Crosslinking Behavior of Dextran Modified with Hydroxyethyl Methacrylate upon Irradiation with Visible Light—Effect of Concentration, Coinitiator Type, and Solvent

Elbadawy A. Kamoun,* Henning Menzel

Institut für Technische Chemie, Technische Universität Braunschweig, Braunschweig 38106, Germany

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ABSTRACT: This study presents the synthesis of a crosslinkable dextran as starting material for the development of new hydrogels as drug delivery system in dental applications. 2-Hydroxyethyl methacrylate (HEMA) was coupled to dextran after activation with carbonyldiimidazole as monitored by FTIR and ^{1}H-NMR spectroscopy. The Dex-HEMA was crosslinked by visible light in the presence of camphorquinone (CQ) as photoinitiator and a coinitiator in a proper solvent. Aliphatic or aromatic amines were used as coinitiators and the content of the coinitiator was varied from 0.25 to 3.0 mol %. Diphenyliodonium chloride was added as a third component to the above photoinitiation system. It was observed that, the degree of swelling decreased upon an increase of Dex-HEMA concentration and the water content in the solvent system due to formation of more crosslinking points, that is, increasing crosslink density (P_x). The type of coinitiator shows a prominent impact on the swelling behavior and crosslinking efficiency of hydrogels. Special cryofixation and cryofracture techniques were used to investigate the surface and interior of swollen Dex-HEMA hydrogel samples by SEM. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 117: 3128–3138, 2010

Key words: hydrogels; photopolymerization; swelling; crosslinking; morphology

INTRODUCTION

Hydrogels are materials that are able to swell rapidly when placed in excess water and to retain large volumes of water. The polymer chains do not dissolve because of the presence of chemical or physical crosslinks.[1] Recently, considerable efforts have been made to synthesize hydrogels from dextran by different methods.[2,3] Dextran is used in several biomedical applications, for example, as plasma expander or as drug delivery system, because of its good water solubility and high biocompatibility.[4,5] Dextran is an amorphous and water soluble bacterial polysaccharide, which consists mainly of α-1,6-linked D-glucopyranose residues and partly of α-1,2 α-1,3 or α-1,4-linked side chains.[2] It has three hydroxyl groups per anhydroglucose unit, which can be used for modification with crosslinking groups, for example, vinyl groups.

2-Hydroxyethyl methacrylate (HEMA) is less harmful to the human body than other reagents commonly used for the incorporation of vinyl groups, such as acryloyl chloride. Poly(HEMA) is used in a wide range of biomedical applications. HEMA can be activated with carbonyldiimidazol (CDI) and attached to the dextran backbone via a carbonate ester group in order to obtain a hydrogel precursor (Dex-HEMA), which has a labile group for improved biodegradability.[6] One of the most important properties of hydrogels, the swelling ratio, can be adjusted by controlling the degree of substitution with methacrylate groups.[7] The precursor polymers can be dissolved and crosslinked by, e.g., photopolymerization. Normally UV-light is used for photocrosslinking. Because of carcinogenic and photoallergic effects, and the risk of tissue burning, the use of irradiation below 400 nm (in the UV region) is restricted in dental applications,[8] wherefore, visible light is used. In these applications, campherquinone (CQ) in combination with tertiary amines, as coinitiators have been the standard initiator system for photopolymerization.

A number of studies have been undertaken to determine the mechanism of initiation and the

**Present address:* Mubarak City for Scientific Research and Technological Applications (MUCSAT), New Materials Research Institute, Polymer Materials Research Department, New Borg El-Arab City, 21934 Alexandria, Egypt.

Correspondence to: H. Menzel (h.menzel@tu-bs.de).

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parameters that affect photopolymerization efficiency. Beside a relatively broad absorption in the UV-region (200–300 nm, $\lambda_{max} = 253.7$ nm) CQ has an absorption band in visible region at (400–500 nm, $\lambda_{max} = 468$ nm).[9,10] However, CQ has a low molar absorption coefficient in the visible light spectrum. To improve the efficiency of the photocuring, CQ is used in a mixture with a coinitiator (effective hydrogen-atom donor) such as amines.[10] Although radiation in the UV range promotes an electron in one of the two carbonyl groups of CQ into a short-lived, excited state (half-life time of $\sim$ 0.05 ms for the CQ triplet),[10] upon exposure of CQ to visible light, the molecule is excited into a singlet state ^{1}CQ*. This singlet state relaxes by intersystem crossing into its triplet state ^{3}CQ*. Amines and the excited CQ form an exciplex (excited complex state). Exciplex free radicals, by electron transfer and hydrogen abstraction, are generated, which can initiate a radical polymerization of, e.g., an acrylate (Fig. 1).[10] Recently, a new class of nonamine coinitiators like 1,3-benzodioxole (BDO) have been introduced.[11] The exact mechanism for this new coinitiator has not yet been reported. However, it is likely that the activated methylene group of the BDO can donate a hydrogen similar to the α-carbon atom of amine coinitiator (as shown in Fig. 1).

Cook[10] described that in the absence of an amine polymerization of a standard acrylate dental formulation proceeds only to a limited extent. Polymerization is also extremely slow in the presence of primary amines or amines with no α-hydrogens. However, tertiary aliphatic amines accelerate the polymerization rate, as do tertiary aromatic amines. Wang et al. had reported that the type of coinitiators affects the rate of polymerization and the final conversion level of HEMA in the presence of water.[13]

By further addition of an iodonium salt [e.g., diphenyliodonium chloride (DPIC)] to photoinitiator system as the third component, the rate of free radical formation is significantly increased.[13] It was proposed that the iodonium salt might act as an electron scavenger from the dye radical.[14,15]

The aim of this study was to synthesize a dextran derivative with hydroxyethyl methacrylate groups for photocrosslinking and to explore the possibilities for a visible light crosslinking using a CQ/coinitiator/DPIC system and a light-emitting diodes (LED) based light curing unit typically used in dental applications.[16] By studying the impact of different factors and coinitiator types on the crosslinking density, as can be deduced from the investigation of the swelling behavior of the resulting hydrogels, a system with optimal properties is sought. It was necessary to use some dimethyl sulfoxide (DMSO) as solvent in the photocrosslinking step, due to the poor solubility of CQ in water. After crosslinking, the gels were swollen in distilled water or buffer solution to remove the DMSO.

