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Nanoscale structures of dextran esters

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Abstract

Multifunctional dextran esters with varying degrees of substitution by furoyl-, pyroglutamyl-, propyl-, and acetyl moieties are able to self-assemble into regular nanospheres during a dialysis process. That means a controlled and slow exchange of the organic solvent *N*,*N*-dimethylacetamide against water results in formation of biopolymer based nanoparticles with a size in the range of 90–520 nm. The size of the nanospheres depends on the ratio of the introduced functional groups, the molecular weight of the polymers, and the preparation conditions. A functionalization of a degree of substitution of at least 2.0 is necessary to get semisynthetic dextran derivatives that are able to form these nanoparticles. According to the encapsulation of the fluorescence probe pyrene, hydrophobic domains were verified inside the dextran ester nanoparticle.

Keywords: Nanoparticles; Esterification; Fluorescence; Functionalization of polymers; Self-organization

1. Introduction

The development of biodegradable nanoparticles as controlled drug delivery systems was of considerable interest over the past few decades (Lemarchand, Gref, & Couvreur, 2004). Beside both drug protection against in vivo degradation and defined disposal of pharmacologic active agents, effective nanoparticles are requested for targeting on specific sites or cells, e.g., in human tissue. One major advantage of polysaccharides as nanoparticle component is their natural molecular recognition since they have specific receptors in certain cells. Moreover, well-documented biocompatibility and biodegradability enable polysaccharides to be used as biomaterial in medical applications (Dimitriu, 1996). Particularly dextran, consisting of mainly $\alpha(1\rightarrow 6)$ linked D-glucose units, represents a valuable biopolymer that is widespread in medicine and pharmacy (blood plasma substitute, coating material to prevent protein opsonization).

The formation of polymeric nanoparticles in water results from self-assembling to regular nanospheres containing hydrophobic domains inside the core and a more hydrophilic shell. One approach to achieve such amphiphilic structures is grafting of dextran with synthetic polymers like poly(ε-caprolactone) (Gref, Rodruiges, & Couvreur, 2002), poly(lactide) (Nouvel et al., 2004), poly(methyl methacrylate) (Sparnacci, Laus, Tondelli, Magnani, & Bernardi, 2002), poly(isobutylcyanoacrylate) (Chauvierre, Vauthier, Labarre, & Hommel, 2004), and poly(ethylene glycole) (Coombes et al., 1997). A more simple path for the preparation of biopolymeric nanoparticles is the modification of dextran with hydrophobic functional groups, e.g., esterification with cholic acid (Nichifor, Lopes, Carpov, & Melo, 1999), 4-hexyl benzoyl chloride (Aparecida Blaz Vieira, Salomao Moscardini, de Oliveira Tiera, & Tiera, 2003), and fatty acids (Rodrigues, 2005). However, only low substituted derivatives were investigated regarding their nanoparticle formation up to now.

Recently, we have shown that even high functionalized dextran derivatives are able to form spherical particles by a

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controlled and slow exchange of the organic solvent from the polymer solution by water applying dialysis (Liebert, Hornig, Hesse, & Heinze, 2005). The presence of the polar carbonyl function and less polar moieties in the molecule is necessary for the self-organization. The acylation of dextran was used as an efficient tool for the introduction of functional groups. An interesting approach in this regard is the defined esterification of dextran via *in situ* activation of the carboxylic acid with *N*,*N*′-carbonyldiimidazole (CDI) generating a number of highly functionalized derivatives with different functional groups and varying values of the degree of substitution (DS) (Hornig, Liebert, & Heinze, in press). In this way, tailored dextran esters with adjustable properties can be obtained. The introduction of furoyl moieties through reaction of dextran with furan-2-carboxylic acid (Fur)/CDI leads to photo-crosslinkable derivatives. Subsequent UV-irradiation decreases the solubility and can consequently improve the mechanical strength (Liebert & Heinze, 2005). The acylation with racemic or enantiomeric pyroglutamic acid (Pyr) may enable the polymer for chiral recognition. The functionalization with small hydrophobic groups (acetate and propionate) via acid anhydrides can subsequently tune the hydrophilic/hydrophobic balance of the entire molecule, which is an important criterion for the formation of nanoparticles (Hornig, Heinze, Hesse, & Liebert, 2005).

