Synthesis, Characterization, and Polymerization of Glycidyl Methacrylate Derivatized Dextran

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ABSTRACT: Glycidyl methacrylate derivatized dextran (dex-GMA) was synthesized by coupling of GMA to dextran in the presence of 4-(*N,N*-dimethylamino)pyridine using DMSO as an aprotic solvent and characterized by GPC, FTIR, and NMR. The structure of the product was established with ^{1}H and CH-COSY NMR. The degree of substitution, as determined by NMR, can be controlled by varying the molar ratio of GMA and dextran. Almost quantitative incorporation of GMA (>90%) was established. Hydrogels were prepared by radical polymerization of aqueous solutions of dex-GMA, using ammonium peroxydisulfate (APS) and *N,N,N′,N′*-tetramethylethylenediamine (TEMED) as the initiating system. The polymerization rate, as determined by FTIR analysis, was dependent on the APS, the TEMED, and the dex-GMA concentration. By proper selection of the polymerization conditions, hydrogels could be obtained in which more than 95% of the methacrylate groups had reacted within 20 min.

Introduction

Dextran is a bacterial polysaccharide, consisting essentially of α-1,6 linked D-glucopyranose residues with a few percent of α-1,2-, α-1,3-, or α-1,4-linked side chains.[1] The low molecular weight fractions of dextran are used as a plasma expander.[2] Furthermore, dextran is widely under investigation as a polymeric carrier in novel drug delivery systems.[3–8]

Because of its good biocompatibility, dextran is also a suitable polymer to be used for the preparation of hydrogels, which are becoming increasingly important in the biomedical, pharmaceutical, and biotechnological fields.[9,10] Dextran hydrogels can be obtained by cross-linking dextran in DMSO with 1,6-hexanediisocyanate[11] or by derivatization of dextran with polymerizable double bonds, followed by radical polymerization of an aqueous solution of the dextran derivative. A glycidyl acrylate derivative of dextran has been synthesized by Edman et al.[12] However, their method lacked control of the amount of acrylate groups incorporated in the dextran molecule, and therefore an additional cross-linker, *N,N′*-methylenebis(acrylamide), had to be added to obtain a network.

In this paper we describe a new procedure for the synthesis of glycidyl methacrylate derivatized dextran (dex-GMA), which allows full control of the degree of substitution. In addition, the formation of hydrogels by polymerization with ammonium peroxydisulfate and *N,N,N′,N′*-tetramethylethylenediamine was examined.

Experimental Section

1. Materials. Dextran (from *Leuconostoc mesenteroides*, T40, M_n = 15 000, M_w = 32 500, as determined by GPC analysis), dimethyl sulfoxide (DMSO, <0.01% water), glycidyl methacrylate (GMA, 95% by GC; systematic name, 2,3-epoxypropyl methylpropenoate), ammonium peroxydisulfate (APS), and *N,N,N′,N′*-tetramethylethylenediamine (TEMED) were obtained from Fluka Chemie AG, Buchs, Switzerland. 4-(*N,N*-Dimethylamino)pyridine (DMAP, 99%) was from Acros Chimica, Geel, Belgium. Other solvents (p.a.) were obtained from Merck, Darmstadt, Germany. Dialysis tubes (cellulose, MW cutoff 12 000–14 000) were purchased from Medicell International Ltd., London, England. PD-10 columns containing Sephadex G-25 M, were supplied by Pharmacia Biotech, Uppsala, Sweden.

2. Methods. *NMR.* NMR spectra were recorded in ^2H_2O (99.8% ^{2}H, Merck) with a Gemini 300 MHz spectrometer (Varian Associates Inc. NMR Instruments, Palo Alto, CA), using ^{2}HOH at 4.8 ppm as the reference line. Approximately 30 mg of (GMA derivatized) dextran was dissolved in 0.8 mL of ^2H_2O. For ^{1}H-NMR, a pulse angle of 87.7° was used with a relaxation delay of 30 s. The water signal at 4.8 ppm was eliminated by solvent suppression with decoupling. The decoupling power was adjusted to a level at which the intensity of the anomeric proton signal was not affected. For the ^{13}C-NMR spectra, the pulse length was 4 μs, the 180° pulse was 25 μs and the relaxation delay was 2 s. The CH-COSY spectra were recorded by observing the ^{13}C signal with a relaxation delay of 2 s. The decoupler was gated on during acquisition and off during delay. A line broadening of 3 Hz was used.

FTIR. FTIR spectra were recorded with a Bio-Rad FTS-25 spectrometer (Bio-Rad Laboratories Inc., Cambridge, MA). The dry materials were powdered, ground with KBr powder and pressed into pellets under reduced pressure. For each sample 16 scans were recorded between 4000 and 450 cm^{-1} with a resolution of 2 cm^{-1}. Win-IR software V 2.03 was used to calculate the peak height of the IR absorptions at 813 cm^{-1} (double bond of GMA) and 763 cm^{-1} (dextran).[13–15] The relative decrease of the ratio of these absorptions was used to calculate the conversion of the methacrylate groups.