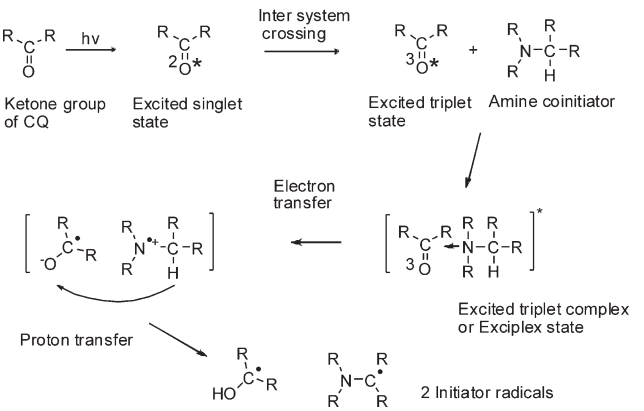

Figure 1 Key steps of the mechanism of visible light photoinitiation of free radical polymerization by CQ/amine systems.[12]

EXPERIMENTAL

Characterization

FTIR characterization

The FTIR spectra of dextran and Dex-HEMA were recorded on an Equinox 55 instrument (BRUKER; Germany). Translucent KBr-disks were prepared by grinding the dry materials together with infrared grade KBr and pressing. The FTIR spectrum was obtained by recording 64 scans between 4000 cm^{-1} and 400 cm^{-1} with a resolution of 2 cm^{-1}.

^{1}H-NMR characterization

NMR spectra were recorded by (NMR-DRX400, BRUCKER, Germany, 300 MHz). Approximately 50 mg of the product were dissolved in 0.8 mL of either D_2O or DMSO-d_6.

SEM investigation

Scanning electron microscopy images were recorded using a JEOL-JSM-6400 instrument (JEOL, Germany) at 20.0 kV. The hydrogel is swollen in distilled water for 48 h and then very quickly frozen using liquid nitrogen.[7] The freezing process has to be very fast to prevent crystallization of the water, which would result in artifacts.[7] The frozen sample is then freeze-dried at low temperatures of −90°C and low vacuum at 0.52 mbar to remove the water from the structure. A very light-weight dry gel was obtained. For SEM images of the interior, the frozen specimens were cryofractured by a very sharp knife at liquid nitrogen temperature and then freeze-dried (Fig. 5). Freeze-dried swollen hydrogels samples were fixed

on aluminum disks with a carbon band and were coated with gold by vapor deposition. Brightness and contrast of each SEM photograph were carefully adjusted to the same level, because the pore size detection by images analysis software is based upon the gray-scale of the images.

Glass transition temperature

The glass transition temperature (T_g) values of dried Dex-HEMA hydrogels were determined using a differential scanning calorimeter (NETZSCH Thermische Analyse, DSC 204 Phoenix, Germany) at a scanning rate of 5°C min^{-1}. The T_g values were determined as mid-point in the thermogram, as measured from the extensions of the pre- and post-transition baselines.

MATERIALS

Dextran from Leuconostoc Mesenteroides (average M_w 35,000–45,000 g/mol), *N*-phenylglycine (NPG, 95%), 1,3-benzodioxole (BDO, purity 99%), 2,6-di-*tert*-butyl-4-methylphenol, 4-(Dimethylamino)pyridine (DMAP), 1,1-carbonyldiimidazol (CDI), and diphenyliodonium chloride (97%, DPIC) were purchased from Sigma-Aldrich Chemie GmbH, (Steinheim, Germany). Dimethyl sulfoxide and 2,2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMAEMA) were obtained from Acros Chemica, (Geel, Belgium). 2-Hydroxyethyl methacrylate (HEMA) was from Fluka Chemie, (Germany). DL-Camphorquinone, 99% (bornanedione,1,7,7-trimethylbicyclo [2.2.1]-heptane-2,3-dione, CQ) was purchased from Acros-Organics, NJ. Tetrahydrofuran (THF) was dried over sodium and distilled immediately before use.

Synthesis of Dex-HEMA

The synthesis of the hydroxyethyl methacrylate modified dextran was carried out according to the procedure of Dijk-Wolthuis.[6] Typically, 1,1-carbonyldiimidazol (CDI, 6.488, 40 mmol) was dissolved in 190 mL freshly distilled anhydrous THF under nitrogen atmosphere and HEMA (5.204 g, 40 mmol) was added. The reaction mixture was stirred for 16 h at ambient temperature. A small amount of 2,6-di-*tert*-butyl-4-methylphenol (4.407 g, 40 mmol) or hydroquinone monomethyl ether was added to prevent premature polymerization. The THF was evaporated, yielding a slightly yellow liquid; this crude product was dissolved in ethyl acetate, extracted with water for at least 10 times to remove the inhibitor and imidazol pyproduct as well as unreacted HEMA and CDI, and subsequently dried over $MgSO_4$. After filteration and evaporation of ethyl acetate, hydroxyethyl methacrylate-imidazolylecarbamate (HEMA-CI) is obtained. The second step is the coupling reaction between HEMA-CI and dextran. Dextran was dissolved in DMSO under nitrogen atmosphere. After addition and dissolution of the required amount of 4-(dimethylamino) pyridine (DMAP), a calculated amount of HEMA-CI was added. The solution was stirred at room temperature for different times to adjust the degree of substitution. The product of the coupling reaction was then placed in dialysis tubes for 4 days in distilled water to remove excess of DMSO. The Dex-HEMA product was lyophilized and the white fluffy product was stored at −20°C until use.[6]

Dex-HEMA hydrogel formation by crosslinking with visible light

A total of 20 wt % Dex-HEMA was dissolved in DMSO and the photoinitiator (CQ, 0.5 mol %) was added. The coinitiator (DMAEMA, NPG or BDO 1.0 mol %) was dissolved in a small amount of water and added to the mixture. Finally, DPIC (1.0 wt %) was added to the mixture. The polymerization mixture was prepared in the absence of visible light and kept in the dark until use on the same day. Shaking and sonication were required to yield well-mixed solutions.

