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Synthesis of water-soluble and water-insoluble amphiphilic derivatives of dextran in organic medium

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ABSTRACT

Hydrophobically modified dextrans were prepared by reacting native polysaccharide with 1,2-epoxydodecane in dimethylsulfoxide. Epoxide oligomerization was shown to occur as a secondary reaction when hydroxide ions were used as base catalysts. By adjusting the amount of epoxide in the feed, dextran derivatives with degrees of substitution (DS) between 0% and 164% were obtained. Polymers with DS above 100% were readily soluble in organic solvents like tetrahydrofuran, dioxane and water-saturated chloroform and dichloromethane. Their solution properties in organic solvent were characterized by capillary viscometry. Water-soluble derivatives were compared to other amphiphilic dextrans obtained using a heterogeneous modification in aqueous medium. The effect of modification conditions on substitution pattern was evidenced.

1. Introduction

In the framework of sustainable development, polymers from renewable resources are attracting an increasing interest from both academia and industry for the synthesis of functional additives in formulated products. One important example is the preparation of stabilizers for colloidal dispersions. Polysaccharides have been widely investigated to that goal. The covalent attachment of hydrocarbon tails onto hydrophilic polysaccharide backbones is a well established way of preparing amphiphilic polymers which are efficient stabilizers of aqueous colloidal dispersions. Almost all the reported studies in the topic are focused on the synthesis of water-soluble amphiphilic polysaccharides. In other words, the amount of attached hydrocarbon tails remains low enough to preserve solubility in aqueous media. As a consequence, the resulting polymeric stabilizers are convenient for formulating colloidal dispersions in which the continuous phase is an aqueous medium. In order to assess the potential applications of amphiphilic polysaccharides to the formulation of water-in-oil emulsions or multiple emulsions, it would be of great interest to prepare polysaccharide derivatives which would exhibit significant solubility in some non water-miscible solvents.

To that goal, the use of a non ionic polysaccharide as starting material seems the best choice. Dextran is a non ionic bacterial polysaccharide which combines biocompatibility and chemical reactivity. Dextran macromolecules consist of a main chain with α-(1 → 6) linked D-glucose units with some short branches. In the commercial dextran T40© α-(1 → 3) links forming short branches represent about 5% as compared to α-(1 → 6) links (Nordmeier, 1993). Dextran repeat unit contains three secondary hydroxyl groups that exhibit sufficient chemical reactivity to be used for attaching functional groups via the formation of ester or ether links. In what follows, dextran derivatives will be characterized by defining the degree of substitution (DS) as the molar ratio of covalently linked functional groups to repeat units. By its definition, DS varies between 0% and 300% (Fig. 1).

In that work we investigated the synthesis of a family of amphiphilic derivatives of dextran by reacting native polysaccharide with 1,2-epoxydodecane in a polar organic solvent, dimethylsulfoxide (DMSO). Our main goal was to control the number of attached hydrocarbon groups and to vary this number over a wide range so as to obtain both water-soluble and water-insoluble derivatives. Dilute solution properties of both types of dextran

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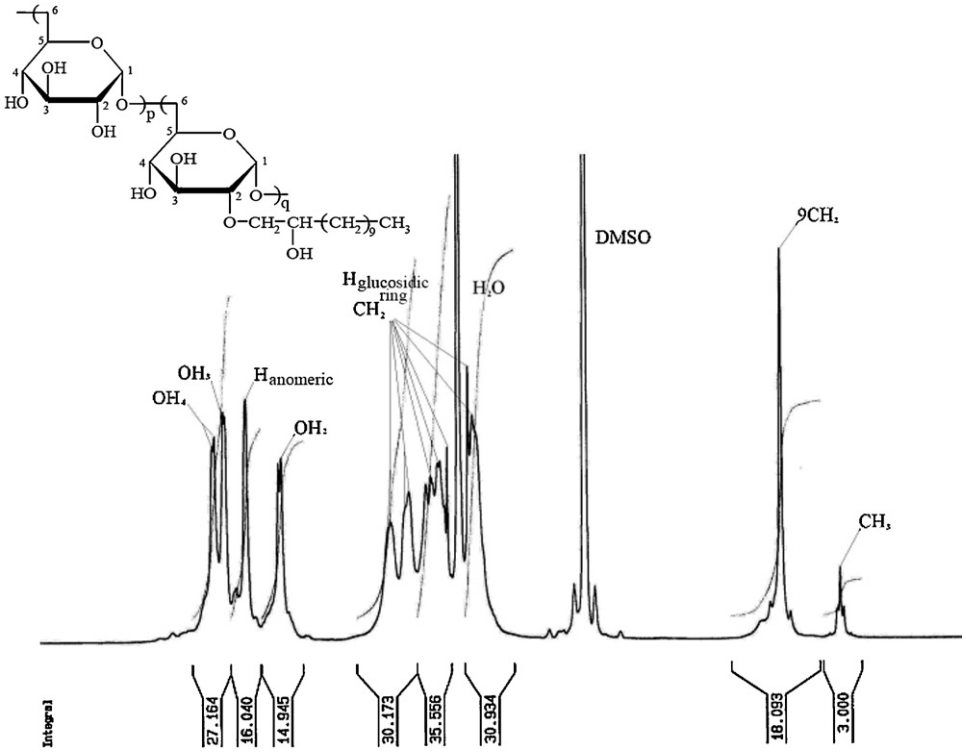