GPC. The molecular weights and molecular weight distributions of dextran and dex-GMA were determined by gel permeation chromatography (GPC) on a system consisting of a Waters 510 HPLC pump and 410 differential refractometer (Waters Associates Inc., Milford, MA) with three thermostated (35 °C) Shodex KW series columns (OH pack KB 800P 8 × 300 mm, precolumn; OH pack KB 802 6 mm × 50 mm, exclusion limit 4 × 10^3; OH pack KB 80M 8 mm x 300 mm, exclusion limit 2 × 10^7; SHOWA Denko, Tokyo, Japan). Degassed 10 mM NaCl in Milli Q water was used as the mobile phase.[16] The flow rate was 1.0 mL/min. The columns were calibrated using dextran standards of known molecular weights

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with narrow molecular weight distributions (Fluka). The chromatograms were analyzed with Millennium 2010 V. 2.0 software (Waters Associates Inc., Milford, MA).

3. Kinetics of the Reaction of Dextran with GMA. Dextran (10.0 g) was dissolved in DMSO (90 mL). After dissolution of DMAP (2.00 g) and bringing the solution to the desired temperature (4, 25, 37, or 50 °C), GMA (4.63 g) was added. For the study at 4 °C, a mixture of 10% (v/v) formamide in DMSO was used to prevent solidification of DMSO. Samples (1 mL) were taken periodically from the reaction mixture and diluted with 1.5 mL of water. dex-GMA was separated from unreacted GMA by elution with water over a Sephadex PD-10 column. The first 3 mL were collected and lyophilized. A control experiment showed that all unreacted GMA was removed by this procedure. The degree of substitution (DS; the amount of methacrylate groups per 100 dextran glucopyranose residues) of dex-GMA was determined by ^{1}H NMR spectroscopy and used to calculate the amount of unreacted GMA.

4. Synthesis of dex-GMA. (Standard procedure). Dextran (50.0 g) was dissolved in DMSO (450 mL) in a stoppered 1 L round bottom flask under nitrogen atmosphere. After dissolution of DMAP (10.0 g), a calculated amount of GMA was added. The solution was stirred at room temperature for 48 h, after which the reaction was stopped by adding an equimolar amount of concentrated HCl to neutralize the DMAP. The reaction mixture was transferred to a dialysis tube and extensively dialyzed for 2 weeks against demineralized water at 4 °C. dex-GMA was lyophilized, and the white fluffy product was stored at −20 °C before use.

5. Synthesis of Glyceryl Methacrylate (2,3-Dihydroxy-1-propyl Methylpropenoate and 1,3-Dihydroxy-2-propyl Methylpropenoate). Glyceryl methacrylate was synthesized essentially according to Refojo:[17] GMA (25.2 g) was added to 40 mL of demineralized water containing 0.1 mL of concentrated sulfuric acid. A small, additional amount of hydroquinone monomethyl ether was added to prevent premature polymerization. The heterogeneous reaction mixture was stirred at ambient temperature for 7 days. The resulting clear solution was neutralized with 0.1 M NaOH, saturated with NaCl, and extracted with dichloromethane. The extract was dried over magnesium sulfate, filtered, and concentrated under reduced pressure; yield 26.0 g, 92%. Part of the crude product (500 mg) was purified by column chromatography (35 g of silica, eluant, $CHCl_3$/MeOH, 10/0 to 9/1, v/v), yielding 350 mg of a colorless viscous liquid.

R_f ($CHCl_3$/MeOH, 9/1, v/v) = 0.39.

^{1}H NMR (^2H_2O): 1,3-dihydroxy-2-propyl methylpropenoate δ 6.18 (m, 1H, H_b), 5.72 (m, 1H, H_b), 5.02 (m, 1H, $H_{d'}$), 3.77 (m, 4H, $H_{e'}$), 1.91 (m, 3H, H_c); 2,3-dihydroxy-1-propyl methylpropenoate δ 6.15 (m, 1H, H_b), 5.72 (m, 1H, H_b), 4.25 (dd, $^2J_{H-H}$ = 11.5 Hz, $^3J_{H-H}$ = 3.8 Hz, 1H, H_{f1}), 4.16 (dd, $^2J_{H-H}$ = 11.5 Hz, $^3J_{H-H}$ = 6.1 Hz, 1H, H_{f2}), 4.00 (m, 1H, H_d), 3.68 (dd, $^2J_{H-H}$ = 11.7 Hz, $^3J_{H-H}$ = 4.7 Hz, 1H, H_{e1}), 3.63 (dd, $^2J_{H-H}$ = 11.8 Hz, $^3J_{H-H}$ = 6.3, 1H, H_{e2}), 1.91 (m, 3H, H_c).

^{13}C NMR (^2H_2O): 1,3-dihydroxy-2-propyl methylpropenoate δ 17.3 (CH_3), 60.3 (CH_2OH), 76.0 ($CHOCOR$), 127.0 (H_2C=), 135.7 (H_2C=C), 169.5 (C=O); 2,3-dihydroxy-1-propyl methylpropenoate δ 17.3 (CH_3), 62.3 (CH_2OH), 65.7 (CH_2OCOR), 69.5 ($CHOH$), 127.0 (H_2C=), 135.7 (H_2C=C), 169.5 (C=O).