When water was added to the solutions, heavy water (deuterium oxide, 99.9%, D_2O, obtained from Aldrich Chemica, USA) was used because of the absence of overlapping of water bands at 1640 cm^{-1} in the IR. D_2O was added to polymerization mixture in different ratios 0, 5, 10, 15, 20, and 30 wt %. For photocrosslinking, a visible light LED lamp (Type: Bluephase, Ivoclar vivadent clinical, Lichtenstein) was used. The wavelength of the light is from 430 to 490 nm with an intensity 1000 mW/cm^2. The light source was placed directly over the polymer solution. The mixture was exposed to the LED lamp for 2 min. The produced gel was removed from the PE vial and soaked in distilled water or buffer solution to remove the DMSO and to determine the swelling ratio as a function of time.

Swelling experiments, gel yield, and Flory-Rehner calculations

The yield of hydrogel after the irradiation process was determined by weighting. Subsequently, the hydrogel was placed in distilled water or buffer solution, respectively. After predetermined intervals, it was removed, the water at the surface of the hydrogel was gently wiped by a paper towel, and the hydrogel was weighted again. This procedure was repeated until no further weight change was detected. Subsequently, the hydrogel was freeze-dried under vacuum and the dry gel weight

determined. The swelling ratio (SWR) of the hydrogel was calculated by the following equation.[17]

$$\text{Swelling ratio, SWR } \% = [(W_S - W_0)/W_0] \times 100$$

where W_S is the weight of the swollen hydrogel and W_0 as the weight of the dried hydrogel. The gel yield (%) was calculated using the equation.[18]

$$\text{Gel yield } \% = [W_0/W_{\text{solid content}}] \times 100$$

where W_0 is the dried gel weight and $W_{\text{solid content}}$ is the weight of prepolymer used in the hydrogel formation. The hydrogel swelling ratio based on mass (Q_m) was calculated by dividing the gel mass after swelling equilibrium by the dry gel mass. To obtain the value of the volumetric swelling ratio Q_v, the following equation was used:

$$Q_v = 1 + (\rho_p/\rho_s)(Q_m - 1)$$

Here, ρ_p is the density of the dry polymer and ρ_s is the density of the solvent (1 g/cm^3 for water). According to Flory-Rehner equation, the crosslink density can be described by the number average molecular weight between two adjacent crosslinks (M_c). M_c was calculated using a simplification of the Flory-Rehner equation:[19]

$$Q_v^{5/3} = (M_c v/V_1)(0.5 - \chi)$$

where v is the specific volume of dry polymer (0.62 cm^3 g^{-1} at 20°C for dextran), V_1 is the molar volume of water (18.062 cm^3 mol$^{-1)}$ and χ is the Flory-Huggins interaction parameter (0.473 for dextran). Using these values, the equation further simplified to:

$$M_c = (18/0.0162)Q_v^{5/3} \quad \text{g mol}^{-1}$$

The crosslink density (P_x) is determined by the following equation.[20]

$$P_x = (M_c v)^{-1} \quad \text{mol cm}^{-3}.$$

RESULTS AND DISCUSSION

Dex-HEMA was synthesized according to literature procedures as described in the materials and methods section.[6] The coupling between dextran and HEMA-CI has been proven by FTIR analysis of the freeze-dried product. It shows a band for a carbonate ester group at 1730–1740 cm^{-1}, which is not present in pure dextran. Further evidence for the successful introduction of the HEMA groups as side chain in dextran is given by ^{1}H-NMR spectra. (Fig. 2).

