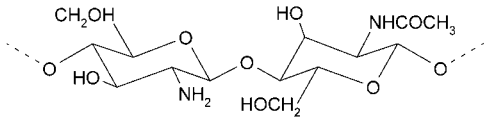
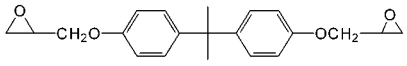
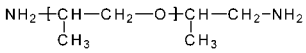
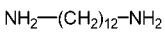
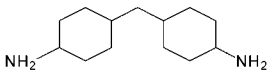
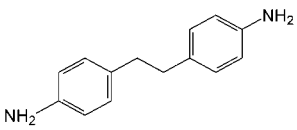
Table 1. Reagents Used for the Polyaddition in Miniemulsion

Substance		Viscosity (cps) or M_w (g·mol^{-1})
Chitosan		LM : 20-200 cps[a)] HM : 800-2000 cps[a)]
	deacetylation degree: 75 - 85 %	
Epoxide		
Epikote E828		312 g·mol^{-1}
Amine		
Jeffamine D2000		2032 g·mol^{-1}
1,12 diaminododecane		200 g·mol^{-1}
4,4'-diaminodicyclo hexylmethane		210 g·mol^{-1}
4,4'-diaminobibenzyl		212 g·mol^{-1}

[a] 1% in 1% acetic acid, at 20 °C.

and nonionic surfactants could be used resulting in differently charged and stable polymer dispersions.[24,25] It was recently shown that the miniemulsion process can be applied in a much broader range than only radical polymerization, e.g., anionic polymerization[26,27] and polyaddition[28,29] can be performed in the dispersed state *after* emulsification. Furthermore, hollow nanocapsules were prepared in a one-step miniemulsion process.[30]

In this paper, it is intended to combine the possibilities opened by the use of the amphiphilic biopolymer chitosan and the miniemulsion route. First, the polymerization of styrene is carried out using a typical miniemulsion procedure with chitosan as stabilizer, producing highly monodisperse particles. Chitosan miniemulsions will then be used for the synthesis of epoxy particles by polyaddition. As chitosan bears amine and alcohol functions, it can react with the epoxide and can be grafted onto the particles, which are obtained by polyaddition reaction. This turns out to be a convenient technique to modify or graft the water-soluble chitosan with nonwater soluble reaction partners, thus resulting in new and previously not accessible chitosan derivates. Here, also other biodegradable polymers can be added for hybrid formation. Finally, nanocapsules consisting of hybrid polyaddition polymers as shell and a hydrophobic oil as core were elaborated. These capsules are biocompatible and biodegradable and can find applications in drug delivery.

Experimental Part

Chemicals. Styrene (Aldrich) was distilled under reduced pressure prior to utilization. The initiator V59 (2,2′-azobis-(2,4-dimethylvaleronitrile)) from Wako-Chemicals, Japan, was used as received. Epikote E828 was obtained from Nagase GMBH. Jeffamine D2000 was donated by Huntsman Corporation. 1,12-Diaminododecane and 4,4′-diaminodicyclohexylmethane were purchased from Fluka and used as received. Gluadin APG was donated by Henkel KGaA. The other products (low molecular weight (LM) and high molecular weight (HM) chitosan, sodium dodecyl sulfate (SDS), cetyl trimethylammonium chloride (CTMA-Cl), hexadecane, toluene, acetic acid, 4,4′-diaminobibenzyl) were purchased from Aldrich and used as received. Deionized water was used for all the experiments. The chemical structure and the molecular weight of the starting materials used in the polyaddition experiments are listed in Table 1.

Synthesis of PS Particles with Only Chitosan as Stabilizer. Chitosan, composed of two different molecular weights (low and high), was dissolved in 1% v/v aqueous acetic acid to obtain a 1% w/w solution. This solution was further diluted with 1% v/v aqueous acetic acid to obtain 0.5, 0.2, and 0.1% w/w solutions, which are used as aqueous phase in the miniemulsion polymerization. The monomer phase composed of a mixture of 2 (or 4) g of styrene, 250

mg of hexadecane as hydrophobe, and 40 (or 80) mg of V59 as oil soluble initiator is added to 24 g of the chitosan solution. After the mixture was stirred at room temperature for 1 h, a miniemulsification was obtained by ultrasonicating for 120 s at 90% amplitude (Branson sonifier W450 Digital) at 0 °C. For polymerization, the temperature was increased to 71 °C and kept at that temperature for 12 h.

