New 2-Hydroxyethyl Methacrylate Resins with Good Swelling Characteristics

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ABSTRACT: 2-Hydroxyethyl methacrylate copolymers with styrene and series of the cross-linkers (divinylbenzene and mono-, di- and triethylene glycol dimethacrylates) with low cross-linking degree (2–5 mol %) were obtained by suspension polymerization. Loading capacity of the resins, their glass transition temperature, and swelling characteristics in 20 solvents were analyzed depending on monomers composition. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 101: 1487–1493, 2006

Key words: 2-hydroxyethyl methacrylate; suspension polymerization; swelling

INTRODUCTION

Polymers and copolymers of 2-hydroxyethyl methacrylate (HEMA) have many practical applications. The hydrophilic character of this monomer renders the obtained polymers to be able to absorb more water than they weigh. HEMA polymers in contrast to the monomer are nontoxic and they are characterized by a very good biocompatibility. Owing to these, they are used, for instance, as soft contact lenses,[1] implants,[2] and in controlled drug release.[3] HEMA copolymers can also be used as carriers for enzyme and protein immobilization,[4,5] as sorbents for chromatographic applications,[6] and in metal ion isolation from a solution.[7] Using HEMA copolymers in organic synthesis was also described.[8]

HEMA polymers are often obtained by bulk or solution-free radical polymerization. In the second case, water is mostly used as a solvent. Depending on water content, homogenous (transparent) or heterogeneous (nontransparent porous sponges) hydrogels can be produced.[9–13] Another useful technique of HEMA polymerization is suspension polymerization, which delivers products as spherical microparticles.[14–20] Terpolymers in this form are easy to manipulate. However, there are many problems with suitable stabilization of the monomers suspension in the water phase because of high HEMA solubility. Protection from agglomeration of monomer drops is particularly difficult when large particles have to be obtained.

Therefore, the water phase was often salted out with NaCl. Mg(OH)$_2$, which was produced in situ from MgCl$_2$ and NaOH, as a suspension stabilizer.

From the biomedical applications point of view, high hydrophilicity of HEMA polymers is particularly required. This feature limits the possibility of using such materials in catalytic and synthetic applications. This problem can be solved when a hydrophobic non-polar monomer is built into a polymer matrix, which provides good swelling characteristics of supports in many nonhydroxylic solvents. Synthesis and characteristics of such type of terpolymers are the aim of this work.

EXPERIMENTAL

Materials

2-Hydroxyethyl methacrylate (HEMA) was distilled under reduced pressure before use. Styrene (S), ethylene glycol dimethacrylate (EGDMA), diethylene glycol dimethacrylate (DEGDMA), triethylene glycol dimethacrylate (TEGDMA), and divinylbenzene (DVB, mixture of isomers) were purified by extraction with 5 wt % NaOH in 20 wt % NaCl solution. Other reagents and solvents (diluents) obtained commercially were used as received.

Resins synthesis

Suspension copolymerization of HEMA with styrene and series of cross-linkers (DVB, EGDMA, DEGDMA, and TEGDMA) were carried out under nitrogen atmosphere in 800 mL cylindrical reactor equipped with a heating coat, mechanical stirrer, reflux condenser, and addition funnel. The dispersion medium was pre-
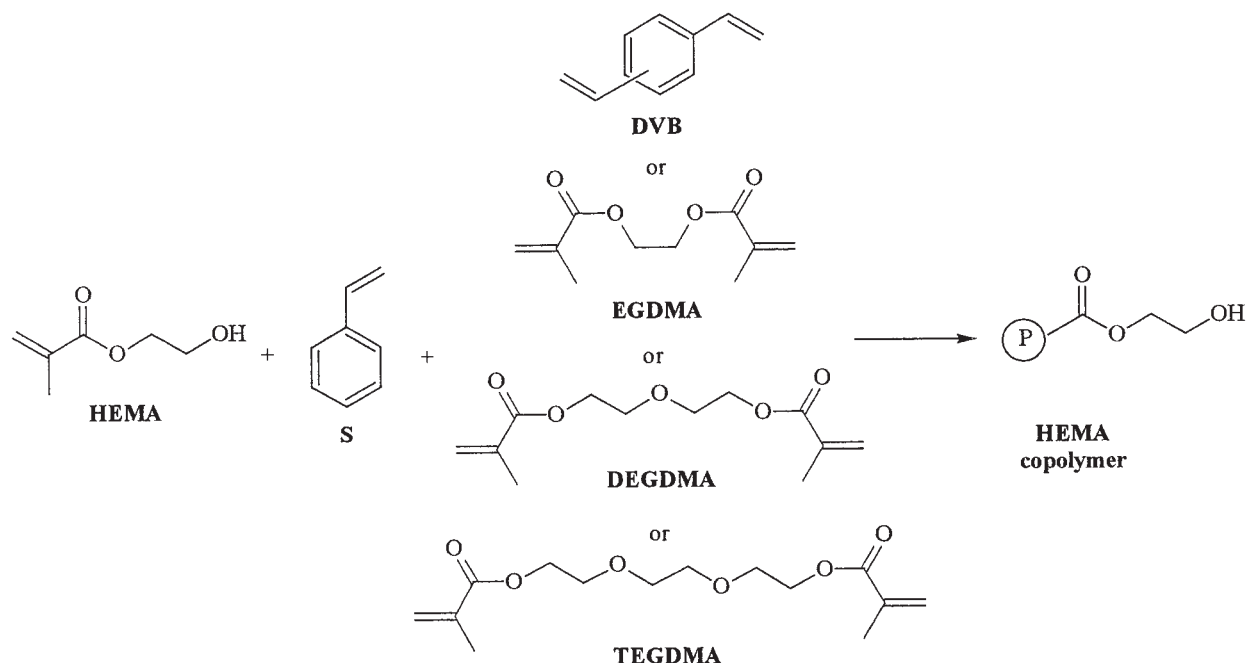
Scheme 1 Preparation of HEMA resins.