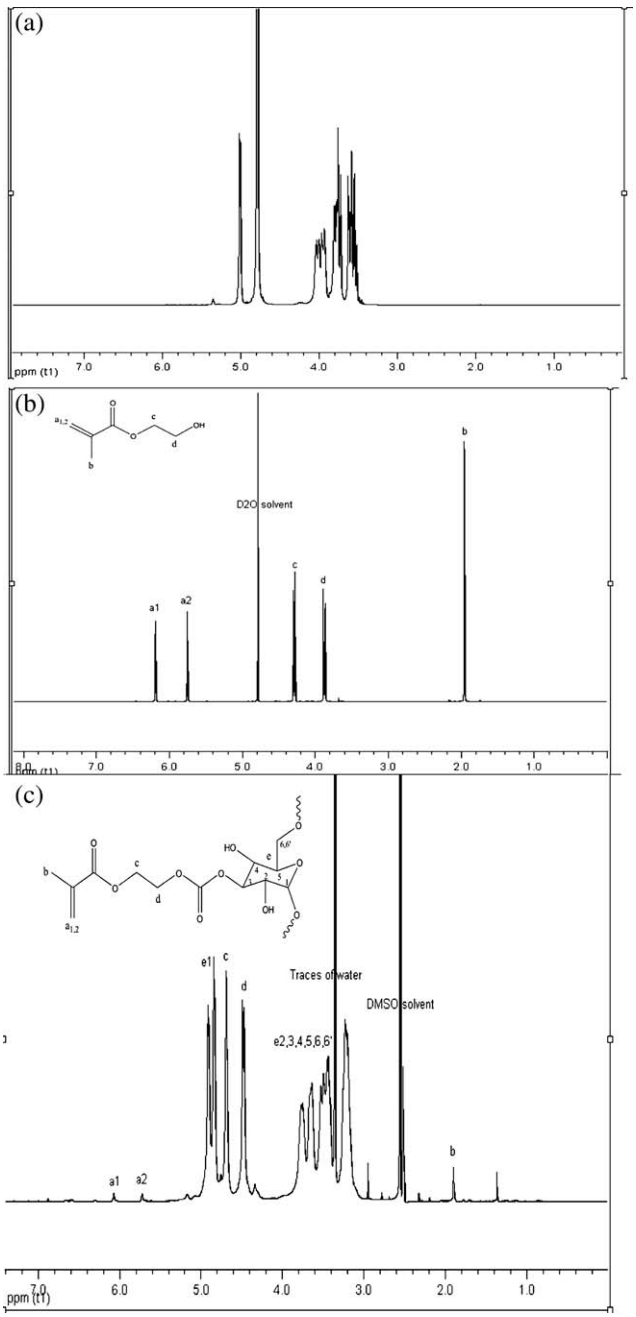

Figure 2 ^{1}H-NMR spectra of pure dextran (a), HEMA (b), and Dex-HEMA (c), in D_2O, D_2O, and DMSO-d_6 solvents, respectively.

From the ^{1}H-NMR spectra, the degree of substitution (DS, average number of methacrylate groups per dextran glucopyranose residue, $0 < DS < 3$) can be calculated. Figure 2 shows ^{1}H-NMR spectra of dextran (a), HEMA (b), and Dex-HEMA (c) after coupling, respectively. The three protons of the methyl group of methyacrylate group are detected at 1.97 ppm (s, 3H, H_b) in Figure 2(b,c), whereas two protons of methacrylate group were found at 6.11 ppm and 5.58 ppm (s, 2H, $H_{a1,a2}$) [Fig. 2(b,c)]. The ethyl group of pure HEMA appeared at 3.9 ppm

TABLE I
Effect of Dex-HEMA Concentration on Gel Yield %, Average Molecular Weight Between Two Adjacent Crosslinks (M_c) and Crosslinking Density (P_x) for Different Three Coinitiators Used

Photoinitiator system	Dex-HEMA (wt %)	Yield %	M_c (10^3 g/mol)	P_x (10^{-6} mol/cm^3)
CQ-DMAEMA-DPIC	10	–	–	–
	15	–	–	–
	20	22	3929	0.424
	30	63	296	5.61
CQ-NPG-DPIC	10	24	868	1.92
	15	56	152	10.94
	20	63	89	18.72
	30	65	41	40.27
CQ-BDO-DPIC	10	20	1155	1.44
	15	53	453	3.68
	20	60	215	7.74
	30	61	99	16.81

–, no hydrogel obtained.

and 4.3 ppm of (m, 4H, $H_{d,c}$) [Fig. 2(b)], but signals from this group shifted after coupling with dextran to 4.44 and 4.71 ppm of (m, 4H, $H_{d,c}$) [Fig. 2(c)]. The signals from the dextran glucopyranose unit appear at 3.28–3.85 ppm (m, 6H, $e_{2,3,4,5,6,6'}$) [Fig. 2(c)], at 4.94 ppm (broad, 1H, e_1), and at 5.13 ppm (broad, e_1 of α-1,3 branch) [Fig. 2(c)]. The degree of substitution (DS) was calculated by integration of the corresponding signals[6] according to:

$$DS = \left[\left(\frac{\text{Area}\,(\delta = 6.0\,\text{to}\,4.95) + \text{Area}\,(\delta = 4.95\,\text{to}\,2.15)}{\text{Area}\,(\delta = 5.1\,\text{to}\,4.95) \times 1.04} - 5\right) \Big/ 7\right]^{-1}$$

The correction factor (1.04) is necessary to take into account the 4% α-1,3-linkages in dextran.[6] The peaks for the solvents (DMSO-d_6 at 2.5 ppm, D_2O at 4.8 ppm and traces of water at 3.33 ppm in case DMSO-d_6 was used) were omitted in the corresponding integrations.

It was found that there are some important factors affect the DS values, e.g., the ratio between HEMA-CI and dextran in the coupling step, the coupling reaction temperature/time and DMAP concentration. Batches of Dex-HEMA having degrees of substitution of 0.033, 0.056, 0.15, 0.25, 1.1, 1.5, and 2.6 were prepared. The Dex-HEMA batches with a DS > 0.15 are not completely soluble in water. Therefore, Dex-HEMA with a DS = 0.056 was used in this study.

Effect of Dex-HEMA concentration and type of coinitiator on the crosslinking

The concentration of Dex-HEMA is considered one of the most important factors affecting the crosslink density. Therefore, experiments with different concentrations of Dex-HEMA were carried out and the crosslink density was determined by swelling measurements (Fig. 4 and Table I).

The most commonly used photoinitiators for crosslinking and curing with visible light are those in which radicals are formed in a bimolecular process comprising an excited state of a dye, such as CQ, and coinitiators that act as an electron donor.[13] This is because CQ can initiate the methacrylate monomer only at low rate, and the electron donating (reducing) amines are used as the photo-accelerator to expedite the photopolymerization. Here three different coinitiators were used.

DMAEMA (Fig. 3) is a tertiary aliphatic amine and used as hydrophilic coinitiator in photocrosslinking with visible light already for many years. According to Cook, the conversion of the exciplex state obtained after electron transfer into free radicals depends on the amine structure/nature and concentration.[10] Thus *N*-phenyl glycine as another tertiary amine was tested. Although CQ/DMAEMA is regarded as the most compatible coinitiator for HEMA with/without water present in the polymerization system, Wang reported that the principle advantage of the CQ/NPG system is that it should

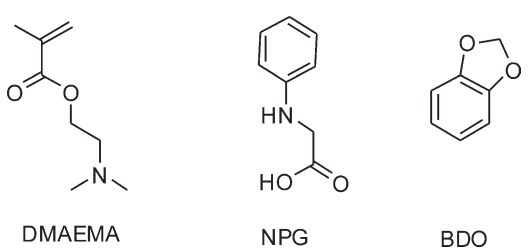

Figure 3 Chemical structures of the different coinitiators used.