FTIR (KBr): 3428 (ν_{O-H}), 1718 ($\nu_{C=O}$), 1636 ($\nu_{C=C}$), 1299 and 1173 (ν_{C-O}, ester), 1051 (ν_{C-O}, alcohol), 813 (ν_{C-H}, C=CH_2).

6. Preparation of dex-GMA Hydrogels. To a solution of dex-GMA (100 mg or 400 mg, DS = 28) in phosphate buffer (0.20 M, pH 8.5) was added APS (100 μL of APS solution in phosphate buffer, 11 or 219 μmol of APS per 100 μL) and the solution was mixed well. The polymerization was started by the addition of TEMED (100 μL of TEMED solution in phosphate buffer, pH adjusted to 8.5, concentration 6.7, 20 and 34 μmol of TEMED per 100 μL). The final concentration of the dex-GMA solution was 10 or 40% w/w. dex-GMA was allowed to polymerize at room temperature for a certain period of time, after which the reaction was stopped by quickly freezing the gels in liquid nitrogen. After lyophilization the conversion of the methacrylate groups was determined by FTIR spectroscopy.

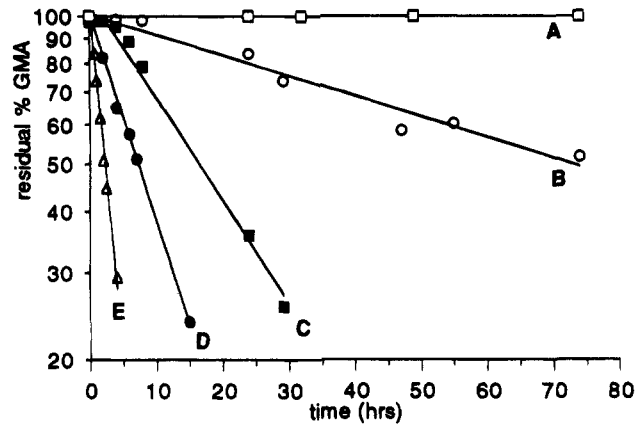


Figure 1. Logarithm of the residual percentage of GMA as a function of time, in the absence of DMAP at 50 °C (A) and in the presence of DMAP at 4 °C (B), 25 °C (C), 37 °C (D), and 50 °C (E).

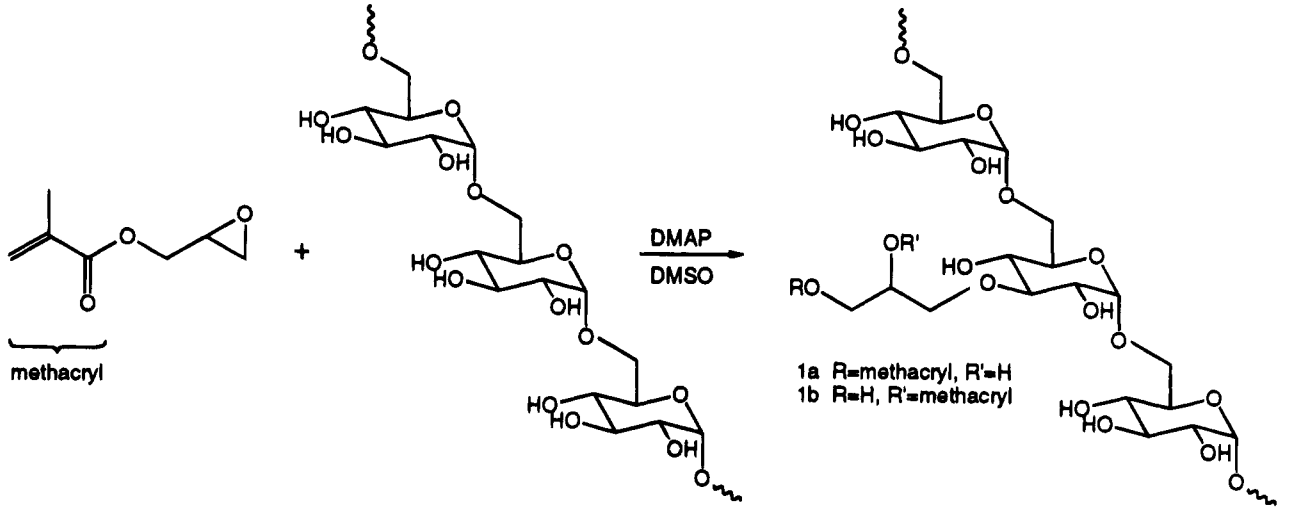
Results and Discussion

Synthesis of Glycidyl Methacrylate Derivatized Dextran. The synthesis of dextran derivatized with polymerizable groups has been described by Edman et al.[12] In their procedure glycidyl acrylate was coupled to dextran in a carbonate buffer at pH 11. The reaction time was 5 days, and the degree of substitution was 5, corresponding to an incorporation of less than 10% of the glycidyl acrylate originally present. The low incorporation of acrylate groups can most likely be ascribed to the aqueous basic reaction conditions. Firstly, the epoxy group can react with water, yielding glyceryl acrylate, which does not react with dextran under these conditions. Secondly, the acrylic ester can be hydrolyzed, before and after reaction with dextran.