pared by dissolving 1 wt % polyvinylpyrrolidone K90 (PVP) in deionized water.

Benzoyl peroxide (BPO) (1 wt %) was dissolved in monomers and then the mixture was diluted with mixed solvent (cyclohexanol/n-octanol, 4/1 w/w) taken in 1/1 w/w proportion. Afterwards, this solution was added dropwise into the dispersion medium for about 30 min. The copolymerization was carried out for 2 h at 70°C and then for 6 h at 80°C. The mechanical stirrer rate was adjusted to 350 rpm. After cooling, a washing procedure was applied to remove the diluents and any unreacted monomers from the products. The spherical beads formed were decanted and washed many times with excess water and then they were transferred to a Soxhlet apparatus where the extraction with acetone for 6 h was

carried out. After that, the microbeads were resuspended in methanol. This procedure protects beads from agglomeration during drying. Copolymers were dried at 40°C under reduced pressure and then they were fractioned using sieves.

Resin characteristics

Resin morphology was estimated using JEOL JSM-5500LV scanning electron microscope and Motic SMZ-143 stereoscope microscope with digital camera.

The hydroxyl group content in beads was determined by analyses of nitrogen content in previously modified copolymers. Modification of HEMA copolymers was carried out in the following way: 0.25 g of an

TABLE I
Characteristics of HEMA Resins

	Terpolymer	Yield (%)	Fraction 75–250 μm (%)	Loading capacity of resin (mmol/g) Calculated	Loading capacity of resin (mmol/g) Determined[a]	T_g (°C)
1	10%HEMA–3%DEGDMA–87%S	69	67	0.9	0.83	106
2	15%HEMA–3%DEGDMA–82%S	75	82	1.34	1.07	105
3	20%HEMA–3%DEGDMA–77%S	61	46	1.76	1.29	106
4	20%HEMA–2%DEGDMA–78%S	71	64	1.78	1.30	104
5	20%HEMA–5%DEGDMA–75%S	79	50	1.72	1.34	110
6	20%HEMA–3%EGDMA–77%S	80	83	1.78	1.23; (1.15)[b]	109
7	20%HEMA–3%TEGDMA–77%S	73	77	1.74	1.34	102
8	20%HEMA–3%DVB–77%S	83	67	1.82	1.27; (1.28)[b]	110
9	30%HEMA–3%DEGDMA–67%S	83	43	2.58	1.81	107