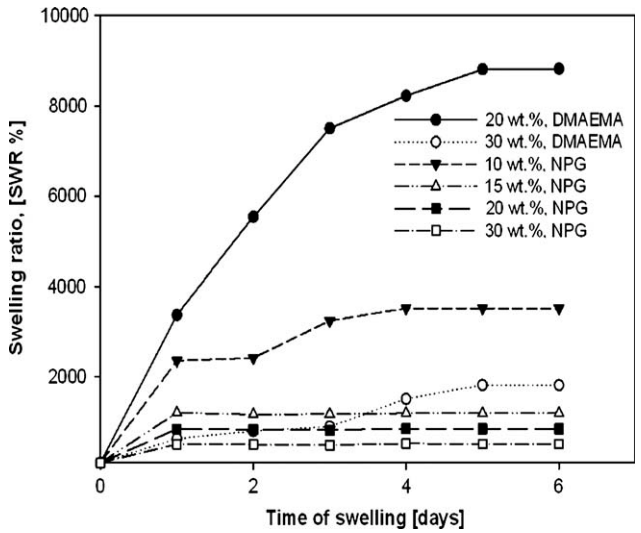

Figure 4 Effect of Dex-HEMA concentration (wt %) on swelling ratio (SWR %) in presence of two different amine coinitiators.

be biologically less toxic than other amine coinitiators.[13] Furthermore, a higher photoreactivity was reported for NPG compared with DMAEMA.[13] On the other hand, unlike the amines, BDO, is a new kind of effective synergist for CQ in photopolymerization process.[11] There are several natural benzodioxole derivatives, such as safrole, isosafrole, and myristicin found in a wide variety of human food, essential oils, and flavors. They are extracted from plants such as sassafras, nutmeg, parsnips, carrots, parsley, pepper, and sesame seeds. Although some of these natural products show toxic or even carcenogenic effects, BDO itself are regarded as safe.[11] Because CQ has very limited water solubility, DMSO was used as a solvent with varying amounts of water added.

Figure 4 shows the swelling degree as a function of the swelling time for the different Dex-HEMA concentrations with two different coinitiators (DMAEMA and NPG). It is noteworthy that the equilibrium swelling degree is reached after 5 days in case CQ/DMAEMA, whereas it is reached after 1 day only with NPG coinitiator initiation system. From the equilibrium swelling ratio the crosslinking density (P_x) and the average number molecular weight between two adjacent crosslinks (M_c) was calculated. The results (Table I) clearly indicate that the swelling degree decreases with increasing of Dex-HEMA concentration, thus more crosslinks are formed and a tighter network structure results. Furthermore, it was noted that no crosslinking takes place with low Dex-HEMA concentrations of 10 and 15 wt % for the CQ/DMAEMA initiating system, while crosslinking was achieved in case of CQ/NPG and CQ/DBO even with low Dex-HEMA concentrations. That is, the reactivity of initiating system containing NPG or BDO as coinitiator is higher than that of DMAEMA. This is in accordance with the results reported by Wang et al.[13]

Besides the influence of the concentration, also an influence of the type of coinitiator can be observed from the data presented in Table I. The highest crosslink densities (P_x) are obtained for hydrogels, which were initiated by CQ/NPG. BDO a new nonamine coinitiator is less effective than NPG but better than the CQ/DMAEMA system.

Although hydrogels have been developed and studied for many years, morphologic observations of hydrogels by SEM, particularly their interior structure in dried or swollen states, are rare.[7,21] The investigation of the structure requires a cryofixation of the hydrogel. Here techniques described by Kim and Chu,[7,21] which allow the observation of the surface and interior structures (see Fig. 5), have been used.

The surface morphology of freeze-dried hydrogels prepared from solutions with 20 and 30 wt % of Dex-HEMA using CQ with DMAEMA, NPG, and BDO as coinitiators, respectively, was investigated by SEM (Fig. 6). There are some clear differences between the gels prepared with the different coinitiators. In case of DMAEMA as coinitiator for both Dex-HEMA concentrations, the hydrogels were fragile structures when compared with hydrogels, which were initiated using NPG or BDO as coinitiators. In

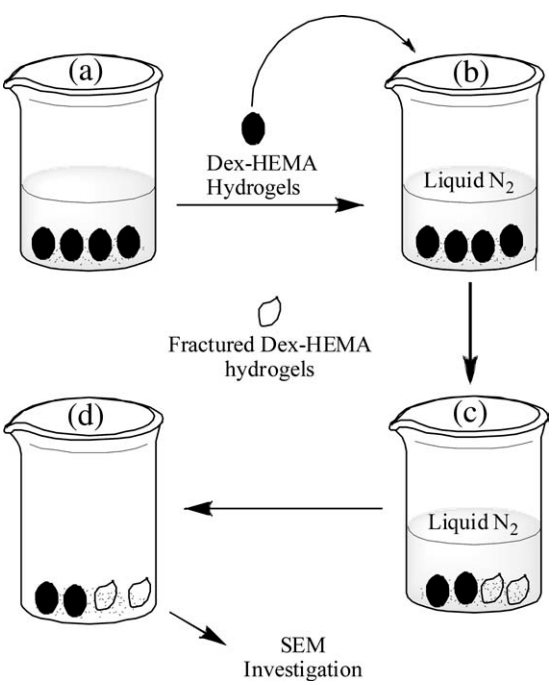

Figure 5 Cryofixation and cryofracturing technique for Dex-HEMA hydrogels, (a) Dex-HEMA hydrogel equilibrated in distilled water, (b) Dex-HEMA frozen in liquid N_2, (c) fracture of some parts to observe the interior, and (d) freeze-drying at 0.5 mbar and −90°C.