Synthesis of Epoxy Resin Particles, Grafting to Chitosan. One or two grams of a mixture containing the Epikote and the desired diamine (for quantities see the Tables) in a mole ratio 2:1 was dispersed in 20 g of a chitosan solution prepared as described above. The monomer mixture contained 250 mg of hexadecane as hydrophobe. Different amounts of Jeffamine D2000 as indicated in detail in the tables were added in the monomer mixture while different amounts of CTMA-Cl were added in the continuous phase, after emulsification. After the mixture was stirred at 0 °C for 1 h, the miniemulsion was prepared by ultrasonicating the emulsion for 120 s at 90% amplitude (Branson sonifier W450 Digital) at 0 °C to prevent polymerization. For polyaddition, the temperature was increased to 68 °C and kept at that temperature for 12 h.

Synthesis of Nanocapsules Made of Chitosan−Epoxy Hybrid Polymers. One-half gram of a mixture containing the Epikote and the diamine in a mole ratio 2:1 was dissolved in 2 g of toluene, and 250 mg of hexadecane was added as the hydrophobe. This solution was dispersed in 24 g of a chitosan solution prepared as described before. After the solution was stirred at 0 °C for 1 h, the miniemulsion was prepared by ultrasonicating the emulsion for 120 s at 90% amplitude (Branson sonifier W450 Digital) at 0 °C to prevent polymerization. For polymerization, the temperature was increased to 68 °C and kept at that temperature for 12 h.

For making protein-*g*-polysaccharide grafted hybrid structures, the water-soluble amphiphilic Gluadin APG was used. Four-tenths gram of the diepoxide was dissolved in 2 g of toluene. Two hundred fifty milligrams of hexadecane acted as hydrophobe. This solution was dispersed in a chitosan solution in which the Gluadin was dissolved too.

Analytical Methods. The particles sizes were measured using a Nicomp particle sizer (model 370, PSS Santa Barbara, USA) at a fixed scattering angle of 90°.

Electron microscopy was performed with a Zeiss 912 Omega electron microscope operating at 120 kV. The diluted colloidal solutions were applied to a 400-mesh carbon-coated copper grid and left to dry. No further contrasting was applied.

All measurements regarding the surface tension were carried out with a K10 processor-tensiometer form Krüss employing the DuNöuy−Ring method. The radius of the Pt−Ir ring RI12 was 9.45 mm and the wire had a radius of 0.185 mm.

Infrared spectroscopy was performed on a Biorad FTS 600 spectrometer in absorbance setup. The samples were measured as pure products with an ATR accessory.

Liquid ^{1}H NMR spectra were recorded with a Bruker DSP400 using D_2O as solvents, adding the potassium salt of hydroquinone sulfonic acid as calibration product for quantitative determination.

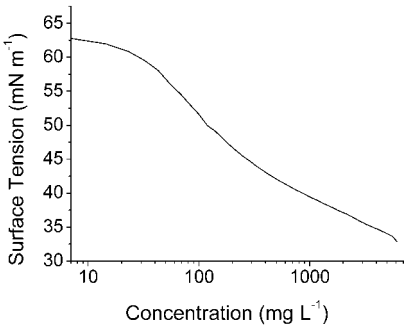


Figure 2. Equilibrium surface tension as a function of concentration for low molecular weight chitosan in 1% v/v aqueous acetic acid at pH 3.

Results and Discussion

For the preparation of miniemulsions (see below), two types of chitosan, which differ in their molecular weight, were employed for this work, one chitosan has low molecular weight and the other has high molecular weight (in the following LM and HM will be used for distinction). The deacetylation of both chitosans was between 75 and 85%, which is close to the reported optimum value for emulsification properties.[4] Concentration-dependent surface tension measurements of the different chitosan solutions show that only the low molecular weight chitosan was able to reduce the surface tension of aqueous acetic acid progressively from 66 mN·m^{-1} to less than 35 mN·m^{-1} at a concentration of 7 g·L^{-1}, but without any sharp break characterizing something as a distinct critical micelle concentration (cmc) value (see Figure 2). No significant decrease of the surface tension was observed in the case of the high molecular chitosan. This is known for larger amphiphilic polymers and tentatively explained by the fact that the entropy factor by adsorbing at the interface seems not to be compensated by the enthalpy win when the length of the chitosan molecule increases.[31] Although a chitosan charge depends obviously on the pH, there is no dependence of the surface tension on the pH values between pH 1 and 4 of the solution.