[a] Determined by Kjeldahl method.
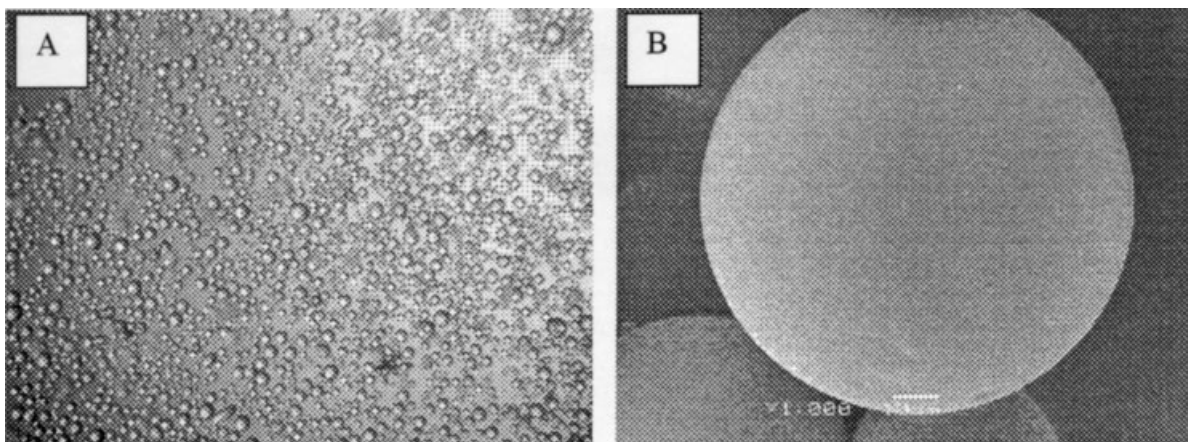[b] Determined by EA 1108 Carlo Erba Instrument.

Figure 1 Microphotographs of 20% HEMA–3% DVB–77% S terpolymer. (A) Stereoscope microscope and (B) scanning electron microscope.

appropriate dry resin was swelled in 5 mL of dichloromethane (DCM) and was allowed to react with 4-nitrophenyl chloroformate (10 equiv) in the presence of triethylamine (5 equiv). The mixture was shaken for 24 h at room temperature. After that, the copolymer was washed several times with DCM and methanol by turns and then was dried at 40°C under reduced pressure. Nitrogen content, which is equivalent to hydroxyl group content, was determined by the classic Kjeldahl method. Selected resins were additionally analyzed using EA 1108 Carlo Erba Instrument.

Glass transition temperature (T_g) measurements were performed with differential scanning calorimetry method by means of Toledo 822^e calorimeter with Star^e System software. The resins were heated from 30 to 300°C and then cooled to 30°C. This procedure was repeated. The rate of heating and cooling were adjusted to 10°C/min.

The volume of the resin after swelling was determined in the following way: 1 g of an appropriate dry resin was added to 10 mL graduated syringe that was equipped with a polypropylene filter. An appropriate solvent was added. After achieving swelling equilibrium (30–60 min), the excess solvent was removed by means of the plunger. The increase of the volume and the swelling ratio was calculated as $\Delta V = V_s - V_d$ and $S = V_s/V_d$, respectively, where V_d is the volume of dry resin and V_s is the volume of swelled resin.

RESULTS AND DISCUSSION

Copolymerization

Suspension polymerization was applied to prepare three-component terpolymers (TCT) of HEMA with styrene and series of cross-linkers (DVB, EGDMA, DEGDMA, and TEGDMA). Some data on the suspension copolymerization of HEMA are available.[14–20] Some organic suspension stabilizers such as 87 and 97% poly(vinyl alcohol) and PVP, solvents for monomers such as toluene, cyclohexanol, and mixtures of cyclohexanol with linear alcohols, and azobisisobutyronitrile and BPO as initiators were taken into considerations. Stereoscopic microscope with digital camera was used to make quality assessment of the products.