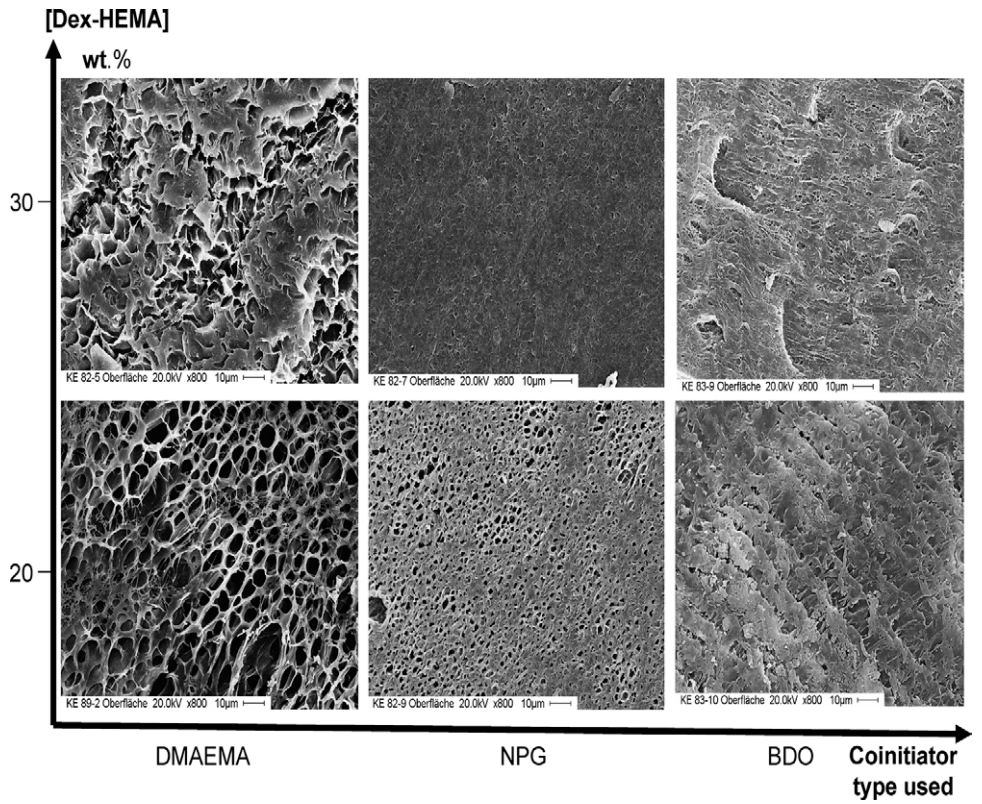

Figure 6 SEM images photographs of hydrogel surfaces with 20 and 30 wt % of Dex-HEMA concentration, initiated with CQ/DMAEMA, CQ/NPG, and CQ/BDO systems (the original magnification was ×800).

two latter cases, the surface structures are also more uniform. The hydrogel surfaces of CQ/DMAEMA crosslinked hydrogels exhibit a highly porous honeycomb-like structure with presence of some of random cracks, holes, and deep caves especially in case of 20 wt % of Dex-HEMA. The pore size distribution was broader than for hydrogels, which were initiated by the CQ/NPG or CQ/BDO systems.

It was observed that the surfaces of hydrogels prepared with CQ/NPG are a relatively smooth, and that there are no more pores or very tiny pores only when the Dex-HEMA concentration is increased. Kim and Chu found that the unswollen dextran-methacrylate hydrogel showed a relatively smooth surface with very tiny pores or without any pores.[7] These results are comparable with the results obtained here for swollen hydrogels, when CQ/NPG and CQ/BDO are used for the crosslinking. These coinitiators give hydrogels with small swelling ratios especially for high Dex-HEMA concentrations. SEM results for CQ/NPG and CQ/BDO exhibit less pores and a denser structure without any random cracks as they appeared at the surface of hydrogels prepared with CQ/DMAEMA. On the other hand, the results obtained with the much stronger swollen gels prepared with the CQ/DMAEMA system are similiar to the rugged and broad porous structure, found by Kim and Chu[7] for highly swollen hydrogels (Figs. 4 and 6). Thus, we can conclude that a higher swelling ratio correlates with a more structured surface. Gels which do not swell as much, because of a higher crosslink density, show a smoother surface.

The difference in efficiency of the crosslinking for the different concentrations and different coinitiators results also in differences of the glass transition temperatures (T_g) of the dried gels as determined by DSC (Table II). To show that the efficiency of the initiating system has an impact on the T_g, crosslinked material prepared with the most effective photoinitiator system CQ/NPG and the least effective system CQ/DMAEMA were investigated. The T_g is higher for the CQ/NPG system. Additionally, T_g values in the CQ/NPG cured gels increase dramatically with

TABLE II
T_g Values of Different Dex-HEMA Concentrations with DMAEMA and NPG Coinitiators

	T_g (°C)	
Dex-HEMA (wt %)	CQ-DMAEMA-DPIC	CQ-NPG-DPIC
10	–	96
15	–	104
20	97	114
30	106	144

–, no hydrogel obtained.

TABLE III
Effect of Coinitiator Concentration for DMAEMA, NPG, and BDO (0.25–3.0 mol %) at Constant CQ (0.25 mol %) and Dex-HEMA Concentration (20 wt %) on Gel Yield, Average Molecular Weight Between Two Adjacent Crosslinks (M_c) and Crosslinking Density (P_x)

Photoinitiator system	Coinitiator (mol %)	Yield %	M_c (10^3 g/mol)	P_x (10^{-6} mol/cm^3)
CQ-DMAEMA-DPIC	0.25	77	880	1.89
	0.5	77	1161	1.44
	1.0	76	3067	0.544
	2.0	78	2375	0.702
	3.0	81	928	1.8
CQ-NPG-DPIC	0.25	64	63	26.3
	0.5	67	81	20.5
	1.0	64	106	15.6
	2.0	62	134	12.4
CQ-BDO-DPIC	0.25	72	66	25.0
	0.5	70	52	31.7
	1.0	73	53	31.4
	2.0	77	48	34.1

an increase of Dex-HEMA concentration due to formation of more crosslinking points and a tighter network structure.