Therefore, we have developed a novel and more efficient method to obtain dextran with polymerizable groups. In our procedure, dextran is reacted with glycidyl methacrylate (GMA) in dimethyl sulfoxide (DMSO) as a polar aprotic solvent. A base is needed as a catalyst for the coupling reaction, because in the absence of a catalyst, no incorporation of GMA could be detected (reaction time 70 h, temperature 50 °C; Figure 1A). Probably, the hydroxyl groups of dextran are polarized by the base and react subsequently with the less hindered methylene carbon of the epoxy group of GMA[18,19] to form the 3-methacryloyl-1-glyceryl ether of dextran, according to Scheme 1. Under the basic reaction conditions, the methacryloyl group can move from position 3 to position 2 on the glyceryl moiety through transesterification, as demonstrated by NMR analysis (*vide infra*). The product therefore consists of two regio isomers, the 3-methacryloyl-1-glyceryl ether of dextran (Scheme 1, **1a**) and the 2-methacryloyl-1-glyceryl ether of dextran (Scheme 1, **1b**).

The coupling reaction of GMA to dextran was studied in the presence of imidazole, triethylamine, pyridine, or 4-(*N,N*-dimethylamino)pyridine (DMAP) as a catalyst. When using imidazole, no incorporation of GMA was detected. On the other hand, triethylamine, pyridine, and DMAP were effective catalysts. However, compared to DMAP, triethylamine and pyridine required significantly longer reaction times in order to obtain a substantial degree of substitution. We therefore studied the kinetics of the coupling reaction catalyzed by DMAP.

Scheme 1. Reaction of Dextran with Glycidyl Methacrylate[22]



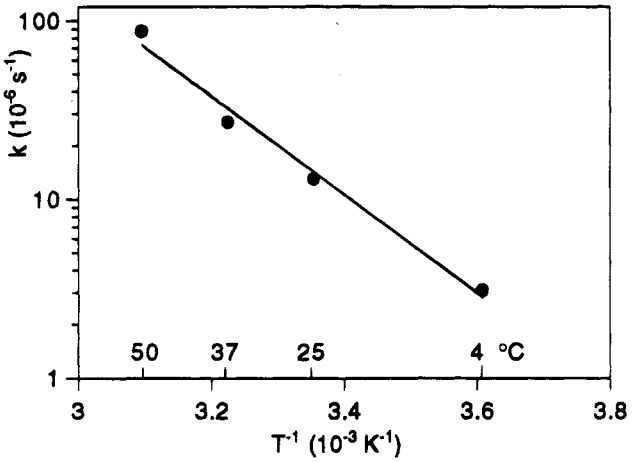


Figure 2. Arrhenius plot of the reaction of dextran with GMA in DMSO in the presence of DMAP (8.8 mol % vs hydroxyl groups).

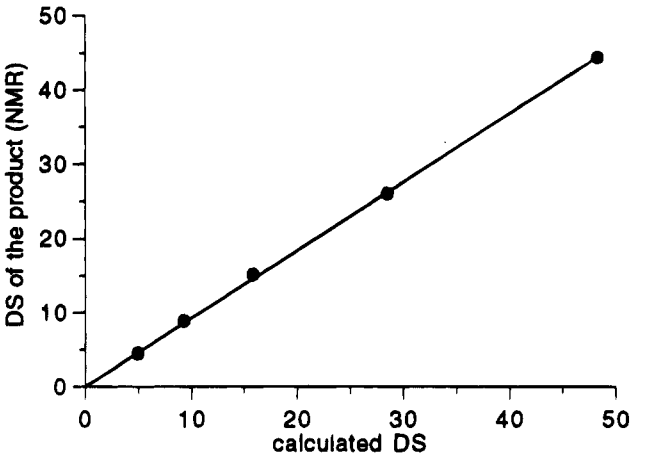


Figure 3. Relationship between the molar ratio of GMA to glucopyranose residues (×100) in the reaction mixture (=the calculated DS) and the DS of the product.

Figure 1 shows the residual amount of GMA in the reaction mixture as a function of the reaction time at various temperatures. From these experiments it can be concluded that the reaction follows pseudo first order kinetics. The activation energy of the coupling of GMA to dextran in the presence of DMAP (8.8 mol % vs hydroxyl groups) is 55(±4) kJ/mol, as derived from the Arrhenius plot (Figure 2).

For the large scale synthesis of glycidyl methacrylate derivatized dextran (dex-GMA), a reaction time of 48 h at ambient temperature was chosen as a suitable reaction condition. Figure 3 shows the relationship between the molar ratio of GMA to glucopyranose residues in the reaction mixture (i.e. the calculated DS) and the degree of substitution (DS) of the products, as determined by NMR analysis. It is shown that more than 90% of the added GMA is incorporated in dextran under these conditions. This means that dex-GMA can be obtained with full control of the DS, ranging from low (4.5) to relatively high (45). Purification of the GMA-derivatized dextran by several cycles of dissolution and precipitation, analogous to the method described by Edman et al.,[12] resulted in low yields of dex-GMA. Therefore, extensive dialysis of the reaction mixture against demineralized water was used to purify dex-GMA. Prior to dialysis, DMAP was neutralized by addition of concentrated hydrochloric acid to prevent alkaline hydrolysis of the methacrylic ester. Hydrolysis was also minimized by dialyzing at 4 °C. After dialysis for 2 weeks and subsequent lyophilization, products in which no DMAP and DMSO could be detected by NMR were obtained in high yields (70–90%).