In the present study, the synthesis of multifunctionalized dextran esters bearing photo-crosslinkable and chiral moieties with high degrees of substitution (DS) was investigated. Dextran samples of different molecular weight and origin were used and examined concerning their self-assembly behavior during dialysis.

2. Experimental

2.1. Materials

N,*N*′-Carbonyldiimidazole (CDI) was purchased from Aldrich and *N*,*N*-dimethylaminopyridine (DMAP) from Merck. Furan-2-carboxylic acid, pyroglutamic acid, and dextran were received from Fluka. Dextran with the weight-average molecular weight (M_w) of 54,800 g mol^{-1} and a polydispersity index (PDI) of 1.56 is produced by *Leuconostoc mesenteroides* strain no. NRRL B-512(F). The other dextran samples originate from *Leuconostoc ssp.* strains and possess a M_w (PDI) of 5400 (2.49); 18,100 (1.86); 454,400 (1.81); and 648,000 g mol^{-1} (3.99). All chemicals were used without further treatment. Reactions containing a furoyl moiety have to be carried out in a dark environment to avoid undefined cross-linking.

2.2. Measurements

NMR spectra were acquired on a Bruker AMX 250 and DRX 400 spectrometer with 16 scans for ^{1}H NMR (room temperature) and 200,000 scans for ^{13}C NMR (70 °C) measurements (25 mg sample mL^{-1} for ^{1}H NMR and 100 mg sample mL^{-1} for ^{13}C NMR studies). FTIR spectra were recorded on a Nicolet AVATAR 370 DTGS spectrometer with the KBr-technique. Elemental analyses were performed by CHNS 932 Analyzer (Leco). M_w was estimated by gel permeation chromatography (GPC) on a JASCO system equipped with three columns (HEMA-Bio linear, HEMA-Bio 1000, HEMA-Bio 100) and a refractive index detector (RI-930) using an aqueous solution of 0.2 M $NaNO_3$/0.1 M NaH_2PO_4/0.05% H_3PO_4 as an eluent with a flow rate of 1.0 mL min^{-1}, by dextran and pullulan calibration at 30 °C. Measurements in DMSO were acquired with a NOVEMA 300 column and a flow rate of 0.3 mL min^{-1} at 70 °C. For SEM studies, one droplet nanoparticle suspension on a mica surface was lyophilized and covered with gold. The images were obtained with a SEM equipment LEO-1 450 VP (LEO, Oberkochen, Germany) operating at 15 kV. For cryo-TEM, a volume of 4 mL of the dispersion was placed onto a grid covered by a perforated carbon support foil (Quantifoil Micro Tools Jena, Germany). The frozen sample was transferred with the Gatan-626 single tilt cryotransfer system into the cryo-electron microscope Philips-CM120. The particle size of the nanospheres was determined by dynamic light scattering (DLS) study, using a laser beam at 650 nm and a scattering angle of 177° (HORIBA LB-550), and by a particle size distribution analyzer (PSDA, Polymer Laboratories Ltd., Shropshire, UK) with a flow rate of 2.1 mL min^{-1} and an injection volume of 20 μL operating at pH 7.