Tests have shown that using 1 wt % PVP in water, mixture of cyclohexanol and *n*-octanol (4/1 w/w
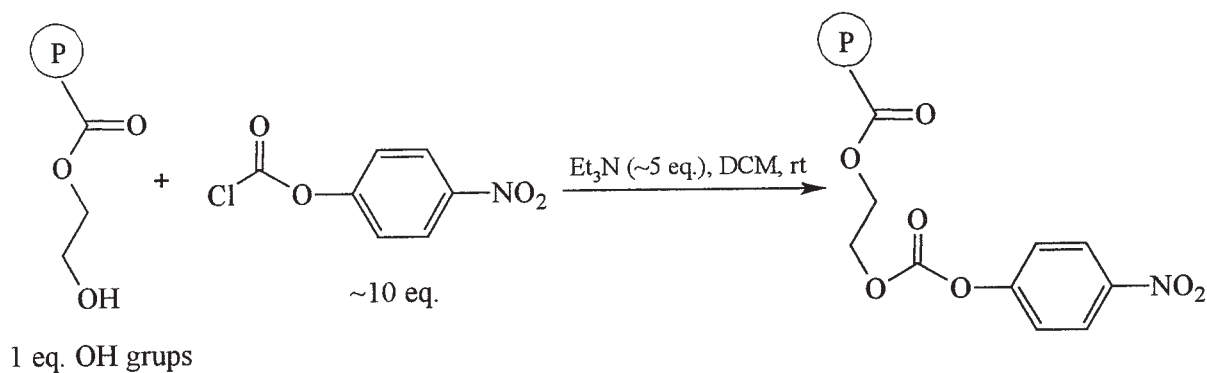
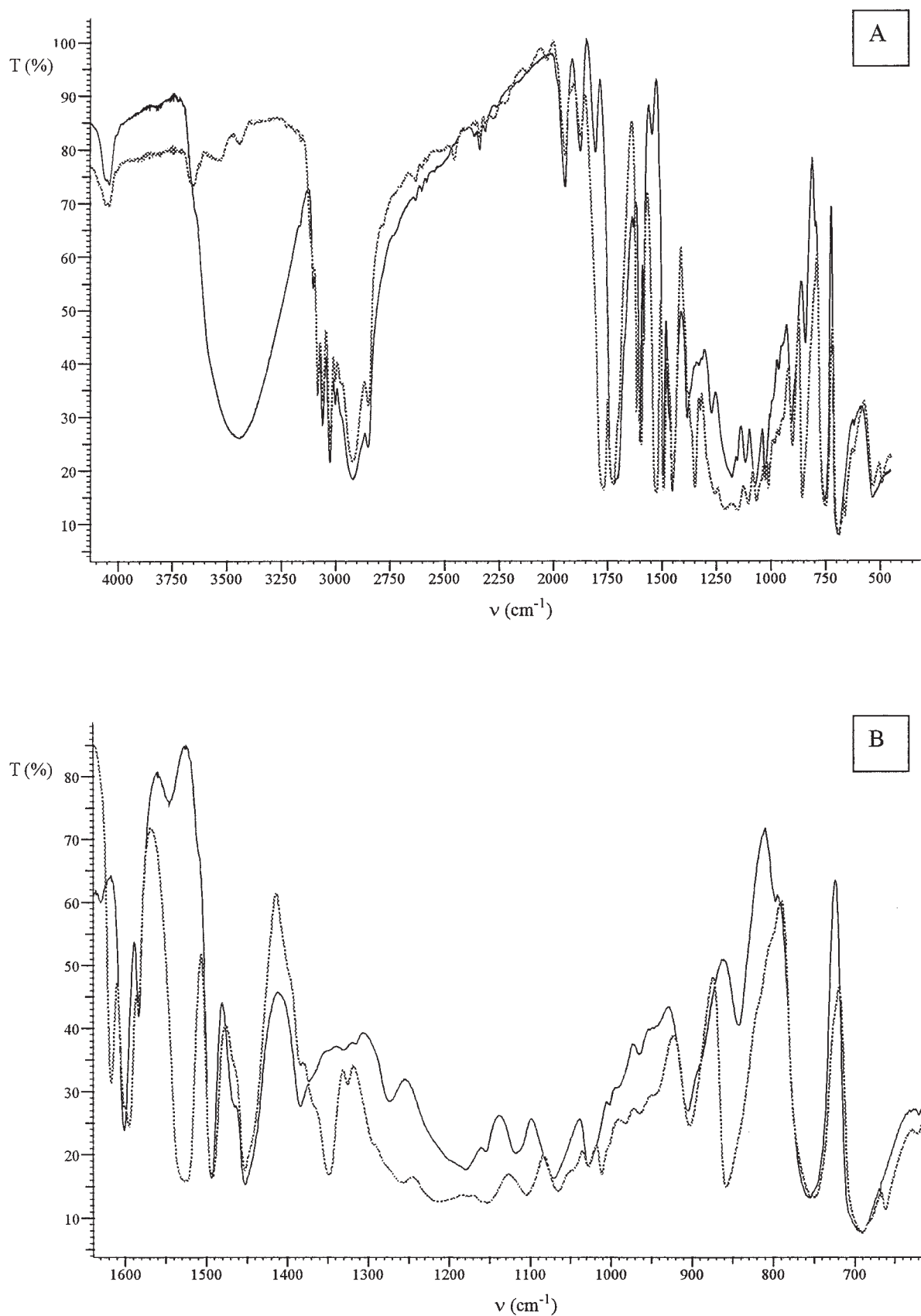**Scheme 2** Chemical modification of resins.