GPC analysis of dex-GMA showed that the elution profile was independent of the DS and not significantly different from dextran. This indicates that the hydrodynamic radii of dextran and dex-GMA are equal. Representative GPC chromatograms of dextran and dex-GMA are shown in Figure 4.

Characterization by NMR. Quantitative determination of the degree of substitution is necessary for a proper characterization of dex-GMA. In Figure 5a the NMR spectrum of dextran is displayed. The signal from the anomeric proton of the glucopyranosyl ring (H_a, δ 5.0 ppm) is well separated from the other proton signals (δ 3.4–4.1 ppm). The low-intensity signal at δ 5.3 ppm is assigned to the proton at the anomeric carbon of the α-1,3 linkages ($H_{a'}$).[1] From the ratio of the integrals of δ 5.3 and δ 5.0 ppm, on the average 4% of α-1,3 linkages was calculated, which is common for the dextran used in this study.

In the spectrum of dex-GMA (Figure 5b) the signals from the methacryloyl group are observed at δ 1.95 ppm (methyl protons, H_c) as well as at δ 5.75 and δ 6.2 ppm (protons at the double bond, H_b), having an integral ratio of 3:2, as expected. However, the signal of the anomeric proton shows a shoulder at δ 5.05 ppm.

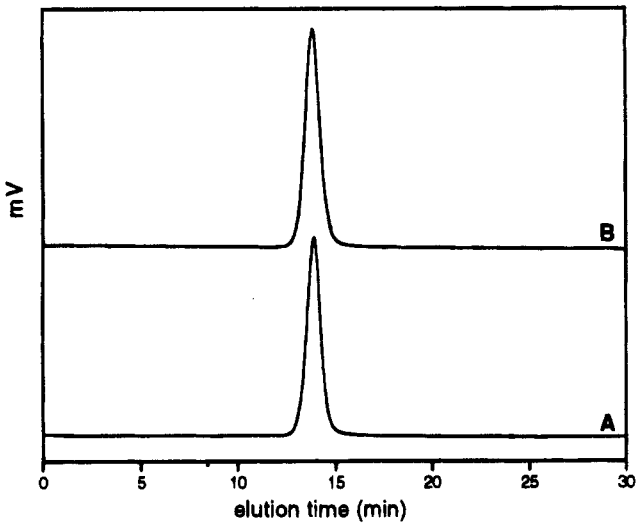


Figure 4. GPC chromatograms of (A) dextran T40 and (B) dex-GMA (DS = 11).

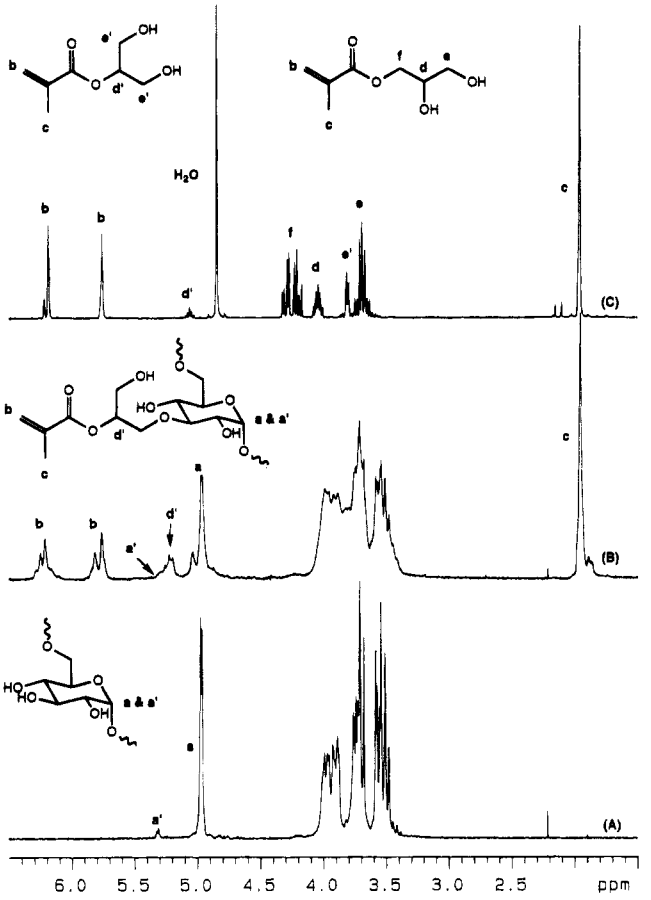


Figure 5. ^1H NMR spectra of (A) dextran T40, (B) dex-GMA (DS = 42), and (C) glyceryl methacrylate, dissolved in ^2H_2O.