2.3. Synthesis

2.3.1. Synthesis of dextran propionate **1** and subsequent peracetatylation, polymer **2**

Pyridine (5 mL), 1.6 mL (12.4 mmol) propionic anhydride and 50 mg DMAP were added to a solution of 1 g (6.17 mmol) dextran (M_w 5400 g mol^{-1}) in 10 mL DMSO. The mixture was allowed to react at 80 °C under stirring for 5 h and precipitated in 200 mL isopropanol, washed two times with 50 mL ethanol and dried at 60 °C under vacuum. Yield: 0.93 g (58.6%); Degree of substitution (DS_{Pro}): 1.70 (polymer **1**, determined by means of ^{1}H NMR spectroscopy after peracetylation, polymer **2**); ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 5.4$–3.5 (H-AGU), 2.3 (CH_2-propionate), 1.0 ppm (CH_3-propionate); ^{13}C NMR (400 MHz, DMSO-d_6): $\delta = 172.9$ (O—CO), 98.4 (C1), 95.3 (C1′), 72.9–67.9 (C2—C5), 65.1 (C6), 54.7 (CH-pyroglutamate), 28.6, 24.3 ppm (CH_2-pyroglutamate); FTIR (KBr): 3482 (OH), 2984 (C—H), 1750 (C=O_{Ester}), 1172 (C—O), 1084 cm^{-1} (C—O).

Propionylation leading to sample **6** was carried out according to this procedure except peracetylation.

2.3.2. Dextran propionate pyroglutamate **3**

To a solution of 0.89 g (3.5 mmol) dextran propionate **1** (DS_{Pro} 1.70) in 10 mL DMSO, 1.75 g (13.5 mmol) DL-pyroglutamic acid, and 2.19 g (13.5 mmol) CDI were added. The mixture was allowed to react at 80 °C under stirring for

24 h. The polymer was precipitated in 400 mL water, washed two times with 50 mL water and dried at 60 °C under vacuum (polymer **3**). Yield: 0.34 g (34.0%); $DS_{Prop} = 1.70$, $DS_{Pyr} = 0.26$ (determined by elemental analysis); ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 7.8$ (NH), 5.4–3.3 (H-AGU), 4.1, 2.3, 2.1 ppm (CH-pyroglutamate), 2.3 (CH_2-propionate), 1.0 ppm (CH_3-propionate); ^{13}C NMR (400 MHz, DMSO-d_6): $\delta = 177.3$ (CO—NH-pyroglutamate), 173.3 (O—CO), 95.9 (C1′), 73.2–65.5 (C-AGU), 55.2 (CH-pyroglutamate), 29.1 (CH_2-pyroglutamate), 27.3 (CH_2-propionate), 25.0 (CH_2-pyroglutamate), 9.2 ppm (CH_3-propionate); FTIR (KBr): 3482 (OH), 2982 (CH), 2943 (CH), 1748 (C=O_{Ester}), 1175 (C—O), 1027 cm^{-1} (C—O); Elemental analysis: C 45.41, H 5.42, N 1.95.

The samples **4** and **5** were prepared according to this procedure using dextran of different molecular weight.

2.3.3. Dextran pyroglutamate

To a solution of 0.5 g (3.1 mmol) dextran possessing a M_w of 54,400 g mol^{-1} in 10 mL DMSO, 2.19 g (9.3 mmol) DL-pyroglutamic acid and 1.49 g (9.3 mmol) CDI were added. The mixture was allowed to react at 80 °C for 20 h. The mixture was then filtered and the product was isolated by precipitation in 250 mL ethanol, washed two times with 50 mL ethanol and dried at 60 °C under vacuum. Yield: 1.12 g (95.6%); $DS_{Pyr} = 1.96$ (determined by elemental analysis); ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 8.0$ (NH), 5.6–3.4 (H-AGU), 4.2, 2.3, 2.1 ppm (H-pyroglutamate); ^{13}C NMR (400 MHz, DMSO-d_6): $\delta = 176.9$ (CO—NH), 172.2 (O—CO), 98.4 (C1), 95.1 (C1′), 76.5–65.6 (C-AGU), 54.7 (CH-pyroglutamate), 28.6, 24.3 ppm (CH2-pyroglutamate); FTIR (KBr): 3362 (OH, NH), 2925 (C—H), 1751 (C=O_{Ester}), 1693 (OC—NH), 1205 (OC—NH), 1017 (C—O) cm^{-1}; Elemental analysis: C 46.54, H 6.67, N 5.66.

Perpropionylation leads to polymer **7**.