Polystyrene Nanoparticle Dispersions Stabilized by Chitosan. As a reference experiment, styrene was dispersed with conventional miniemulsion methods[32] in a chitosan solution. Using either low or high molecular weight chitosan as a biocompatible surfactant produced stable styrene miniemulsions with as low as 0.5% chitosan compared to the monomer phase. However, during polymerization only a part of the polystyrene formed could be stabilized by the chitosan, the other part coagulated resulting in a solid content lower than expected (see Table 2). With an increase of the chitosan-to-styrene ratio, less coagulate was formed while keeping the particle size constant. Typical latex particles obtained are depicted by transmission electron microscopy (TEM) in Figure 3.

The surface tension values of the final dispersions prepared by the low molecular weight chitosan were measured to be around 66 mN·m^{-1}, indicating that in this case all the chitosan is mainly adsorbed on the particles. As chitosan bears amine functions, it can be grafted onto the particles via a hydrogen abstraction mechanism.[5,6]

As already stated and quantified in Table 2, chitosan alone as a stabilizer for nanometer-sized droplets is insufficient,

Table 2. Synthesized Polystyrene Particles Using Different Styrene/Chitosan Ratios by Varying the Amount of Styrene and the Concentration of the Chitosan Solution, Using 20 mL of Chitosan Solution[a]

latex	chitosan[b]	chitosan/ styrene (%)	dispersed/ continuous phase (%)	solid content %)	diameter (nm)
EM174	HM	1	9	3.1	227
EM176	HM	2	9	3.4	214
EM178	HM	5	9	5.2	238
EM175	HM	0.5	16.6	3.5	281
EM177	HM	1	16.6	5.3	261
EM179	HM	2.5	16.6	7.1	264
EM180	LM	1	9	2.8	234
EM182	LM	2	9	2.4	231
EM184	LM	5	9	5.7	321
EM181	LM	0.5	16.6	3.5	218
EM183	LM	1	16.6	4.8	376
EM185	LM	2.5	16.6	7.6	236

[a] The pH is about 3. [b] Key: LM, low molecular weight; HM, high molecular weight.

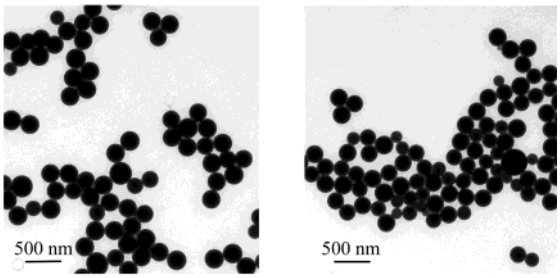


Figure 3. TEM pictures of polystyrene latexes stabilized by chitosan: left, low molecular weight chitosan (EM185); right, high molecular weight chitosan (EM178).

Table 3. Influence of a Second Surfactant Added after Ultrasonication (chitosan/styrene, 1%; 4 g of styrene, 20 g of dilute acetic acid; continuous/dispersed phase, 16.6%; pH = 3)

latex	surfactant	amount (mg)	solid content (%)	diameter (nm)
EM237	SDS	38	3.8	392
EM241	SDS	89	4.1	379
EM243	Lutensol	39	3.2	191
EM229	Lutensol	199	3.8	189
EM242	CTMA-Cl	38	13.8	95
EM256	CTMA-Cl	40	12.7	81
EM250	CTMA-Cl	77	12.8	79
EM253	Jeffamine D2000	21	11.0	227
EM254	Jeffamine D2000	41	14.9	149
EM255	Jeffamine D2000	80	15.8	107
EM225	Jeffamine D2000	145	15.6	108

and a large amount of coagulate is formed which might be originated by the fact that the chitosan cannot protect the final polymer particles against collision. Therefore, it was tried to support chitosan emulsification by additional small amounts of other low molecular weight surfactants after the miniemulsification process or synthetic polymers added to the oil phase. The experiments are listed in Table 3.