Fig. 1. ^{1}H NMR spectrum of a modified dextran (DS = 6%) in DMSO d_6.

derivatives were characterized by capillary viscometry in aqueous and organic solutions. In what follows, dextran derivatives obtained by modification with 1,2-epoxydodecane will be named DexC10$_\tau$ in which τ will be the degree of substitution expressed in %.

2. Experimental

2.1. Materials

All chemicals were from Aldrich with the highest purity available. MilliQ water was used in all experiments. A commercial dextran sample, T40® from Amersham Pharmacia was used. Its weight-average and number-average molar masses were characterized by size exclusion chromatography and found equal to 40 000 g/mol and 33 000 g/mol, respectively.

2.2. Dextran modification in dimethylsulfoxide with tetrabutylammonium hydroxide

Dextran (5 g) was dissolved in 100 mL of distilled water. The required amount of tetrabutylammonium hydroxide (40% wt solution in water) was added (1.5 mol per repeat unit). After 1 h stirring, the mixture was freeze-dried. The resulting solid was dissolved in 100 mL dimethylsulfoxide (DMSO) and, if required, heated to 50 °C. Then, the required amount of 1,2-epoxydodecane was added. The reaction was left proceed during 96 h under magnetic stirring. The crude reaction medium was transferred to a dialysis bag (molar mass cut off equal to 6–8000 g/mol according to the data of the supplier) and dialyzed against water/ethanol mixtures (50/50, v/v) and finally water. The aqueous solution recovered after dialysis was freeze-dried and sampled for analysis by ^{1}H NMR. The solid product was put in a Soxhlet extractor and washed with absolute ethanol during 24 h. The recovered ethanol was fully evaporated and the resulting solid was analyzed. Alternatively, 1,2-epoxyoctadecane was used in one experiment and in that case ethanol was replaced by tetrahydrofuran in Soxhlet extractor.

2.3. Dextran modification in dimethylsulfoxide with t-BuOK

Dextran (5 g) was dissolved in 100 mL commercial DMSO under nitrogen current. The required amount of *t*-BuOK was added (either 1.5 or 3.0 mol per repeat unit). The required amount of 1,2-epoxydodecane was added and the reaction was left proceed during 48 h. Alternatively, anhydrous DMSO was used following the same procedure.

2.4. Structural analyses

^{1}H and ^{13}C NMR spectra were obtained with a Brücker Avance 300 spectrometer (300.13 MHz and at 300 K). Polymers were dissolved in DMSO d_6.

Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-ToF) spectra were acquired on a Voyager-DE STR instrument (Applied Biosystems) equipped with a nitrogen laser (337 nm) to desorb and ionize the samples. The instrument was operated in linear mode. The matrix was obtained from a mixture of tetrahydrofuran/dithranol/NaI, 50/45/5, v/v/v.

Size exclusion chromatography analyses were performed with a system comprising a Merck L6200A pump (0.7 mL/min), a Degazys DG 1310, Uniflow unit, a 200 μL injection loop, a PL aquagel-OH Guard pre-column followed by 2 PL aquagel-OH 40 and PL aquagel-OH 50 columns (Polymer Laboratories). The detection system was a miniDawn (Wyatt Technology Corporation) photodiffusiometer (wavelength 690 nm and detection at 41.6°, 90° and 138.4°) followed by a Merck RI-71 differential refractometer. The eluent was 0.1 mol/L $NaNO_3$ with 0.2 g/L NaN_3. The refractive index increment value (dn/dc) used for calculations was 0.145 mL/g.