2.3.4. Synthesis of dextran furoate

To a solution of 0.5 g (3.1 mmol) dextran possessing a M_w of 54,400 g mol^{-1} in 20 mL DMSO, 1.04 g (9.3 mmol) furan-2-carboxylic acid and 1.49 g (9.3 mmol) CDI were added. The mixture was allowed to react at 60 °C under stirring for 5 h. The product was isolated by precipitation in 250 mL ethanol, washed two times with 50 mL ethanol and dried at 60 °C under vacuum. Yield: 0.49 g (61.3%); $DS_{Fur} = 1.87$ (determined by means of ^{1}H NMR spectroscopy); ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 7.9$, 7.2, 6.6 (H-furoyl), 5.5–3.5 ppm (H-AGU); ^{13}C NMR (400 MHz, DMSO-d_6): $\delta = 157.8$ (O—CO), 147.9, 144.2, 118.9, 112.6 (C-furoyl), 99.1 (C1), 96.1 (C1′), 77.0–65.7 ppm (C-AGU); FTIR (KBr): 3409 (OH), 2925 (CH), 1723 (C=O_{Ester}), 1577 (C—H_{Fur}), 1103 (C—O), 1077 (C—O), 1052 cm^{-1} (C—O).

Perpropionylation leads to polymer **8**.

2.3.5. Esterification of dextran with pyroglutamic- and furan-2-carboxylic acid

In a typical synthesis, 1.99 g (14.4 mmol) DL-pyroglutamic acid, 1.73 g (15.4 mmol) furan-2-carboxylic acid, and 4.98 g (30.8 mmol) CDI were added to a solution of dextran (1 g, 6.2 mmol) possessing a M_w of 5400 g mol^{-1} in 40 mL DMSO (molar ratio AGU:Fur:Pyr:CDI = 1:2.5:2.5:5) and the mixture was allowed to react for 22 h at 80 °C under stirring. The product was isolated by precipitation in 350 mL ethanol, washed two times with 50 mL ethanol and dried at 60 °C under vacuum, polymer **9**. Yield: 1.38 g (60.3%); $DS_{Fur} = 0.79$ (determined by means of ^{1}H-NMR), DS_{Pyr}: 1.27 (determined by elemental analysis); ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 7.9$, 7.2, 6.7 (H-furoyl), 7.2 (NH), 5.6–3.5 (H-AGU), 4.2, 2.3, 2.1 ppm (H-pyroglutamate); ^{13}C NMR (400 MHz, DMSO-d_6): $\delta = 176.6$ (CO—NH-pyroglutamate), 171.9 (O—CO-pyroglutamate), 156.5 (O—CO-furoyl), 147.9, 144.3, 120.7, 112.0, (C-furoyl), 98.3 (C1), 95.4 (C1′), 76.2–65.1 (C-AGU), 54.6 (CH-pyroglutamate), 28.5, 24.2 ppm (CH_2-pyroglutamate); FTIR (KBr): 3373 (OH), 3144 (NH), 2943 (CH), 1725 (C=O_{Ester}), 1577 (C—H_{Fur}), 1298 (CH), 1181 (C—O), 1112 cm^{-1} (C—O); Elemental analysis: C 50.32, H 4.69, N 4.55.

Perpropionylation leads to polymer **10**. Samples **11** to **15** were synthesized according to the described procedure using dextran of different molecular weight and a molar ratio of AGU:Fur:Pyr:CDI = 1:1:2:3.

2.3.6. Peracylation of the dextran esters, general procedure

To determine the DS of the dextran ester by means of ^{1}H NMR spectroscopy, peracylation with acetic- or propionic anhydride was carried out. For this purpose, 0.2 g of sample in 6 mL pyridine was allowed to react with 6 mL of the corresponding anhydride in the presence of 50 mg of DMAP as catalyst for 24 h at 80 °C. The polymer was precipitated and washed with ethanol (250 mL) two times and dried at 60 °C. The sample was reprecipitated from 3 mL chloroform in 100 mL ethanol followed by filtration and drying at 60 °C under vacuum. FTIR (KBr): no ν(OH).