Figure 2   Comparison IR spectra of copolymer 20% HEMA–3% DVB–77% S before (——) modification with the modified one (_ _ _).

taken in 1/1 w/w proportion to monomers) and BPO (1 wt %) ensured the only minor agglomeration of particles. Series of HEMA TCT (Scheme 1), whose composition and selected properties are shown in Table I, were obtained in mentioned conditions. Figure 1 presents typical morphology of the resins.

The aim of our work was to obtain HEMA terpolymers that have good swelling characteristics in common organic solvents. Therefore, content of cross-linking agent in the monomer mixture was ranged from 2 to 5 mol %. HEMA contents were settled on 10, 15, 20, and 30 mol % level.

Loading capacity of the resins

Loading capacity of hydroxyl group resins is often determined by reacting the beads with an excess of reagents containing a chromophore. Cleavage of the chromophore after accurate washing away of physically absorbed parts makes indirect determination of OH groups content in polymer by UV–vis method easy. In this way, Fréchet et al. estimated the loading capacities of PEG resins using 4-nitrophenyl chloroformate as a chromophore.[8]

In our experiments, we have also used an excess of 4-nitrophenyl chloroformate (10 equiv) in the presence of triethylamine in DCM (swells strongly the resins) to modify chemically the HEMA terpolymers (Scheme 2). The modification was carried out for 24 h. Comparison IR spectra of a resin before modification to modified one showed practically quantitative conversion of OH groups (3450 cm^{-1}) [(Fig. 2(A)]. Strong bands from carbonate carbonyl (1769 cm^{-1}) and nitro groups appear simultaneously (1530, 1350, and 860 cm^{-1}) [Fig. 2(B)].

The experimentally determined loading capacity of the TCT resins ranged from 0.8 to 1.8 mmol/g. It was 69–92% of the value calculated from the monomers composition (Table I). The difference between calculated and determined hydroxyl groups content increased with increasing HEMA content in the feed
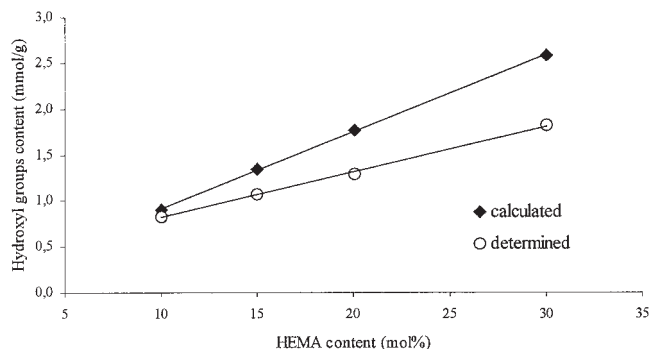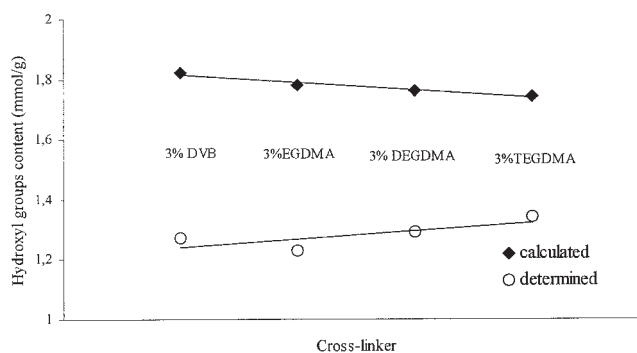

Figure 4 Hydroxyl groups content in 20% HEMA–3% cross-linker–77% S resins depending on the cross-linker nature.

(Fig. 3). It was an unexpected result because the reverse picture should be observed. Taking into consideration coefficients of reactivity of HEMA and S (dominating monomers in polymer matrix), 0.85 and 0.5 respectively, the loading capacity should enrich with increasing HEMA content. The difference between calculated and determined hydroxyl groups content also slightly increased toward decreasing distance between double-bonds in the cross-linking monomers (Fig. 4). It was presumably due to lower availability of internal hydroxyl groups for 4-nitrophenyl chloroformate during modification. The effect of cross-linking degree was not observed.

Glass temperature (T_g)

Glass temperature is one of the parameters that define properties of polymers. The mobility of polymer chains increase considerably above T_g and displacing of noncross-linking polymer chains can take place. For cross-linked polymers, moving of chains is limited by cross-linkers, which tide them together in three-dimensional network.