3. Results and discussion

3.1. Dextran modification in polar organic medium

Dextran modification has been already carried out in a polar organic solvent, DMSO, which permitted dissolving both polysaccharide and epoxide, thus providing a homogeneous reaction medium (Rotureau, Chassenieux, Dellacherie, & Durand, 2005). A basic catalyst was required to increase the reactivity of dextran hydroxyls. Sodium hydroxide could not be used in DMSO since the addition of a concentrated NaOH aqueous solution to DMSO containing solubilized dextran led to the formation of a gel-like medium and prevented further reaction. As a result, a 40 wt% aqueous solution of tetrabutylammonium hydroxide (TBAOH) was used. Nevertheless, with 1,2-epoxyalkanes, DS values remained always lower than 100%.

In order to obtain dextran derivatives that could exhibit significant solubility in non-water miscible solvents, we chose to use a very hydrophobic epoxide, 1,2-epoxydodecane and to design reaction conditions in order to reach DS values above 100%. To that goal, we attempted to minimize the amount of water in reaction medium. The two expected effects were reducing hydrolysis of epoxide and increasing the solubility of both epoxide and modified dextran in reaction medium. Indeed, long 1,2-epoxyalkanes have a limited solubility in a mixture of DMSO and water. TBAOH was commercially available under the form of an aqueous solution, a mixture containing the required amounts of dextran and TBAOH aqueous solution was first freeze dried before dissolution in DMSO together with the epoxide.

Apart from epoxide hydrolysis, epoxide oligomerization has been shown to occur when dextran modification was carried out in aqueous medium with 1,2-epoxydodecane (Covis, Ladaviere, Desbrières, Marie, & Durand, under review). In addition, the oligomers formed were difficult to extract because of their very low solubility in mixtures of water and organic solvents contrary to what was observed with epoxides having shorter hydrocarbon chains like 1,2-epoxyoctane. In order to check the occurrence of that reaction, we followed the purification procedure established for the modification in aqueous medium which combined dialysis and Soxhlet extraction. Finally, the influence of the nucleophilicity of the base catalyst was investigated by changing TBAOH by *t*-BuOK.

All modified dextrans were characterized by ^{1}H NMR in order to check their purity and determine their DS (Fig. 1). The value of DS was calculated using the ratio of the areas of the peaks corresponding to alkyl chains to the area of the peak of anomeric hydrogen present in all repeat units (modified or not).

The degradation of dextran backbone in alkaline organic medium was checked by control experiments where no epoxide was added. The polymer was characterized by size exclusion chromatography before and after the time corresponding to the reaction (96 h for TBAOH and 48 h for *t*-BuOK, at 50 °C). For each base, the amount was 1.5 mol per mol of glucose unit. The initial weight-average molar mass of dextran was 48 000 g/mol. After 48 h stirring with *t*-BuOK, the weight-average molar mass was found equal to 44 000 g/mol while it dropped down to 36 000 g/mol with TBAOH. In both cases polydispersity index remained close to 1.3, i.e. close to the value of the commercial sample.

3.2. Use of tetrabutylammonium hydroxide as the base catalyst

Several experiments were carried out varying the initial amount of 1,2-epoxydodecane. 1,2-Epoxyoctadecane was used in one experience (Table 1). The amount of base catalyst, TBAOH was kept constant and equal to 1.5 mol per mol of epoxide.

The overall recovery yields were between 60 and 80%. By varying the initial amount of epoxide between 0.3 and 2 in mol ratio relative to glucose units, the final DS of dextran derivatives ranged between 2% and 164% according to reaction temperature. When the synthesis was carried out at 50 °C, the obtained DS were much higher than those obtained at room temperature with the same conditions. The followed procedure allowed preparing modified dextrans with DS values controlled by feed composition and reaching values up to almost 200%. These results can be attributed to the reduction of water content in the reaction medium by freeze drying dextran/TBAOH mixture prior to dissolution in DMSO. Thus, this synthesis procedure allows preparation of both water-soluble and water-insoluble dextran derivatives.

In addition, Soxhlet extraction evidenced that a part of epoxide was involved in oligomerization reactions. As in the previous work about modification in aqueous medium, dialysis step was not sufficient to completely extract oligomer by-products (Covis et al., under review). The chemical structure of oligomers formed in DMSO (Table 1, entry 4) was characterized by NMR and MALDI-ToF (Figs. 1 and 2). This product contained oligomers of 1,2-epoxydodecane with degrees of polymerization between 2 and 7. In addition, the spectra confirmed that end groups were hydroxyls, consistently with the idea of a hydroxide-initiated oligomerization. The mass of residual oligomers extracted by Soxhlet increased with increasing epoxide load and was higher when the reaction was carried out at room temperature. These amounts of oligomers were much lower than those obtained when doing the reaction in aqueous medium.