The experiments suggest that the anionic SDS does not improve this situation, which has to be expected: in this case, interaction of the anionic surfactant with the cationic polymer leads even to a lowering of the polymer activity. The nonionic Lutensol leads to significantly smaller particles, but still low solid contents are obtained. On the contrary, the cationic surfactant CTMA-Cl allows high solid contents and synthesis of very small particles with diameters less than 100 nm. Indeed, the cationic polymer/cationic surfactant pair gives the required stability, and the comparison to the case of chitosan as the only interfacial active component shows that those particles are already the product of a coarsening process throughout polymerization (from 100 to 200 to 300 nm) and do not represent the original miniemulsion state. This shows that in any case pure chitosan is not suited for the miniemulsion process. The choice of CTMA-Cl on the other hand has to be just seen as a cross-test to show the deficiencies of the system, since its use is prohibited by demands of biocompatibility and biodegradability.

Table 4. Synthesized Particles with Epikote E828 and Jeffamine D2000 (mole ratio 2:1)[a]

latex	chitosan[b]	chitosan/ monomer (%)	dispersed phase (%)	diameter (nm)	std dev σ
EM189	LM	2	5	223	0.61
EM188	LM	4	5	173	0.37
EM208	LM	10	5	149	0.45
EM191	LM	2	9	205	0.41
EM209	LM	5	9	170	0.49
EM210	LM	2.5	16.6	173	0.63
EM200	HM	2	5	228	0.60
EM197	HM	4	5	222	0.55
EM199	HM	10	5	226	0.54
EM198	HM	2	9	186	0.51

[a] The pH is about 3. [b] Key: LM, low molecular weight; HM, high molecular weight.

This is why we also added a synthetic biocompatible polymer, Jeffamine D2000, which was shown earlier to have interfacial properties,[29] to the monomer phase to ensure cationic stabilization of the "weak spots" during the polymerization process. In this case, indeed high solid contents were obtained already at small amounts of Jeffamine (between 0.5 and 2.5% with respect to the monomer phase), and very small and monodisperse latexes without any coagulate could easily be synthesized. It is interesting to see that beyond 1% of Jeffamine, the particle size saturates at a similar value as in the case of the cationic surfactant CTMA-Cl. We expect this to be the primary particle size, which is now stabilized throughout the process.

Epoxy Hybrid Particles Using Chitosan as Reactive Surfactant. It has recently been shown that the miniemulsion process is not restricted to radical polymerization but can also be applied to the polyaddition of different diepoxides with various diamines.[29] In these examinations, the standard surfactants SDS and Lutensol AT50 were used. Here, it is desired to synthesize polyaddition latexes with chitosan/Jeffamine D2000 as the stabilizer/costabilizer system. Since both chitosan and Jeffamine are bearing amine functionalities, they can react with the diepoxides and can be considered as reactive stabilizers.

In a first set of experiments, a monomer mixture containing the diepoxide Epikote E828 and the diamine Jeffamine was dispersed in the chitosan solution, using the classical miniemulsion procedure (see Table 4).

Stable and coagulate-free latexes were obtained with relatively broad size distributions. The results suggest that

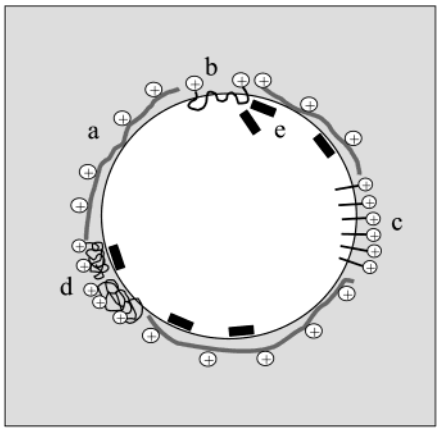


Figure 4. Schematic view of the formation of nanocapsules by interfacial reaction. Chitosan acts as a reactive biocompatible stabilizer from the water phase forming patches on the interface (a); costabilizer like oligomeric diamines (b) (e.g., Jeffamine D2000) or low molecular cationic surfactants (c) (e.g., CTMA molecules) can improve the surface layer structure from the inside of the droplets and the coupled stabilization efficiency. A stabilization from the water phase can also be provided by a water soluble but amphiphilic protein, e.g., Gluadin (d). A diepoxide (e) can additionally be used as stabilizing cross-linking agent.

the particle size decreases with the amount of low molecular weight chitosan, as is the case for the conventional surfactants[24] and also decreases with increasing ratio of the dispersed to continuous phase. No clear tendency was obtained in the case of high molecular weight chitosan. This result is reminiscent of the interfacial properties of chitosan in solution, as pointed out through surface tension measurements.