Glass temperature (T_g) of our HEMA TCT determined by DSC method is in the range 103–112°C (Table I), which is closer to T_g of polystyrene (100°C)[21] and then polyHEMA (55°C).[21] Typical DSC curve is presented in Figure 5.

Theoretically, glass temperature of copolymers should tend to increase with increasing degree of cross-linking and with decreasing distance between polymer chains, which is determined by a cross-linker. Our results correlate with theoretical considerations (Table I).

Swelling

Swelling is the main factor that decides on access to internal functional groups in gel-type polymers.[22] It allows molecules to penetrate and chemically explore all polymer network. Swelling characteristics are help-

Figure 3 Hydroxyl groups content versus HEMA content in HEMA–3% DEGDMA–S resins.
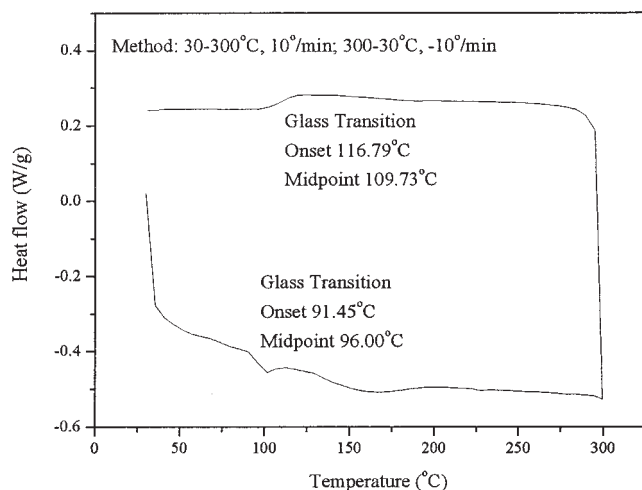
Figure 5 DSC curve of 20% HEMA–3% DVB–77% S terpolymer.

ful in the selection of a good solvent for a reaction on the polymer.

We have studied the swelling of our TCT in 20 common solvents. Measurements were carried out in syringes equipped with a filter that makes removing of excess solvent possible and thus they provide credible results. Griffith and coworkers[23] used the syringe method in study of swelling of some commercial resins in 39 solvents.

The results presented in Table II showed that growth of copolymer volume after swelling is not only a function of the solvent nature but also the composition of the copolymers play a role as well. Theoreti-

cally, essential factor for swelling of resins should be the affinity of polymer–solvent, which is defined by compatibility of Hildebrand's solubility parameters (δ).[21] Hildebrand's solubility parameter of polystyrene (styrene is the "main" monomer in our TCT) equals 17.9 [MPa$^{1/2}$].[21] Therefore, in the case of our polymers, we could expect the best swelling characteristics in the solvents with δ about 18 [MPa$^{1/2}$], if we assume that the minor monomers in TCT does not affect the solubility parameter considerably.

From the results (Table II), it follows that all solvents with δ close to 18 [MPa$^{1/2}$] can be numbered among "good" or "moderately good" solvents. However, DCM, 1,2-dichloroethane (EDC), and 1,4-dioxane are also "good" solvents, although their Hildebrand's solubility parameters are somewhat larger. Moreover, acetone that has δ closer to 18 [MPa$^{1/2}$] than 1,4-dioxane turned out to be "worse" solvents for our TCT. Furthermore, amide solvents, such as N,N-dimethylformamide (DMF) and N,N-dimethylacetamide (DMA), with δ substantially different from those mentioned, strongly swell our resins.

Depending on the swelling degree, the solvents can be divided into several groups. Chloroform turned out to be the best solvent. DMA, 1,4-dioxane, DCM, THF, DMF, EDC, diethylene glycol dimethyl ether (diglyme), and benzene belong to the second group. They also strongly swelled the resins. In toluene, ethyl acetate, isobutyl methyl ketone, and acetone, the copolymers swelled clearly less. Hexane, acetonitrile, acetic acid, and alcohols turned out to be "bad" solvents for the resins.