2.4. Nanoparticle preparation

Preparation of the nanoparticles was carried out by a dialysis process. Forty milligram of dextran ester was dissolved in 10 mL purified DMAc and was dialyzed against distilled water (Spectra/Por® membrane, molecular weight cut-off 3500 g mol^{-1}) for 4 d. The deionized water was exchanged 5 times in a period of three days. For SEM images, a droplet of approximately 0.2 mL was placed on a mica surface. The system was lyophilized for 6 h and sputtered with gold.

2.5. Fluorescence spectroscopic study

A stock solution of pyrene (6×10^{-6} mol L^{-1}) in acetone was added to 10 mL of various concentrations of nanoparticle suspension to give a final pyrene concentration of 6×10^{-7} mol L^{-1}. The mixture was heated at 60 °C for 3 h to remove acetone. The fluorescence intensity was measured by a fluorometer (Fluorolog Jobin Yvon-Spex, ISA Horiba Group) applying an emission wavelength of 335 nm. The

excitation and emission bandwidths were 1.0 and 1.0 nm, respectively.

3. Results and discussion

Applying the synthesis concept of the defined introduction of multiple functionalities via *in situ* activation of carboxylic acids, a large variety of dextran derivatives bearing furoate-, pyroglutamate-, propionate-, and acetate groups in different ratios is accessible. Dextran propionate, -propionate pyroglutamate (Fig. 1a), -furoate pyroglutamate (Fig. 1b), perpropionylated dextran furoate, -pyroglutamate (Fig. 1c), -furoate pyroglutamate, and peracetylated dextran propionate are potential derivatives for the preparation of nanoscale particles. During dialysis of the dextran derivatives, an exchange of the solvent *N*,*N*-dimethylacetamide (DMAc) against water occurs, while the formation of nanoparticles is based on the self-assembly of highly functionalized dextran molecules. It is important that a certain balance of a polar, i.e., the carbonyl function and nonpolar moiety is introduced into the polymer backbone. The character of functional groups, the DS, the course of reaction, and consequently the distribution of the substituents influences the size of the resulting nanoparticles. It should be mentioned that under the conditions of peracylation a *N*-acylation of pyroglutamyl moieties takes place (compare Figs. 1a and c) (Bernardi et al., 2002).

Five different dextran samples relating to their origin and molecular weight distribution were used in our studies for the biopolymer preparation. The structure determination was carried out extensively by NMR spectroscopy, IR spectroscopy, elemental analysis, and gel permeation chromatography. Table 1 shows an assortment of dextran derivatives that form nanoparticles after dialysis of DMAc solutions against water.

The results demonstrate that a degree of functionalization of at least 2 by the mentioned substituents is necessary for the organisation into regular spheres. For example,

