Preparation and Characterization of Thermoplastic Polymers from Hydroxyalkyl Methacrylates

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Synopsis

Soluble polymers have been produced from technical-grade 2-hydroxyethyl methacrylate (HEMA) and hydroxypropyl methacrylate (HPHA) using a combination of vacuum distillation and solvent extractions to purify the monomers prior to solution polymerization. These extractions, particularly of HEMA with hexane and corn oil, were found to reduce the level of ethylene glycol dimethacrylate to < 1%, according to gas chromatographic analysis. Homopolymers of HEMA and HPMA and copolymers of HEMA with methyl methacrylate were prepared with a wide range of molecular weights and characterized by viscometry in dimethyl formamide, infrared spectroscopy including deuterium exchange experiments, and high resolution proton and carbon nuclear magnetic resonance (NMR) spectroscopy. The latter was used to determine copolymer composition and tacticity distribution.

INTRODUCTION

Hydrogels based on the hydroxyalkyl methacrylates (usually 2-hydroxyethyl methacrylate) have found use in the ophthalmic industry as soft contact lenses and, in the future, may be used in a variety of other applications (e.g., controlled drug-release matrix, burn dressing) because of their favorable tissue implant compatibility.[1]

Encouraging preliminary results with insulin permeability studies[2] lead us to believe that soluble polymers based on the hydroxyalkyl methacrylates, perhaps copolymerized with a hydrophobic monomer such as methyl methacrylate, could also find use as mammalian cell microencapsulation matrices. We, therefore, initiated a program of research to prepare a number of such polymers for evaluation.

Crosslinked hydroxyalkyl methacrylate polymers are relatively easy to prepare as the monomers are viscous and usually contain high concentrations of crosslinking agents as side products of monomer synthesis.[3,4] Nonetheless,

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vacuum distillation, hexane extraction, and alumina treatment are recommended for purifying the monomer to prepare pure hydrogels.[1] With great care taken to purify the monomers[5] or in conducting the polymerization it is possible to prepare polymers soluble in common organic solvents. Dilute solutions,[6] an automated monomer feed technique,[7] and batch polymerization with monomer which had been purified by absorption chromatography,[8] have all been used for this purpose. In this paper we discuss an alternative method which we found better suited to the production of large quantities of soluble polymer from relatively inexpensive but impure technical-grade hydroxyalkyl methacrylates, using a combination of simple distillation and solvent extractions to purify the monomers prior to polymerization.

MATERIALS AND METHODS

Reagent Purification

Ethanol (95%, solvent grade) was redistilled with small cuts (5% top and bottom). All other solvents were reagent grade. Azobisisobutyronitrile (AIBN, Polysciences, Warrington PA, technical grade) was recrystallized in low yield from warm methanol, vacuum dried, and stored at −20°C until use. Methyl methacrylate (MMA, Polysciences, technical grade) was double distilled, using a water aspirator pump, with small cuts (10% top and bottom), stored at −20°C and used within 24 h (purity ≥ 98% by gas chromatography). Glycerol trioleate (edible-grade corn oil, Mazola™ Canada Starch, Toronto, Ontario) was boiled with 10 wt% Vega™ bleaching clay (courtesy Canada Packers Ltd., Toronto, Ontario), hot filtered through Whatman No. 114 paper, extracted with equal volume aliquots of ethanol (×2) and distilled water (×2), refrigerated and centrifuged (15,000 rpm × 10 min), decanted, filtered through a 0.8 μm cellulose filter cartridge (Canlab, Toronto, Ontario) and stored in a dark bottle at 0°C. 2-Hydroxypropyl methacrylate (HPMA, Polysciences, technical grade) was double distilled under rotary pump vacuum with cuts (10% top/20% bottom then 10% top and bottom), stored at −20°C, and used within 24 h. 2-Hydroxyethyl methacrylate (HEMA, Polysciences, technical grade) was double distilled under rotary pump vacuum (10% top/40% bottom then 10% top and bottom cuts) for series 1 polymers. The monomer was then extracted with two equal volume aliquots of hexane for series 2 polymers, or with two half volume aliquots of glycerol triolate then with two equal volume aliquots of petroleum ether (35–60) for series 3 polymers. In each case, the monomer was stored at −20°C and used within 24 h of the last purification step.

Preparation of Azobismethylisobutyrate (AMIB)

For one series of polymers, AMIB was used to minimize the incorporation of nitrogen in the final polymer. Briefly, AIBN in methanol (20 g in 130 mL) was converted to the diaminoester hydrochloride salt by reaction at 0°C with dry HCl gas, and hydrolyzed to the ester by addition of water.[9] The product was washed with excess 5% $NaHCO_3$ and recrystallized from methanol/water (1/4) (melting point 27–28°C, yield 85%).