Table 1
Dextran modification in DMSO in the presence of TBAOH with various amounts of 1,2-epoxyalkane (for details see text).

Entry	Epoxide		Temperature	DS (%)[b]	Yield (%)[c]	Oligomer (%)[d]
	Nature	Amount[a]				
1	1,2-Epoxydodecane	0.3	50 °C	10	61	2
2		0.6	50 °C	52	80	3
3		1.0	50 °C	80	80	5
4		2.0	50 °C	137	69	n.d.
5[e]		2.0	50 °C	164	81	20
6		0.3	RT	2	80	5
7		0.6	RT	15	72	3
8		1.0	RT	32	61	23
9[f]	1,2-Epoxyoctadecane	0.1	50 °C	6	59	8

[a] Molar ratio of 1,2-epoxyalkane to glucose units in the feed.
[b] Degree of substitution of the dextran derivative analyzed by ^{1}H NMR after purification.
[c] Mass of modified dextran divided by the expected mass of dextran derivative based on feed composition.
[d] Mass of recovered homopolymer after Soxhlet extraction divided by the mass of epoxide in the feed.
[e] For that experiment, the volume of DMSO was increased by a factor 1.6.
[f] For that synthesis, ethanol was replaced by tetrahydrofuran for Soxhlet extraction.

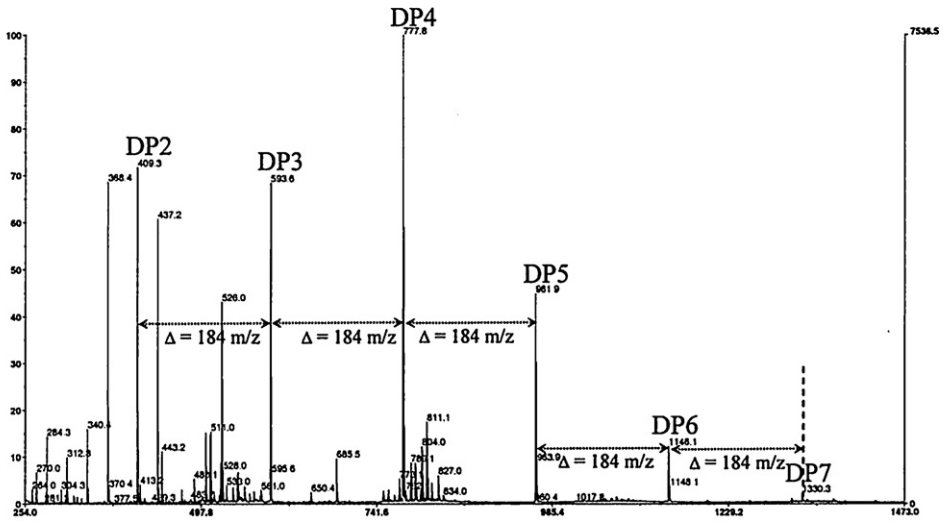

Fig. 2. MALDI-ToF spectrum of poly(1,2-epoxydodecane) recovered after Soxhlet extraction.

Thus, dextran modification in DMSO was in competition with epoxide oligomerization. The latter reaction was initiated by hydroxide ions from TBAOH. Increasing reaction temperature was more favorable to reaction between dextran and epoxide and thus gave rise to a significant increase of the resulting DS.

For an epoxide molar ratio equal to 2 (Table 1, entries 4 and 5), 1,2-epoxydodecane was not completely dissolved in the volume of DMSO. This led to a degree of substitution significantly lower than the expected value (137% compared to 200% from feed composition) contrary to other experiments. Increasing the volume of DMSO by a factor 1.6 allowed to reach complete dissolution of epoxide and provided a higher degree of substitution (164%). Replacing 1,2-epoxydodecane by 1,2-epoxyoctadecane led to amphiphilic dextran with an overall yield comparable to other experiments. Nevertheless, we used a low amount of epoxide (0.1 mol/glucose unit) in order to avoid any problem of solubility similar to that encountered with high amounts of 1,2-epoxydodecane.