TABLE II
Swelling Characteristics of HEMA Resins

Solvent	δ (MPa$^{1/2}$)	Terpolymer ΔV^a (S)							
		1	2	3	4	5	6	7	8
Hexane	14.9	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
iso-butyl methyl ketone	17.2	2.5 (2.7)	2.5 (2.7)	2.5 (2.7)	3.5 (3.3)	1.5 (2.0)	1.5 (2.0)	1.5 (2.0)	1.5 (2.0)
Toluene	18.2	5.0 (4.3)	4.0 (3.7)	2.5 (2.7)	4.5 (4.0)	2.0 (2.3)	2.0 (2.3)	1.5 (2.0)	1.5 (2.0)
Ethyl acetate	18.6	3.0 (3.0)	2.5 (2.7)	2.5 (2.7)	3.5 (3.3)	1.5 (2.0)	1.5 (2.0)	2.0 (2.3)	1.5 (2.0)
THF	18.6	6.5 (5.3)	5.5 (4.7)	5.0 (4.3)	7.5 (6.0)	3.0 (3.0)	3.5 (3.3)	3.5 (3.3)	2.5 (2.7)
Benzene	18.8	6.0 (5.0)	4.0 (3.7)	4.0 (3.7)	6.5 (5.3)	2.0 (2.3)	2.5 (2.7)	2.0 (2.3)	2.0 (2.3)
Chloroform	19.0	8.5 (6.7)	6.5 (5.3)	7.0 (5.7)	9.5 (7.3)	2.0 (2.3)	2.0 (2.3)	2.5 (2.7)	3.0 (3.0)
DCM	19.8	6.5 (5.3)	5.0 (4.3)	5.0 (4.3)	8.0 (6.3)	3.0 (3.0)	3.5 (3.3)	3.5 (3.3)	3.0 (3.0)
1,2-Dichloroethane	20.1	6.0 (5.0)	4.5 (4.0)	4.5 (4.0)	7.0 (5.7)	3.0 (3.0)	3.0 (3.0)	3.0 (3.0)	2.5 (2.7)
Acetone	20.3	1.5 (2.0)	1.5 (2.0)	2.0 (2.3)	2.5 (2.7)	1.5 (2.0)	1.5 (2.0)	1.5 (2.0)	1.5 (2.0)
1,4-Dioxane	20.5	7.0 (5.7)	5.5 (4.7)	5.5 (4.7)	9.0 (7.0)	3.0 (3.0)	3.5 (3.3)	3.0 (3.0)	2.5 (2.7)
Acetic acid	20.7	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
DMA	22.1	6.0 (5.0)	5.5 (4.7)	6.5 (5.3)	8.0 (6.3)	3.5 (3.3)	3.5 (3.3)	3.5 (3.3)	2.5 (2.7)
n-Butanol	23.3	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
2-Propanol	23.5	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
Acetonitrile	24.3	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
DMF	24.8	5.5 (4.7)	4.5 (4.0)	5.5 (4.7)	7.5 (6.0)	3.0 (3.0)	4.0 (3.7)	3.5 (3.3)	2.5 (2.7)
Methanol	29.7	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
Ethylene glycol	29.9	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)	0.5 (1.3)
Diglyme	—	5.5 (4.7)	5.0 (4.3)	5.0 (4.3)	6.5 (5.3)	3.0 (3.0)	3.0 (3.0)	3.0 (3.0)	2.5 (2.7)

^{a} Per 1 g of the resin.

Figure 6 Swelling characteristics of 20% HEMA–DEGD-MA–S resins in series of the solvents.
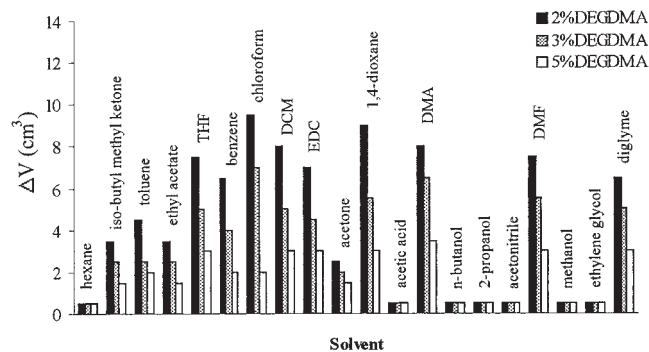

Figure 8 Swelling characteristics of HEMA–3% DEG-DMA–S resins in series of the solvents.

According to expectations, swelling ability decreased with cross-linking of the resins (Fig. 6).

Theoretically, ability to swell should rise with increasing the distance between polymer chains, which is determined by a cross-linker (i.e., from DVB to TEGDMA). Our results generally correlate in this way in the following order DVB < EGDMA < DEGDMA. However, the polymer with the longest cross-linker (TEGDMA) swells less than the one with DEGDMA (Fig. 7).

Increase of HEMA content in polymer matrix practically does not affect its swelling characteristics. It is shown in the Figure 8.