Moreover, an additional signal is observed at δ 5.2 ppm ($H_{d'}$), which partly overlaps the signal from the anomeric proton of the α-1,3 linkages ($H_{a'}$). Therefore, a CH-COSY spectrum of dex-GMA was recorded (Figure 6). In this spectrum a correlation between the peak at δ 5.05 ppm and the anomeric carbon at δ 98 ppm is shown. This shoulder therefore belongs to the anomeric proton. The shift is most likely caused by the attachment of the methacryloyl glyceryl moiety to the glucopyranosyl ring.

Figure 6 also shows that the signal at δ 5.2 ppm has a correlation with a carbon signal at δ 76 ppm, demonstrating that this peak is not part of the anomeric proton. The ^{13}C signal at δ 76 ppm does not occur in the ^{13}C NMR spectrum of either dextran or GMA (results not shown) and must therefore be ascribed to a carbon exclusively present in dex-GMA. To elucidate this correlation (δ 5.2 with δ 76 ppm), glyceryl methacrylate was synthesized as a model compound, which shows similarity to the glyceryl methacryloyl moiety of dex-GMA. The ^1H NMR of glyceryl methacrylate shows, on the basis of multiplicity and the integral of the different signals, that it consists of two isomers: 1-glyceryl- and 2-glyceryl methacrylate (Figure 5c). This was confirmed by HH-COSY NMR (results not shown). 2-Glyceryl methacrylate is formed through transesterification of 1-glyceryl methacrylate, with a molar ratio of about 1:10, respectively (NMR integrals). In this spectrum (Figure 5c), a small peak is observed at δ 5.0 ppm, originating from the $H_{d'}$ of 2-glyceryl methacrylate. The CH-COSY spectrum of glyceryl methacrylate (Figure 7) shows that this peak at δ 5.0 ppm has a correlation with a carbon signal at δ 76 ppm. Since the peak at δ 5.2 ppm in dex-GMA also correlated with a carbon signal at δ 76 ppm (Figure 6), this gives a strong indication that this signal at δ 5.2 ppm in Figure 5b can be attributed to the $H_{d'}$ of the 2-glyceryl methacryloyl moiety of dex-GMA. The intensity of the latter peak is approximately 75% of the intensity of the signal from the double bonds. This means that in dex-GMA the 2-methacryloyl ester is predominantly present, as opposed to glyceryl methacrylate, in which the 1-methacryloyl ester is the main component. This indicates a much higher extent of transesterification for dex-GMA, very likely caused by the basic reaction conditions during the synthesis. Compared with glyceryl methacrylate, the peaks at δ 5.75 and δ 6.2 ppm (protons at the double bond, H_b) are broader in Figure 5B. An additional HH-COSY spectrum (result not shown) demonstrated that these peaks are a combination of signals from two different isomers.

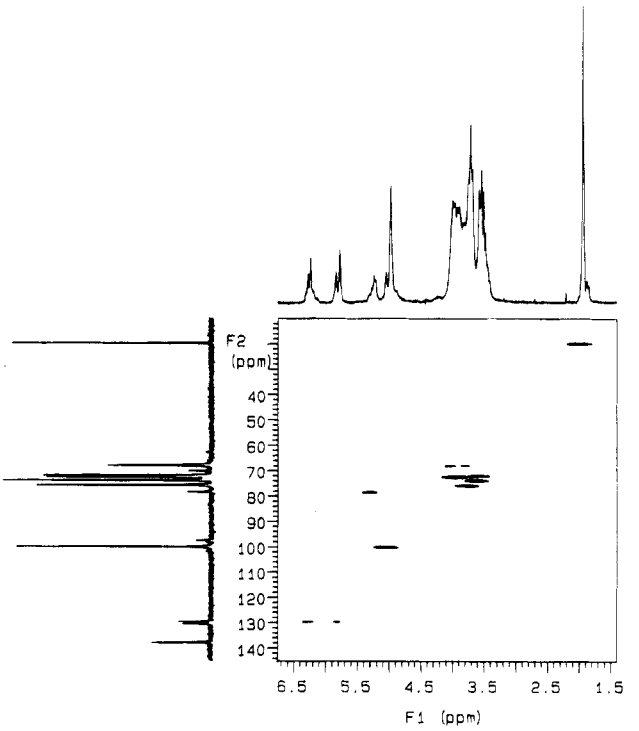


Figure 6. CH-COSY NMR spectrum of dex-GMA (DS = 42).

Based on the assignment of the ^1H-NMR spectrum, the degree of substitution of the dex-GMA is calculated