3.3. Use of t-BuOK as the base catalyst

In order to reduce oligomerization of epoxide, we replaced hydroxide ions by a much less nucleophilic base, *t*-BuOK. Several dextran modifications were carried out at 50 °C varying the amount of 1,2-epoxydodecane (Table 2).

Contrary to what has been observed with TBAOH, products extracted by Soxhlet extractor were not solids but mixtures of liquid and precipitates. ^{1}H NMR spectra (data not shown) revealed that these products contained mainly unreacted 1,2-epoxydodecane and traces of oligomers. Thus, the use of *t*-BuOK strongly reduced the formation of epoxide oligomers which was the expected result of using a non-nucleophilic catalyst.

In our experimental conditions, the use of *t*-BuOK did not favor dextran modification since degrees of substitution were even lower than with TBAOH. Furthermore, increasing the amount of *t*-BuOK up to 3 times the number of glucose units significantly lowered the extent of dextran modification. This result can be explained by considering that reactions were not carried out under inert atmosphere. Consequently, because of the hygroscopic character of DMSO, water from atmosphere converted a significant part of *t*-BuOK into the corresponding tertiary alcohol and prevented dextran reaction with epoxide.

These results demonstrate that epoxide oligomerization can be considerably reduced (if not completely suppressed) by the use of a non-nucleophilic base.

3.4. Solution behavior of dextran derivatives

Dexran derivatives modified with 1,2-epoxyoctane having degrees of substitution up to 30% were soluble in water up to concentrations equal to 50 g/L. The same result was observed with dextran derivatives modified with 1,2-epoxydodecane having degrees of substitution up to 15%. DexC10$_{25}$ gave clear aqueous solutions up to 20 g/L (Rotureau et al., 2005).

DexC10$_{137}$ and DexC10$_{164}$ were soluble in dioxane and tetrahydrofuran up to 80 g/L. DexC10$_{164}$ was soluble in chloroform and dichloromethane saturated with water, up to 60 g/L.

3.4.1. Viscometric study of highly modified dextrans in organic solvents

To the best of our knowledge, the solution behavior of dextran derivatives in low polarity organic solvents has never been published.

The viscosity of dilute polymer solutions is conveniently depicted by Huggins equation (Eq. (1)) which includes both polymer concentration (C in g/L) and two physico-chemical parameters related to the polymer-solvent system ($[\eta]$ and k_H) (Huggins, 1942). The first one is the intrinsic viscosity ($[\eta]$ in L/g) which is related to the specific volume of the macromolecular species present in the solution (isolated macromolecules or aggregates). The second parameter is Huggins coefficient (k_H) which is an indication of the interactions between solvent molecules and the macromolecular species in solution.

$$\eta_{red} = [\eta] + k_H[\eta]^2 C \quad (1)$$

In Eq. (1), η_{red} is the reduced viscosity (in L/g) which is defined by $\eta_{red} = \eta - \eta_s/\eta_s C$ where η and η_s are the viscosity of the polymer solution and that of the pure solvent (Pa s), respectively. For a polymer in good or theta solvent, Huggins coefficient is lower than 0.8 (Graessley, 1974; Huggins, 1942). On the contrary in bad solvent conditions, Huggins coefficient can reach values higher than unity.

Capillary viscometry experiments were carried out with DexC10$_{164}$ solubilized in tetrahydrofuran (THF), chloroform (saturated with water) and DMSO at 25 °C. Plotting reduced viscosity as a function of polymer concentration within the range 5–45 g/L provided linear variations which allowed reliable estimation of intrinsic viscosity and Huggins coefficient (Table 3). For comparison, the intrinsic viscosity of native dextran in DMSO, taking into account the degradation of polysaccharide backbone (Section 3.1) can be estimated to 23 mL/g (Catiker & Güner, 1998).

Table 2
Dextran modification in DMSO with 5 g of native dextran (31 mmol glucose units) in 100 mL DMSO (either commercial or dried) in the presence of *t*-BuOK with various amounts of 1,2-epoxydodecane at 50 °C.

Entry	1,2-Epoxydodecane[a]	*t*-BuOK[b]	DS (%)[c]	Yield (%)[d]	Extracted products (%)[e]
10[f]	0.3	1.5	6	62	25
11[f]	0.6	1.5	21	51	20
12[f]	1.0	1.5	33	79	62
13[f]	2.0	1.5	48	61	83
14[g]	0.3	3.0	5	84	39
15[g]	0.6	3.0	14	82	34
16[g]	1.0	3.0	14	85	69

[a] Molar ratio of 1,2-epoxydodecane to glucose units in the feed.
[b] Molar ratio of *t*-BuOK to 1,2-epoxydodecane.
[c] Degree of substitution of the dextran derivative analyzed by ^{1}H NMR after purification with ethanol in a Soxhlet extractor.
[d] Mass of modified dextran divided by the expected mass of dextran derivative based on feed composition.
[e] Mass of recovered liquid after Soxhlet extraction divided by the mass of epoxide in the feed.
[f] Commercial DMSO.
[g] Anhydrous DMSO.