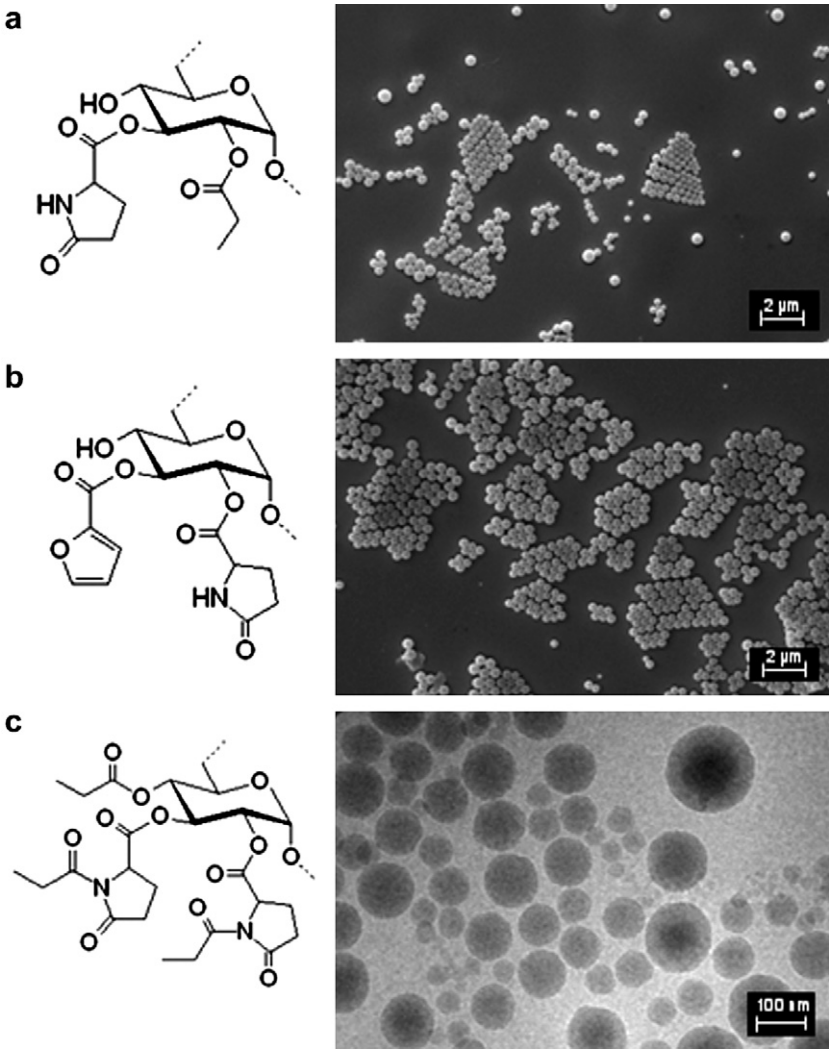

Fig. 1. Schematic structures of dextran derivatives and corresponding images (SEM for a and b, cryo-TEM for c) of the nanoparticles formed by dialysis (DMAc/H_2O); (a) dextran propionate pyroglutamate (sample **3**, $d = 384$ nm); (b) dextran furoate pyroglutamate (sample **9**, $d = 520$ nm); (c) perpropionylated dextran pyroglutamate (sample **7**, $d = 87$ nm).

Table 1
Molecular weight (M_w) of starting dextran, degree of substitution (DS) of functionalized dextran with furoyl- (DS_{Fur}), pyroglutamyl- (DS_{Pyr}), propyl- (DS_{Prop}), and acetyl moieties (DS_{Ac}), and mean diameters of the resulting nanoparticles after dialysis (DMAc/H_2O) determined by dynamic light scattering (DLS) or a particle size distribution analyzer (PSDA)

No.	M_w dextran[a] in g mol^{-1}	DS_{Fur}[b]	DS_{Pyr}[c]	DS_{Prop}	DS_{Ac}	Mean diameter in nm	
						by DLS	by PSDA
2	5,400	–	–	1.70	1.30	128	–
3	5,400	–	0.26	1.70	–	384	–
4	18,100	–	0.33	2.20	–	413	–
5	54,400	–	0.26	2.16	–	446	–
6	54,400	–	–	2.16	–	360	–
7	54,400	–	1.96	3.00	–	87	–
8	54,400	1.02	–	1.98	–	101	–
9	5,400	0.79	1.27	–	–	–	520
10	5,400	0.79	1.27	2.21	–	–	498
11	5,400	0.12	1.13	1.87	–	–	460
12	18,100	0.31	1.20	2.69	–	399	–
13	54,400	0.22	1.34	2.78	–	–	267
14	454,400	0.32	0.72	2.68	–	247	–
15	648,000	0.35	0.84	2.65	–	197	–

[a] Determined by GPC.
[b] Determined by means of ^{1}H NMR spectroscopy after perpropionylation.
[c] Determined by elemental analysis.

mainly irregular particles of different size were obtained after dialysis of a dextran furoate pyroglutamate (DS_{Fur} 0.12, DS_{Pyr} 1.13) as revealed by means of SEM. After perpropionylation, i.e., after complete modification of the remaining hydroxyl groups, regular nanoparticles with 460 nm in diameter are accessible (sample **11**) as discussed in (Hornig et al., 2005). However, a derivative, which possesses a degree on pyroglutamyl groups in the same range as polymer **11** but possessing a higher degree on furoyl moieties, generates nanoparticles before (sample **9**) and after perpropionylation (sample **10**).