Effect of coinitiator concentration

It has already been mentioned that the DMAEMA, BDO, and NPG have different efficiencies as coinitiators in the photocrosslinking of Dex-HEMA with CQ, and it was noticed that in the absence of coinitiators, no crosslinking took place. This result refers to the inability of CQ itself to initiate the system without coinitiator. In a further set of experiments, the concentration of the coinitiators was varied from 0.25 to 3.0 mol % at constant CQ concentration (0.25 mol %). The gel yield, M_c, and P_x were determined as function of the concentration of coinitiator. The results shown in Table III indicate that there is no significant influence of the coinitiator concentration on the gel yield.

On the other hand, Table III illustrates that at low DMAEMA concentration; the M_c values grow toward a maximum at 1.0 mol % DMAEMA concentration and then slightly decrease. Accordingly, the crosslink density P_x significantly decreases to a minimum and then slightly increases again. That is, the most effective crosslinking is observed for the lowest concentration of coinitiator (0.25 mol %). At higher concentrations of the coinitiator, the crosslinking is less effective resulting in a lower crosslinking density and longer chains between the crosslinks. This result was explained according to Cook[10] by the fact that an excess of amine coinitiator acts as retardant in the crosslinking reaction. This result was confirmed also by Sastre and coworkers.[22] A similar observation can be made in case of NPG as coinitiator. The P_x values decrease with increasing NPG concentration. Thus, also for this coinitiator increasing the concentration makes the photocrosslinking less effective. On the other hand, in the case of BDO, the M_c values monotonically decrease and the crosslinking densities (P_x) increase with increasing BDO concentration. Thus, the non-amine coinitiator BDO does not show any retarding effect on the phtocrosslinking. We can conclude from the presented results that both amine coinitiators (DMAEMA and NPG) have almost the same behavior regarding the crosslinking efficiency, whereas the nonamine coinitiator (BDO) shows a different behavior. The exact reaction mechanism for the CQ/BDO system is still unknown. It can be speculated that it is similar in transferring a hydrogen from the activated α C—H, however, it seems as if neither the BDO nor its reaction products act as retarder as it is the case for the amine coinitiators. Further experiments will be necessary to elucidate this effect in detail. The results which have been presented in this study suggested that BDO is a very effective alternative to conventional amine coinitiators used in the dental resin formulations.

Effect of water content in the photocrosslinking mixture solution

For dental adhesives, on the basis of HEMA/BisGMA, a distinct influence of water on the photoreaction was found.[13] For dental resins and CQ/DMAEMA as an initiation system, Wang et al.[13] and Paul et al.[23] reported that a water content of more than 5% inhibits the photopolymerization of HEMA, even when the concentration of photoinitiator was increased. On the other hand, it was reported that the addition of water promoted the polymerization of HEMA in the case of NPG as coinitiator.[24] This might have to do with the hydrophilicity of the

TABLE IV
Effect of Water Content on the Photopolymerization as Measured by Gel Yield, Average Molecular Weight Between Two Adjacent Crosslinks (M_c) and Crosslinking Denisty (P_x) for Three Different Coinitiators

Photoinitiator system	Water content (wt %)	Yield %	M_c (10^3 g/mol)	P_x (10^{-6} mol/cm^3)
CQ-DMAEMA-DPIC	0	–	–	–
	10	–	–	–
	20	59	3464	0.481
	30	77	855	1.95
CQ-NPG-DPIC	0	56	138	12.0
	10	61	88	18.9
	20	70	66	25.1
	30	79	67	25.3
CQ-BDO-DPIC	0	–	–	–
	10	25	237	7.01
	20	65	60	27.6
	30	75	48	34.4

–, no hydrogel obtained.

components in the dental resins and their compatibility with each other and with water. Wang et al. proved that hydrophilic coinitiators (DMAEMA and NPG) outperformed the hydrophobic coinitiator dihydroxyethyl-*p*-toluoidine (DHEPT). CQ photoinitiator system containing only the hydrophobic coinitiator did not initiate the polymerization of HEMA.[13]

Wang found that the addition of diphenyliodonium hexaflorophosphate as a third initiator component in BisGMA/HEMA as a model of dental resin instead of DPIC increased the efficacy of the photopolymerization. In systems with different water content, the polymerization rate decreased with the increase of water content.[25] This does not necessarily mean that the degree of conversion is also decreased. Furthermore, Wang and coworkers suggested that there might be an increase in the degree of conversion in the presence of water in these resins, due to the lower viscosity of the monomer mixture.[25]

We have investigated the influence of the solvent for the gel formation by increasing the amount of water in the DMSO based solution from 0 to 30 wt %. The gel yield, M_c, as well as the crosslink density were determined for the different solvents and the different coinitiators. As can be seen from the results