Table 3
Intrinsic viscosity and Huggins coefficient of $DexC10_{164}$ dissolved in various organic solvents at 25 °C.

Solvent	$[\eta]$ (mL/g)	k_H
$CHCl_3$ saturated with water	11.9	0.9
THF	12.7	0.7
DMSO	10.6	2.4

Since in the three solvents, intrinsic viscosity is about half the value of unmodified dextran homologue, we can assume that $DexC10_{164}$ macromolecules are under the form of compact globules. To discuss this result, we need to separate the less polar solvents, THF and water-saturated $CHCl_3$ from DMSO.

In THF and water-saturated $CHCl_3$, the presence of hydroxyl groups along polymer backbone is not favorable to coil swelling. With $CHCl_3$, water molecules are even required for solvating macromolecules. Thus, macromolecules collapse and expose hydrocarbon tails to surrounding solvent. These units have much better affinity for solvent molecules but do not generate significant interactions between globules. This interpretation may explain why in THF and water-saturated $CHCl_3$ Huggins coefficient remained close to 0.8.

In DMSO, the higher value of Huggins coefficient (2.4) indicates that macromolecules tend to self-associate. In that solvent, the situation is just reversed in comparison to THF and chloroform. Indeed, hydroxyl groups have affinity for DMSO while hydrocarbon tails exhibit limited compatibility with that solvent. Thus, polymeric chains are still collapsed but tend to self-associate because of hydrocarbon tails (in a similar way as "hydrophobic effect" encountered in aqueous solutions). This phenomenon could explain the high value of Huggins coefficient in DMSO.

It has been showed recently that dextran derivatives soluble in water-saturated chloroform exhibited surface-active properties and could be used as stabilizers for water-in-oil nanoemulsions (Carrier, Covis, Marie, & Durand, 2011). This has been, as far as we are aware, the first example of polysaccharide-based stabilizer used in reverse nanoemulsions.

Table 5
Distances between solvents and dextran derivatives in the Hansen diagram. $\Delta\delta = [(\delta_{D\text{solvent}} - \delta_{D\text{polymer}})^2 + (\delta_{P\text{solvent}} - \delta_{P\text{polymer}})^2 + (\delta_{H\text{solvent}} - \delta_{H\text{polymer}})^2]^{1/2}$ in $J^{1/2}/cm^{3/2}$. The situations corresponding to experimental non-dissolution are in grey.

	Dextran	$DexC10_{100}$	$DexC10_{200}$
Water	19.1	32.9	35.4
DMSO	24.9	13.6	13.8
$CHCl_3$	32.9	11.0	8.1
THF	30.0	9.0	6.5
Dioxane	31.7	9.5	6.5

3.4.2. Use of solubility parameters

Solubility parameters have been already applied to discuss the solubility behavior of dextran in organic solvents (Antoniou & Alexandridis, 2010; Antoniou, Tsianou, & Alexandridis, 2005; Antoniou, Buitrago, Tsianou, & Alexandridis, 2010; Antoniou, Themistou, Sarkar, Tsianou, & Alexandridis, 2010; Güner, 2004; Icoz & Kokini, 2007) as well as dextran fatty esters (Kaewprapan, Baros, Marie, Inprakhon, & Durand, 2012). Here, using group contributions from Van Krevelen and Hoftizer, we calculated the solubility parameters of native dextran, $DexC10_{100}$ and $DexC10_{200}$ (assuming only mono- and disubstituted units for the last two polymers, respectively) and compared these values to those of water, DMSO, chloroform and THF (Tables 4 and 5).

Qualitative discussion of solution behavior can be proposed on the basis of solubility parameters. It must be noticed that the attachment of β-hydroxyalkyl groups along dextran backbone does not modify the number of hydroxyl groups in the chain in comparison to native dextran. Consequently, hydrogen bonding ability of solvents should be a major aspect of solubility for dextran derivatives.