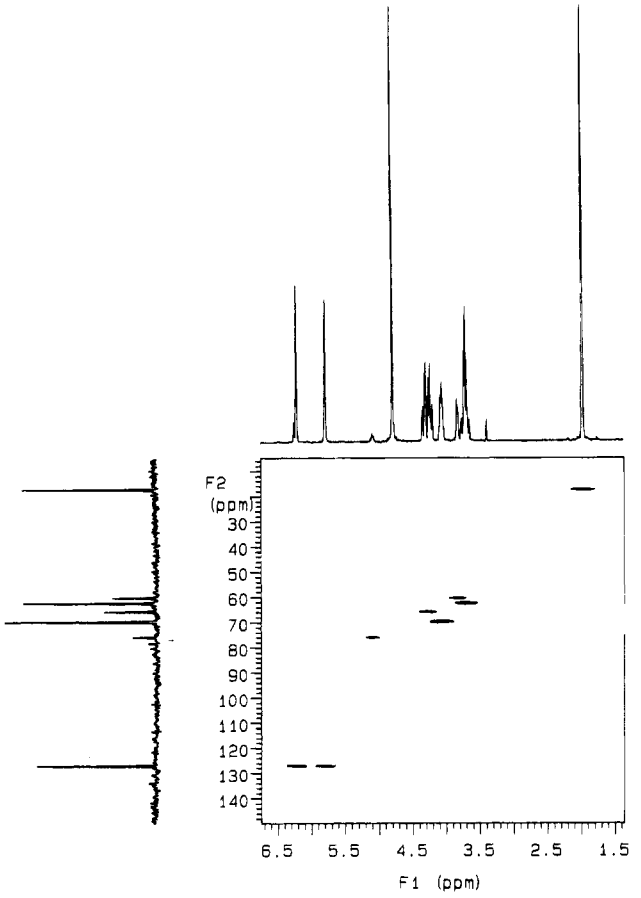


Figure 7. CH-COSY NMR spectrum of glyceryl methacrylate.

as $(100x)/y$, in which x is the average integral of the protons at the double bond at δ 5.75 and δ 6.2 ppm and y is the integral of the anomeric proton at δ 4.95–5.1 ppm with addition of 4% of α-1,3 linkages.

Hydrogel Formation. The methacrylate groups in dex-GMA can polymerize to form a cross-linked structure. When this polymerization is carried out in water, a hydrogel is formed. The polymerization of methacrylate groups can be initiated using ammonium peroxydisulfate (APS) and *N,N,N′,N′*-tetramethylethylenediamine (TEMED). TEMED accelerates the homolytic scission of APS, yielding the sulfate free radical ($SO_4^{\bullet -}$). Besides, also the TEMED free radical $(CH_3)_2NCH_2$-$CH_2(CH_3)NCH_2^{\bullet}$ and the hydroxyl free radical $OH^{\bullet}$ are generated.[20] The kinetics of the polymerization were followed by quantitative determination of the residual amount of methacrylate groups by FTIR spectroscopy.

Figure 8 shows the FTIR spectra of dextran (a) and dex-GMA (b). In the latter spectrum the absorptions at 1710 and at 813 cm^{-1} are clearly visible, which are indicative of the carbonyl group and the double bond of the methacrylate group, respectively. In Figure 9 an expansion of the region around the 813 cm^{-1} peak of IR spectra of dextran (a), dex-GMA (b), and polymerized dex-GMA (c) is shown. It can be seen that the peak originating from the double bond (813 cm^{-1}, Figure 9b), has disappeared after polymerization (Figure 9c).

Polymerization appeared to be slow in the presence of APS only. Therefore, TEMED was added to the solution as an accelerator. The influence of the TEMED concentration on the polymerization rate was studied at a fixed concentration of APS and dex-GMA (Figure 10). It can be seen that the polymerization started immediately after the addition of TEMED. The polymerization rate was high: within 20 min more than 95% of the double bonds were converted. Further, it appeared that an increasing TEMED concentration re-

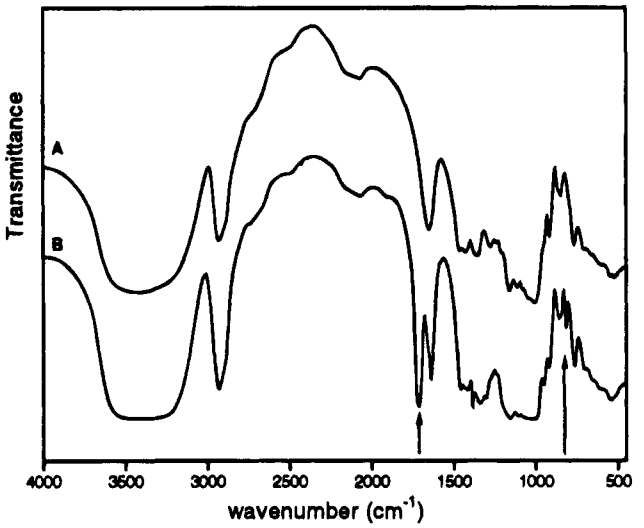


Figure 8. Transmittance FTIR spectra of (A) dextran and (B) dex-GMA. The arrows indicate the peaks, appearing at 1710 and 813 cm^{-1}, which originate from the methacrylate groups.

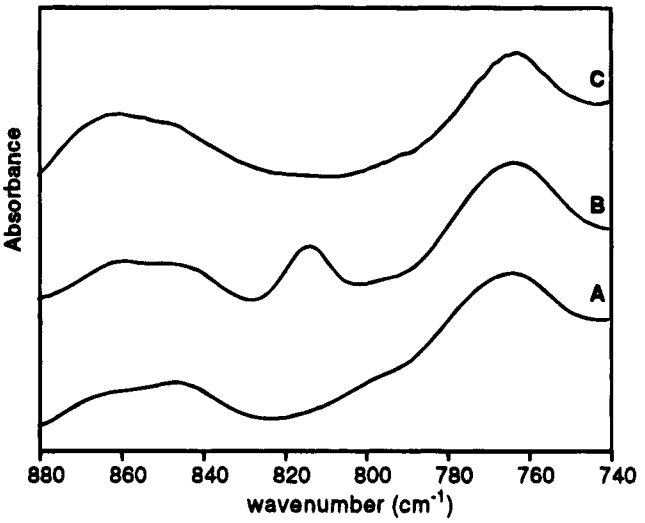


Figure 9. Expanded absorbance FTIR spectra of (A) dextran, (B) dex-GMA, and (C) polymerized dex-GMA.