The nanoparticles formed in aqueous suspensions were analyzed regarding their size and shape by dynamic light scattering (DLS), by particle size distribution analyses (PSDA), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). Nanospheres in the range of 87–520 nm possessing a narrow size distribution are detectable. The nanoparticle suspensions are stable under neutral conditions for at least 3 weeks. Particles below 200 nm do not agglomerate and sediment even up to one year after the preparation.

Another influence on the size of dextran ester nanoparticles is the molecular weight (M_w) of the dextran derivatives. One major advantage of the conversion of carboxylic acids via *in situ* activation with CDI is that no polymer degradation or side reactions take place leading to intermolecular linkages of polymer chains (Heinze, Liebert, Heublein, & Hornig, 2006). A comparison of the particle sizes of dextran propionate pyroglutamate, possessing similar DS values but prepared from dextran of different M_w (samples **3**–**5**), shows an increase in size with decreasing M_w. Otherwise, nanoparticles composed of perpropionylated dextran furoate pyroglutamate (samples **11**–**15**) become smaller with increasing M_w. Nevertheless, a direct correlation between the size of the nanospheres and the M_w of the starting dextran and, thus, the M_w of the dextran derivative is hardly feasible because even small changes in the DS can influence the particle size significantly.

The formation of the nanoparticles during dialysis is based upon the slow exchange of the organic solvent against the nonsolvent water. Dimethylsulfoxide (DMSO) and DMAc are appropriate solvents regarding the prepared dextran derivatives. DMSO is less toxic than DMAc and, thus, seems to be more suitable for biological applications. Nevertheless, a comparison of the solvents shows that a nanoparticle suspension prepared from a DMSO solution still contains residues of the organic solvent leading to a change of the structure of the particles after freeze drying (Fig. 2). The absence of residual DMAc is evidenced by ^{1}H NMR spectroscopy and elemental analysis of freeze dried nanoparticles prepared from a DMAc solution. Nanoparticles of polymer **11** prepared in DMSO are in the range of 374 nm, which are on the average about 85 nm smaller than after preparation in DMAc.

Pyrene was used as hydrophobic probe for fluorescence spectroscopy to investigate the structure of the dextran ester nanoparticles (Rodrigues, 2005; Winnik & Regismond, 1996). The vibrational structure of the fluorescence bands of pyrene is known to be sensitive to the local polar-

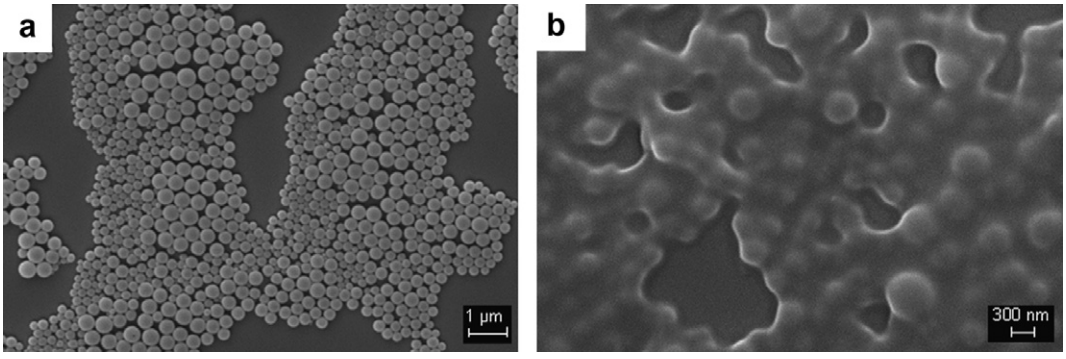

Fig. 2. SEM images of perpropionylated dextran furoate pyroglutamate nanoparticles (sample **11**) prepared by dialysis of (a) DMAc against water ($d = 460$ nm) and (b) DMSO against water ($d = 374$ nm).