THF and dioxane become good solvents for $DexC10_\tau$ with $\tau > 100\%$ essentially because of their low polarity component (δ_P). Chloroform cannot be a solvent for dextran derivatives because of

Table 4
Hansen solubility parameters of dextran, dextran derivatives and solvents calculated by group contribution method from Van Krevelen and Hoftyzer.

Compound	δ ($J^{1/2}/cm^{3/2}$)	δ_D ($J^{1/2}/cm^{3/2}$)	δ_P ($J^{1/2}/cm^{3/2}$)	δ_H ($J^{1/2}/cm^{3/2}$)
Dextran	46.3	26.0	17.9	33.8
$DexC10_{100}$	25.6	19.0	4.4	16.5
$DexC10_{200}$	23.2	18.4	3.1	13.7
Water	48.1	12.3	31.3	34.2
DMSO	26.4	18.4	16.4	10.2
$CHCl_3$	18.8	17.7	3.1	5.7
THF	19.5	16.8	5.7	8.0
Dioxane	20.5	19.0	1.8	7.4

Table 6
Viscometric results in water at 25 °C.

Polymer	Synthesis[a]	$[\eta]$ (mL/g)	k_H
$DexC10_{10}$	In DMSO	9.8	3.1
$DexC10_4$	In aqueous micellar medium	19.5	0.5
$DexC10_{10}$		103.0	1.2

[a] "In DMSO" refers to the procedure described in Section 3.2. "In aqueous micellar medium" refers to the procedure described in Covis et al. (under review) and Durand (2006).

its very low hydrogen bonding component (δ_H). Nevertheless, chloroform saturated with water could dissolve $DexC10_{164}$ (Table 3). Finally, DMSO, because of its high polarity and hydrogen bonding components cannot be a good solvent for dextran derivatives having degrees of substitution higher than 100%. Nevertheless, we have showed that DMSO behaved as a good solvent for dextran derivatives modified with shorter hydrocarbon chains with degrees of substitution up to 40% (Léonard et al., 2008).

As a conclusion, solubility parameters provided tendencies that were fully consistent with what had been deduced from capillary viscometry experiments.

3.4.3. *Solution behavior of low modified dextrans in water: influence of modification procedure*

The solution behavior of water-soluble dextran derivatives has been already reported in detail (Rotureau et al., 2005). Here, we wanted to compare dextran derivatives which were synthesized using two different procedures. One derivative was prepared in DMSO in the presence of TBAOH (Table 1, entry 1). The two others were prepared following a procedure in aqueous micellar medium using cationic surfactant (Covis et al., under review; Durand, 2006). Briefly, in that second modification procedure, the reaction was carried out in water containing a cationic surfactant (dodecyltrimethyl ammonium bromide) and sodium hydroxide. The epoxide, was dispersed in water under the form of droplets and partly solubilized in surfactant micelles.

Both types of polymers were fully soluble in water but led to very different viscometric characteristics (Table 6). For comparison, taking into account the dextran backbone degradation in the conditions used in DMSO and in aqueous micellar medium, the intrinsic viscosity of unmodified dextran would be equal to 21.6 mL/g and 17.5 mL/g respectively (Ioan, Aberle, & Burchard, 2000).

The polymer synthesized in DMSO exhibited the associative behavior that is characteristic of amphiphilic dextrans having DS lower than 15% (Rotureau et al., 2005). The critical association concentration, above which the variation of reduced viscosity deviated from linearity was estimated to 20 g/L. The intrinsic viscosity was about half the value of unmodified dextran which is also consistent with previous results.

On the contrary, the polymers prepared in aqueous micellar medium exhibited a viscometric behavior similar to particles, with a linear variation of reduced viscosity over the whole concentration range. The found values of intrinsic viscosity were close to or much higher than that of unmodified dextran. This result is consistent with the representation of the polymer under the form of nano-size aggregates involving several macromolecules. This behavior would be expected for DS values above 20% for polymers synthesized in DMSO (Rotureau et al., 2005). Thus the synthesis in aqueous micellar medium induced a substitution pattern which enhanced the associative tendency. This can be related to an increase of hydrocarbon tails attachment onto neighboring glucose units resulting from the accumulation of epoxide molecules in cationic micelles. The relation between conditions of modifications and solution properties has already been demonstrated in the case of cellulose derivatives (Hirrien, Desbrières, & Rinaudo, 1996). More work has to be carried out on that point but these results already show that both types of modification may provide dextran derivatives with very different properties even with similar DS.