Using other diamines such as 1,12-diaminododecane and 4,4′-diaminodicyclohexylmethane, chitosan alone was not able to stabilize the polymerizing particles, underlining the importance of Jeffamine as a cosurfactant. With minor amounts of Jeffamine, it was possible to synthesize a great variety of epoxy resins, which however are not presented in detail.

Formation of Nanocapsules. With the hybridization and stabilization chemistry established in the previous experiments, it should be also possible to cross-link chitosan and its cosurfactant Jeffamine D2000 with diepoxies to capsule structures. Here, the amphiphilic hybrid copolymer is built up in situ around the material to be encapsulated, as long as it does not interfere with the polyaddition process in miniemulsion. Previously synthesized chitosan capsules were quite big and not very well defined, and the interfacial hybridization reaction in miniemulsions is expected to extend the accessible size range toward the nanocapsule region. A scheme of this interface reaction around the inert droplet is shown in Figure 4.

In a first set of experiment, toluene containing the diepoxide, Epikote E828, and the Jeffamine was dispersed in the chitosan solution. The starting oil-phase products are miscible, and a stable miniemulsion can be formed. During the cross-linking reaction between the chitosan and the epoxide, phase separation between the toluene and the polymer product occurs, and in the case of appropriate speading coefficients, as reported earlier, capsules are formed.[30]

Table 5. Synthesized Capsules with Epikote E828 and Various Diamines, Mole Ratio 2:1 (chitosan compared to dispersed phase, 1.6%; 4 g of dispersed phase in 20 g of chitosan solution (dispersed/continuous phase, 11%))[a]

latex	amine	Jeffamine (mg)	diameter (nm)
EM33	Jeffamine		126
EM41	1,12-diaminododecane	0	>1000
EM574	1,12-diaminododecane	55	279
EM264	1,12-diaminododecane	88	263
EM341	1,12-diaminododecane	129	249
EM342	1,12-diaminododecane	149	247
EM40	4,4′diaminodicyclohexylmethane	0	>1000
EM232	4,4′−diaminodicyclohexylmethane	156	212
EM42	4,4′-diaminobibenzyl	0	>1000
EM233	4,4′-diaminobibenzyl	157	153

[a] The pH is about 3.

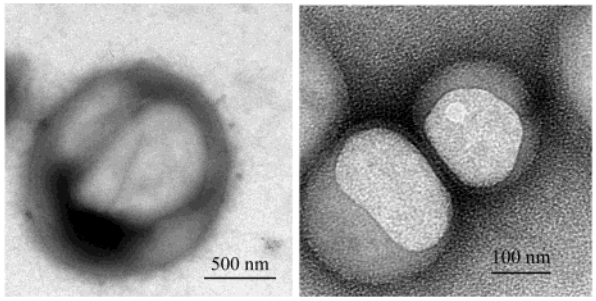


Figure 5. TEM pictures of the capsule preparation.

As a first hint, the toluene could not be detected after the reaction and could not be separated by centrifugation, indicating that it was indeed encapsulated. As expected, the capsules were in the presence of Jeffamine were small (126 nm) and well defined, whereas they were rather big without.

It was not possible to obtain TEM pictures of those samples as the material constituting the shell is a low T_g polymer and degrades in the electron beam. This is why some other diamines were also used to synthesize nanocapsules with higher T_g values (see Table 5). A small amount of Jeffamine was required to control the stability and formation of the capsules, as delineated above. No free toluene could be detected after the reaction. Due to a higher T_g and the higher stability against electron degradation, the shells of nanocapsules could be depicted by TEM as empty hulls (Figure 5) since the toluene is evaporated in the vacuum.

In a last set of experiments, an attempt was made to extend the cross-linking/hybridization reaction to include another water-soluble, amphiphilic, biocompatible and more easily biodegradable amine, namely, Gluadin APG, which is a partially hydrolyzed wheat gluten protein with a molecular weight of about 5000 g·mol^{-1}. Toluene containing Epikote and Jeffamine D2000 was thus dispersed in a solution of chitosan and Gluadin using the conventional miniemulsion process (see Table 6). It is underlined that in this case, the costabilizer is water soluble and approaches the droplet surface from the water phase. After the reaction, again no free toluene was found in the latexes, indicating efficient encapsulation.