CONCLUSIONS

Suspension polymerization of HEMA with styrene and such vinyl monomers as DVB and mono-, di-, and triethylene glycol dimethacrylates in the presence of the mixture of cyclohexanol/n-octanol (4/1 w/w) as a solvent for monomers, BPO as a initiator, and 1 wt % solution of PVP in water as dispersion medium delivers well swellable and easily modifiable resins with hydroxyl group.

The loading capacity of the resin can be easily determined by the reaction of OH groups with 4-nitrophenyl chloroformate with consequent analysis of nitrogen.
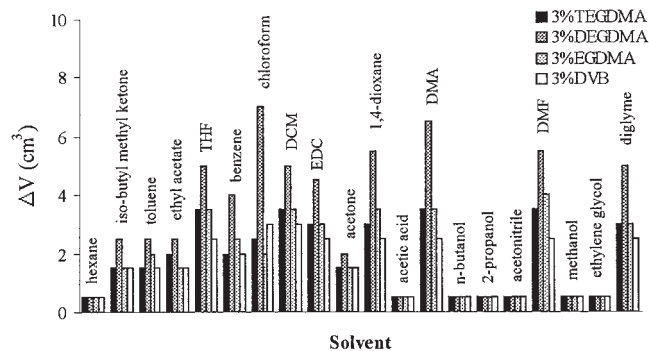
The correlations between the nature of cross-linkers as well as their content in the monomer mixture and T_g of the resins have been observed.

The swelling ability of the HEMA resins can be changed with the nature and quality of cross-linkers. HEMA TCT resins swell the best in chloroform. DMA, 1,4-dioxane, DCM, THF, DMF, EDC, diglyme, and benzene also belong to the "good" solvents for the polymers. Hexane, acetonitrile, acetic acid, and alcohols do not swell HEMA TCT.

References

1. Peppas, N. A. Hydrogels in Medicine and Pharmacy, Vol. 2.; CRC: Boca Raton, 1987.
2. Hutcheon, G. A.; Messiou, C.; Wyre, R. M.; Davies, M. C.; Downes S. Biomaterials 2001, 22, 667.
3. Robert, C. C. R.; Buri, P. A.; Peppas, N. A. J Controlled Release 1987, 5, 151.
4. Arica, M. Y.; Hasirici, V.; Alaeddinoglu, N. G. Biomaterials 1995, 16, 761.
5. Gök, E.; Kiremitci, M.; Ates, I. S. React Polym 1994, 24, 41.
6. Kahovec, J.; Coupek, J. React Polym 1988, 8, 105.
7. Salih, B.; Denizili, A.; Engin, B.; Piskin, E. React Funct Polym 1995, 27, 199.
8. Kita, R.; Svec, F.; Fréchet, J. M. J. J Comb Chem 2001, 3, 564.
9. Chirila, T. V.; Chen, Y. Ch.; Griffin, B. J.; Constable, I. J Polym Int 1993, 32, 221.
10. Chen, Y. Ch.; Chirila, T. V.; Russo, A. V. Mater Forum 1993, 17, 57.
11. Clayton, A. B.; Chirila, T. V.; Dalton P. D. Polym Int 1997, 42, 45.
12. Lou, X.; Chirila, T. V.; Clayton, A. B. Int J Polym Mater 1997, 37, 1.
13. Clayton, A. B.; Chirila, T. V.; Lou X. Polym Int 1997, 44, 201.
14. Hohenstein, W. P.; Mark, H. J Polym Sci 1946, 1, 127.
15. Scranton, A. B.; Mikos, A. G.; Scranton, L. C.; Peppas, N. A. J Appl Polym Sci 1990, 40, 997.
16. Jayakrishnan, A.; Thanoo, B. Ch. J Biomed Mater Res 1990, 24, 913.
17. Jayakrishnan, A.; Sunny, M. C.; Thanoo, B. Ch. Polymer 1990, 31, 1339.
18. Okay, O.; Gürün, C. J Appl Polym Sci 1992, 46, 401.
19. Kiremitci, M.; Cukurova, H. Polymer 1992, 33, 3257.
20. Horak, D.; Lednicky, F.; Rehak, V.; Svec, F. J Appl Polym Sci 1993, 49, 2041.
21. Brandrup, J.; Immergut, E. H. Polymer Handbook, 3rd ed.; Wiley: New York, 1989.
22. Sherrington, D. C. Chem Commun 1998, 2275.
23. Santini, R.; Griffith, M. C.; Qi, M. Tetrahedron Lett 1998, 39, 8951.

Figure 7 Swelling characteristics of 20% HEMA–3% cross-linker–77% S resins in series of the solvents.