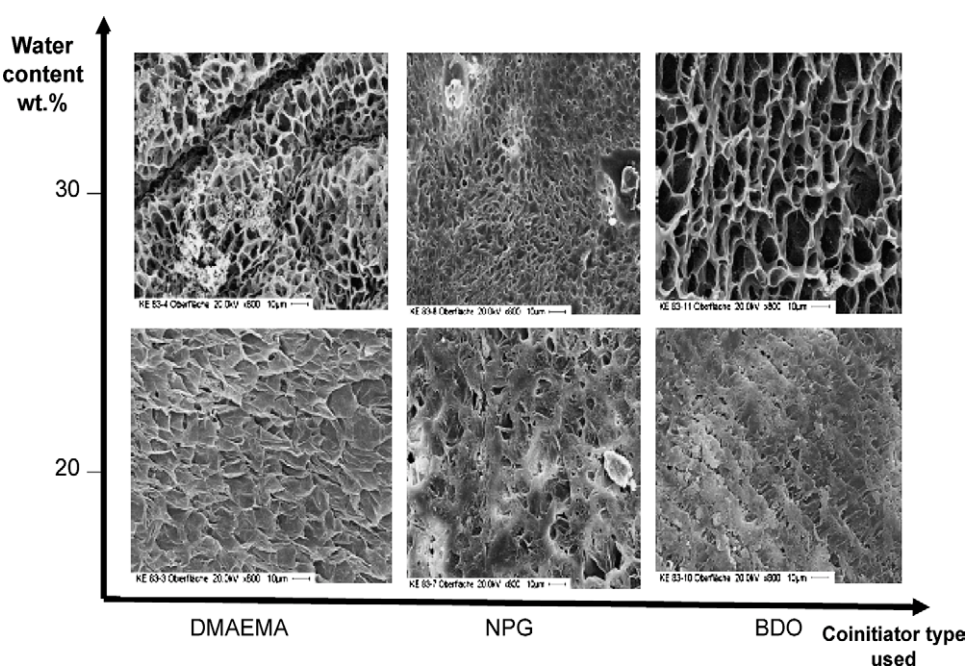

Figure 7 SEM photographs of swollen Dex-HEMA hydrogel surfaces using different coinitiators (original magnification ×800).

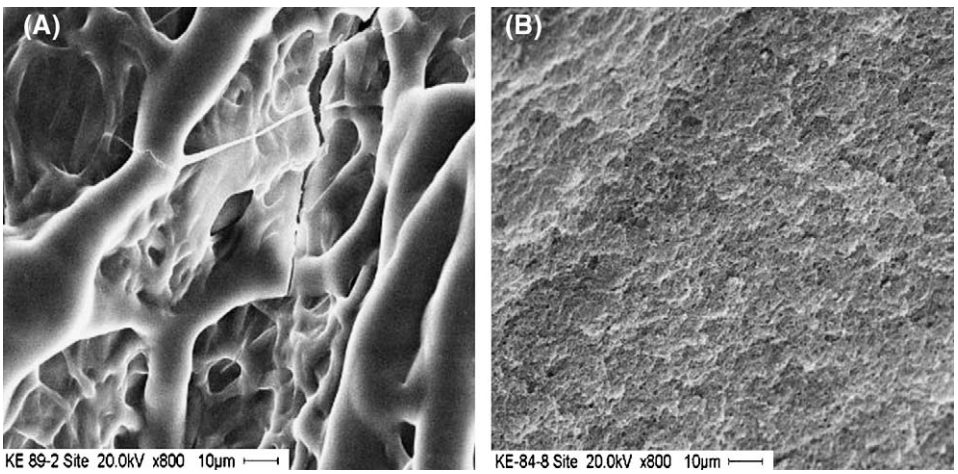

Figure 8 SEM photographs of cross sectional interior of swollen Dex-HEMA hydrogels with coinitiators, DMAEMA (A) and NPG (B), 20 wt % water content in both samples (original magnification ×800).

shown in Table IV, there is a distinct influence of water content on the gel yield. The yield increases with water content. Furthermore, for all coinitiators an increase in crosslinking density with higher amounts of water in the solvent can be observed. Thus, efficiency of the photocrosslinking increases with increasing water content. When comparing the different coinitiators, BDO is the most effective under these conditions.

Figure 7 shows SEM images of the surface structure of freeze-dried Dex-HEMA hydrogels. The images show a relatively smooth surface with some tiny and uniform porous in case NPG coinitiator, whereas in case of DMAEMA as coinitiator the hydrogels exhibit a rugged and highly porous honeycomb-like structure. The width of the pores decreased with water content increased (Fig. 7).

In the contrary, in case of the CQ/BDO initiation system, the porosity in terms of density and width increased with an increase of water content (Fig. 7). This might be caused by the more hydrophobic coinitiator. In fact, BDO is much less soluble in water than the amines (BDO solubility in water: 0.25% at 25°C, DMAEMA and NPG are completely miscible with water).

In Figure 8 the interior structure of the cryofractured hydrogels is depicted. It is evident that different sizes of pores can be observed at the surface and within the same hydrogel by comparing Figure 8(A,B), respectively, with the corresponding surface image of the same hydrogel in Figure 7. We found a fibrillar structure in case of the CQ/DMAEMA systems [Fig. 8(A)], whereas the surface seems to be smoother. The inner structure of the gel which was initiated by the CQ/NPG system [Fig. 8(B)] is denser, whereas the surface exhibits some pores.

Results regarding the influence of the water content on the photocrosslinking and gel formation can be attributed to the compatibility and homogeneity of the different components with water and with each other and are generally in line with the previous studies; although here hydrophilic materials were investigated in solution, whereas previously mostly more hydrophobic materials were investigated in bulk.

CONCLUSIONS

Dex-HEMA was synthesized and photocrosslinked in DMSO by visible light using photoinitiator systems used so far only in dental restoratives materials. The photoinitiation system based on camphorquinone combined with different coinitiators, namely, DMAEMA, NPG or BDO. It was found that the swelling behavior and the crosslinking density of hydrogel networks dependent on the Dex-HEMA concentration, coinitiator type used, and water content.

The Dex-HEMA concentration has a profound impact on the crosslinking density and with that the swelling behavior as well as glass transition temperature of the dried sample. A higher concentration results in higher crosslink densities. In addition, the surface becomes more smooth with increasing concentration. Furthermore, a prominent effect of coinitiator type and concentration on the crosslinking density and morphology of the surface was found. BDO is more effective than the amine coinitiators (DMAEMA and NPG) and shows increasing efficiency with increasing concentration. On the other hand, higher concentrations of amine result a decrease of crosslink density, which might be attributed to a kind of retarding effect.

The water content in the polymer solution has an effect on the crosslinking efficiency, crosslinking density, and morphology. The crosslinking density

improved with an increase of water content, particularly with hydrogels initiated by CQ/NPG and CQ/BDO.

SEM data showed clear differences in morphology of the surface of freeze-dried hydrogels prepared with the different coinitiators. Dex-HEMA hydrogels initiated by CQ/DMAEMA system displayed rugged surfaces with irregular wide pores, some random cracks, and an irregular pore size distribution. On the contrary, hydrogels which were initiated by CQ/NPG or CQ/BDO have much smoother and less porous surfaces.

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