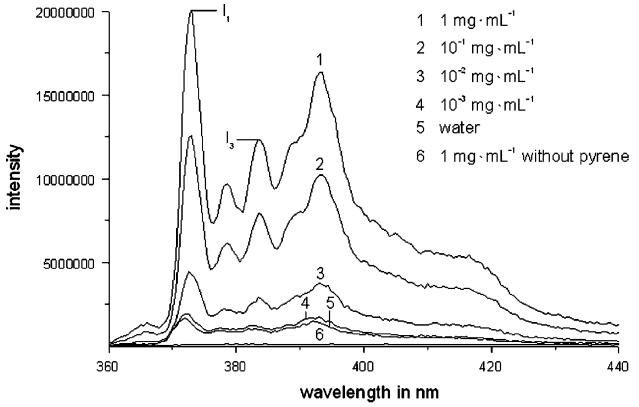

Fig. 3. Fluorescence emission spectra of pyrene (6×10^{-7} mol L^{-1}) in the presence of decreasing concentrations of perpropionylated dextran pyroglutamate (DS_{Pyr} 1.96, DS_{Pro} 3.00, sample **7**) with the excitation at 335 nm.

ity of the microenvironment (Kalyanasundaram & Thomas, 1977). Fig. 3 shows the change in total fluorescence intensity depending on polymer concentrations ranging from 10^{-3} to 1 mg ml^{-1}. A nanoparticle suspension of perpropionylated dextran pyroglutamate (DS_{Pyr} 1.96, sample **7**), possessing a mean diameter of 87 nm, was used for this fluorescence study. The nanoparticle suspension itself shows no fluorescence (graph 6, Fig. 3). At low concentrations (10^{-3} mg ml^{-1}), the change in fluorescence intensity is negligible compared to the aqueous pyrene solution without nanoparticles (graph 5, Fig. 3). With an increased concentration, an increase in the total fluorescence intensity and a red shift of the I_1 (372.5 nm) and I_3 (384 nm) band can be observed. This fact indicates the transfer of pyrene from the aqueous media to the less polar microdomains. The peak ratio I_1/I_3 increases with increasing dipole moment (Karpovich & Blanchard, 1995) and exhibits values of approximately 1.3 at polymer concentrations of 10^{-2} to 1 mg ml^{-1}. Consequently, it is lower than the values of water ($I_1/I_3 \approx 1.87$) or aqueous solutions of unmodified dextran ($I_1/I_3 \approx 1.8$–1.9) (Aparecida Blaz Vieira et al., 2003; Winnik & Regismond, 1996) and just slightly more polar than the interior of anionic sodium dodecyl sulphate micelles ($I_1/I_3 \approx 1.15$). The polarity of the nanoparticle core is comparable to hydrophobically modified dextran- and cellulose micellar systems in aqueous solutions (Aparecida Blaz Vieira et al., 2003; Evertsson & Nilsson, 1999). The presence of a hydrophobic core enables the dextran derivatives examined for the encapsulation of nonpolar substances for potential applications as controlled, e.g., drug delivery systems. They may be a suitable biopolymer based alternative to commonly used biodegradable synthetic block-copolymers (Brannon-Peppas, 1995).

4. Conclusions

Self-assembling nanoparticles were prepared using multifunctionalized dextran bearing furoyl-, pyroglutamyl-, propyl-, and acetyl moieties in varying proportions. The slow exchange of water against DMAc (as organic solvent) via dialysis results in the formation of regular nanospheres of the respective semisynthetic biopolymer derivative. The size of the nanospheres depends on the ratio of the introduced functional groups, the molecular weight of the polymer, and the preparation conditions. The ability to design dextran ester nanoparticles by a dialysis process does not result from a particular substituent but from a certain balance of functional groups with an inherent difference in polarity. Less polar microdomains in the core of the nanospheres can be used for the encapsulation of hydrophobic drugs. The substituents may be valuable for certain molecular recognition or subsequent modification to improve the stability and affect drug release properties.

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