NMR measurements were performed, and the spectra were compared with the spectrum of pure Gluadin solutions. Three major observations were made:

Table 6. Synthesized Capsules with 400 mg of Epikote E828 (chitosan/monomer, 1.6 %; dispersed/continuous phase, 11%).

latex	Gluadin (mg)	Jeffamine (mg)	diameter (nm)
EM381	65	0	250 and 900
EM379	117	0	250 and 900
EM380	180	0	250 and 900
EM413	65	165	282
EM411	117	165	158
EM412	180	165	114

[a] Gluadin is introduced in the continuous phase. The pH is about 3.

In the Gluadin spectrum, sharp peaks between 3.5 and 4.1 ppm are detected, whereas in the latexes with the Gluadin, these peaks are much broader indicating a high immobilization caused by reaction of the protein.

In the latex EM412, the latex with the highest amount of costabilizer, the broad peaks are superimposed by small sharp ones, which can be attributed to a minor fraction of mobile and unreacted Gluadin. Here, the capacity of the high surface area of the miniemulsions to bind and react with Gluadin starts to saturate.

In all latex spectra as well as in the Gluadin spectra, at 2.12 ppm a significant and sharp peak appears which might be attributed to a water-soluble, mobile, and nonreactive component in the Gluadin (purely water soluble degradation products). Whereas the intensity of this peak does not change in the latexes (using potassium salt of hydroquinone sulfonic acid as standard), the intensities of all the other peaks (even though they are broadened) decrease to less than 10% indicating that a high amount of the Gluadin is reacted and cannot be detected at all in the 10 ppm range or only as immobilized component (broad peaks).

An exact quantification of the reacted Gluadin is not possible since not only the Gluadin might be immobilized that much that it cannot detected in this experiment but also parts of the other components. However, it is estimated that about 90% of the Gluadin has reacted. This means that a majority of the Gluadin can bind to the miniemulsion droplets, react with the oil soluble diepoxy derivative, and bridge to the chitosan.

It is speculated that the chitosan, due to its rather stiff polysaccharide backbone, shows rather flat adsorption and leaves out larger unstablized "patches", which due to packing reasons cannot be filled by the chitosan itself. This is why addition of a second, more flexible component, such as CTMA-Cl (ideally, but not biocompatible), Jeffamine D 2000, or Gluadin has such a profitable influence. Similar effects are known from microemulsions and are called the "tree-grass" principle.[33] The fact that the Gluadin still has problems arranging with the chitosan at the droplet interface is seen in the data set where both Jeffamine D2000 and Gluadin had to be added to the recipe in order to obtain a Gaussian distribution of the nanocapsules without the formation of larger ones (Table 6). Here, the particle size depends on the amount of Gluadin added, as should be expected for linear costabilizer efficiency.

Conclusions

Emulsions, latexes, and nanocapsules with diameters down to 100 nm and a cationic chitosan surface layer were generated using miniemulsion procedures. While chitosan in itself results in rather large droplets and a major amount of coagulate, addition of a low molecular weight surfactant or a more flexible polymer costabilizer significantly improves the surface layer structure and the coupled stabilization efficiency and allows production of structures in the diameter range between 100 and 300 nm.

Polyaddition of the chitosan stabilizer with two biocompatible costabilizers, Jeffamine D2000 and Gluadin, and a linking diepoxide in the presence of an inert oil results, via an interface reaction, in thin but rather stable nanocapsules. Since both water- and oil-soluble aminic costabilizers can be used, these experiments show the way to a great variety of capsules with different chemical structure. These capsules are expected to be biocompatible and biodegradable and might find applications in drug delivery.

Another point is that in the presented scenario, polymer reactions on biopolymers take place at the relative high internal surface areas of miniemulsions in a preoriented state (by the gradient of cohesion energy). Therefore, reaction in miniemulsions also allows both hydrophilic and hydrophobic modification of chitosan with rather high efficiency, up to the otherwise rather complicated coupling or grafting with a polypeptide, as delineated by the coupling with Gluadin. This will be explored in more detail in forthcoming work.

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