4. Conclusion

In that work we establish a modification procedure of dextran in organic medium which allowed the preparation of wide series of dextran derivatives with both water-soluble and water-insoluble compounds. We demonstrated that epoxide oligomerization occurred as secondary reaction when hydroxide ions were present while it was almost negligible when *t*-BuOK was the base catalyst. Dextran derivatives with degrees of substitution higher than 100% were soluble in several organic solvents (THF, dioxane) and in water-saturated chloroform and dichloromethane. The viscometric behavior of these polymers in organic solvents was characterized. A low modified dextran derivative (DS = 10%) was studied in aqueous solution and compared to another dextran derivative with similar DS but synthesized following a heterogeneous procedure in aqueous micellar solution. The comparison revealed that the substitution pattern should be significantly different according to the synthesis procedure. Current work examines the use of water-insoluble dextran derivatives for preparing inverse miniemulsions and further characterization of solution behavior of water-soluble amphiphilic dextrans according the method of synthesis (homogeneous or heterogeneous).

References

Antoniou, E., Tsianou, M., & Alexandridis, P. (2005). Solution properties of polysaccharides in water and polar organic solvents. *Polymeric Preprints*, *46*, 532–533.

Antoniou, E., & Alexandridis, P. (2010). Polymer conformation in mixed aqueous-polar organic solvents. *European Polymer Journal*, *46*, 324–335.

Antoniou, E., Buitrago, C. F., Tsianou, M., & Alexandridis, P. (2010). Solvent effects on polysaccharide conformation. *Carbohydrate Polymers*, *79*, 380–390.

Antoniou, E., Themistou, E., Sarkar, B., Tsianou, M., & Alexandridis, P. (2010). Structure and dynamics of dextran in binary mixtures of a good and a bad solvent. *Colloid and Polymer Science*, *288*, 1301–1312.

Carrier, O., Covis, R., Marie, E., & Durand, A. (2011). Inverse emulsions stabilized by a hydrophobically modified polysaccharide. *Carbohydrate Polymers*, *84*, 599–604.

Catiker, E., & Güner, A. (1998). Unperturbed molecular dimensions and theta temperature of dextran in dimethylsulfoxide (DMSO) solutions. *Polymer Bulletin*, *41*, 223–230.

Covis, R., Ladaviere, C., Desbrières, J., Marie, E. & Durand, A. under review.

Durand, A. (2006). Synthesis of amphiphilic polysaccharides by micellar catalysis. *Journal of Molecular Catalysis A*, *256*, 284–289.

Graessley, W. W. (1974). The entanglement concept in polymer rheology. *Advances in Polymer Science*, *16*, 1–179.

Güner, A. (2004). The algorithmic calculations of solubility parameter for the determination of interactions in dextran/certain polar solvent systems. *European Polymer Journal*, *40*, 1587–1594.

Hirrien, M., Desbrières, J., & Rinaudo, M. (1996). Physical properties of methylcelluloses in relation with the conditions for cellulose modification. *Carbohydrate Polymers*, *31*, 243–252.

Huggins, M. L. (1942). The viscosity of dilute solutions of long-chain molecules. IV. Dependence on concentration. *Journal of the American Chemical Society*, *64*, 2716.

Icoz, D. Z., & Kokini, J. L. (2007). Examination of the validity of the Flory-Huggins solution theory in terms of miscibility in dextran systems. *Carbohydrate Polymers*, *68*, 59–67.

Ioan, C. E., Aberle, T., & Burchard, W. (2000). Structure properties of dextran. 2. Dilute solution. *Macromolecules*, *33*, 5730–5739.

Kaewprapan, K., Baros, F., Marie, E., Inprakhon, P., & Durand, A. (2012). Macromolecular surfactants synthesized by lipase-catalyzed transesterification of dextran with vinyl decanoate. *Carbohydrate Polymers*, *88*, 313–320.

Léonard, M., Marie, E., Wu, M., Dellacherie, E., Camesano, T., & Durand, A. (2008). Preparation of polysaccharide-covered polymeric nanoparticles by several processes involving amphiphilic polysaccharides. *ACS Symposium Series*, *996*, 322–340.

Nordmeier, E. (1993). Static and dynamic light-scattering solution behavior of pullulan and dextran in comparison. *Journal of Physical Chemistry*, *97*, 5770–5785.

Rotureau, E., Chassenieux, C., Dellacherie, E., & Durand, A. (2005). Neutral polymeric surfactants derived from dextran: A study of their aqueous solution behavior. *Macromolecular Chemistry and Physics*, *206*, 2038–2046.