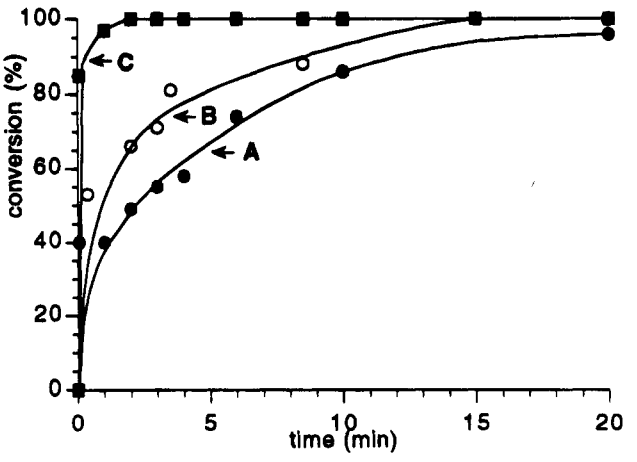


Figure 10. Effect of the TEMED concentration on the conversion of the methacrylate groups as a function of time, at a fixed concentration of dex-GMA (10% w/w) and APS (11 μmol/g of gel): 6.7 μmol (A), 20 μmol (B), and 34 μmol (C) TEMED per g of gel.

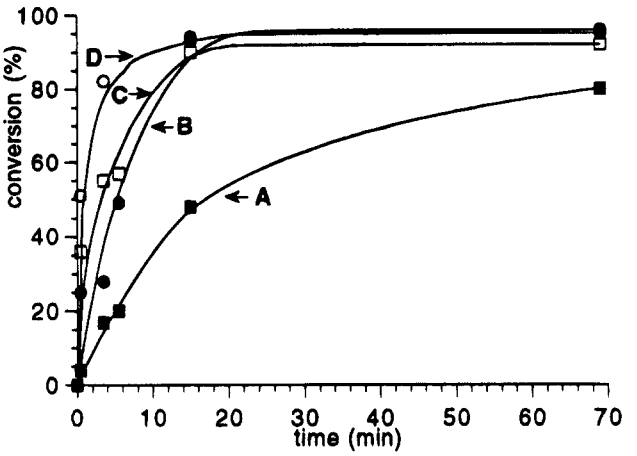


Figure 11. Effect of the dex-GMA and APS concentration on the conversion of the methacrylate groups as a function of time, at a fixed TEMED concentration (6.7 μmol/g of gel): 40% dex-GMA and 11 μmol APS (A), 10% dex-GMA and 11 μmol APS (B), 40% dex-GMA and 219 μmol APS (C), and 10% dex-GMA and 219 μmol APS (D) per g of gel.

sulted in a faster polymerization process. At TEMED concentrations higher than 34 μmol/g of gel the conversion was almost instantaneous.

Figure 11 shows the influence of the APS and the dex-GMA concentration on the polymerization rate. At a low dex-GMA concentration (10% w/w), 95% of the methacrylate groups had reacted within 20 min, irrespective of the APS concentration (Figure 11B, D). A higher APS concentration resulted in faster polymerization. On the other hand, in gels containing 40% dex-GMA, prepared with a low APS concentration, the conversion was only 75% after 70 min (Figure 11A) and did not increase further at longer reaction times (up to 24 h; results not shown). The low final conversion at high initial dex-GMA concentration (40%) and low APS concentration can be explained as follows. Above a dex-GMA concentration of 13% the polymer chains start to entangle.[21] This means that at a dex-GMA concentration of 10%, intramolecular reaction is predominant, whereas at 40% dex-GMA concentration intermolecular cross-linking is occurring to a larger extent. Therefore, in solutions containing 40% dex-GMA, the gel point is reached at a low conversion, resulting in severe mobility restrictions of the unreacted methacrylate groups. On the other hand, at high APS concentration and 40% dex-GMA, more than 95% conversion was reached in 20 min (Figure 11C). This is probably caused by the high concentration of initiating species, which results in a higher conversion. An increasing conversion with increasing initiator concentration has also been observed in other network forming systems.[13]

Conclusions

An efficient method has been developed for the synthesis of glycidyl methacrylate derivatized dextran (dex-GMA). The degree of substitution can be fully controlled by the feed ratio of GMA to dextran, due to the almost quantitative incorporation of GMA in dextran. Upon polymerization of an aqueous solution of dex-GMA with ammonium peroxydisulfate and *N,N,N′,N′*-tetramethylethylenediamine, it is feasible to obtain hydrogels with a virtually complete conversion of methacrylate groups within 20 min. These hydrogels are presently under investigation as a matrix for the controlled release of proteins.

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