TABLE I
Reaction Conditions Used in Solution Polymerization[a]

(a) Monomer Charge(s) (moles)

Series	poly MMA a	poly HEMA-MMA 25-75 b	poly HEMA-MMA 50-50 c	poly HEMA-MMA 75-25 d	poly HEMA e	poly HPMA f
1 (MMA)	0.5(1)	0.375(1) 0.125(2)	0.25 (1) 0.25 (2)	0.125(1) 0.375(2)	0.5 (2)	0.5 (3)
2 (HEMA)	0.5(1)	0.375(1) 0.125(2)	0.25 (1) 0.25 (2)	0.125(1) 0.375(2)	0.5 (2)	0.5 (3)
3 (HPMA)	1.0(1)	0.75 (1) 0.25 (2)	0.5 (1) 0.5 (2)	0.25 (1) 0.75 (2)	1.0 (2)	1.0 (3)

(b) Reaction Conditions

Series	Temperature of polymerization (°C)	Volume solvent [95% ethanol, (L)]	Time of polymerization (h)	Initiator (mol%)
1	(70 ± 0.05)	0.5	4	1 (AIBN)
2	~ 75	0.5	4	0.1 (AMIB)
3	(70 ± 0.05)	1	4	0.01 (AIBN)

[a] Monomer charges corrected for hexane content of monomer phase (see Table IV).

Bulk Polymerization

Bulk polymerization was investigated as an alternative to solution polymerization and to examine the effect of trace amounts of extraction solvents (e.g., corn oil) on polymerization. Redistilled monomer on its own or with initiator (with or without additional components) was extensively degassed on a vacuum line, sealed into a glass ampoule, and polymerized in a water or oil bath. The flask was then cracked open and the product mixture (if soluble) diluted with solvent, precipitated and reprecipitated in petroleum ether (35–60), and vacuum pumped to constant weight.

Solution Polymerization

Polymerizations were performed under research-grade nitrogen, in 95% ethanol, using AIBN or AMIB as initiator, in a standard 2 L Pyrex reaction kettle equipped with Trubore™ mechanical stir shaft, inlet bubbler, thermometer well, pressure-equalizing addition flask, and reflux condensor with exit gas bubbler (all Ace Glass Co., Vineland, NJ).

Briefly, the kettle with solvent was brought to the reaction temperature and flushed with nitrogen. Purified monomer was then admitted. After an equilibration period, the catalyst in 20 mL solvent was added to initiate the polymerization. The reaction was allowed to proceed for 4 h and quenched by cooling the kettle to room temperature. Reaction conditions and monomer feed ratios are given in Table I.

Poly(methyl methacrylate) homopolymers precipitated from solution as the reaction mixture cooled. They were isolated by filtration, dissolved in mini-

mum acetone, precipitated in petroleum ether (35–60), and vacuum dried to constant weight. All other polymers were coagulated by addition to excess petroleum ether. The polymer phase (swollen with solvent and HEMA or HPMA) was dissolved in minimum acetone or methanol, reprecipitated in excess distilled water containing 4 mM $CaCl_2$ (to prevent emulsification of the polymer), extracted 24 h with distilled water to remove residual monomer, and freeze dried to constant weight.

Gas Chromatography (GC) and Gas Chromatography / Mass Spectrometry (GC / MS)

Monomer mixtures were analyzed by gas chromatography (GC) at 140°C using 8′ × OV17 packed columns in a Hewlett Packard 5730A gas chromatograph with flame-ionization detector. A semiquantitative analysis of the GC results was performed by comparing peak areas which had been integrated by a Perkin Elmer Sigma 10 chromatographic data station.

Components of the mixture were identified by comparing their retention times with those of reference materials (various sources) and by the use of GC/MS using a Finnegan E1-C1 automated GC/MS system with spectral library, coupled to a Finnegan 4010 electron impact mass spectrometer. For this experiment, materials with short retention times in the GC experiment were separated on 3 m × Chromosorb 102 packed columns under programmed conditions (180–230°C at 5°C/mm) while those with longer retention times were separated on 8′ × OV17 packed columns at 120°C.

Viscosity Measurements

The viscosities of monomer mixtures at (35 ± 0.05)°C were obtained with a Cannon #200 suspended-level Ubbelhode viscometer. The viscosities of polymer solutions in dimethylformamide (DMF, Aldrich, Gold Label, Milwaukee, WI) at the same temperature were obtained in the usual manner with a Cannon #100 suspended-level Ubbelhode viscometer.[10]

Infrared Spectroscopy

Infrared (IR) spectra were obtained with a Perkin Elmer 1500 Fourier Transform (FT-IR) spectrometer using 100 scans at a resolution of 4 cm^{-1} Thin films of polymer were cast onto NaCl salt plates from methanol and/or tetrahydrofuran, vacuum pumped at 60°C, and transferred, while warm, to the spectrometer.

Deuterium exchange experiments were performed on thin films of polymer which were deposited onto the inner surface of NaCl salt dishes which were affixed to a gas phase IR cell. Infrared spectra before and after exposure to deuterated (d_4) methanol vapor (Sigma Chemical Co., St. Louis, MO) were compared by spectral subtraction and used to assign bands associated with hydroxyl groups in the polymer.

Nuclear Magnetic Resonance (NMR) Spectroscopy

Proton (^1H) NMR spectra of monomers and polymers were obtained at 400 MHz using a Bruker AM-400 Fourier transform (FT-NMR) spectrometer.

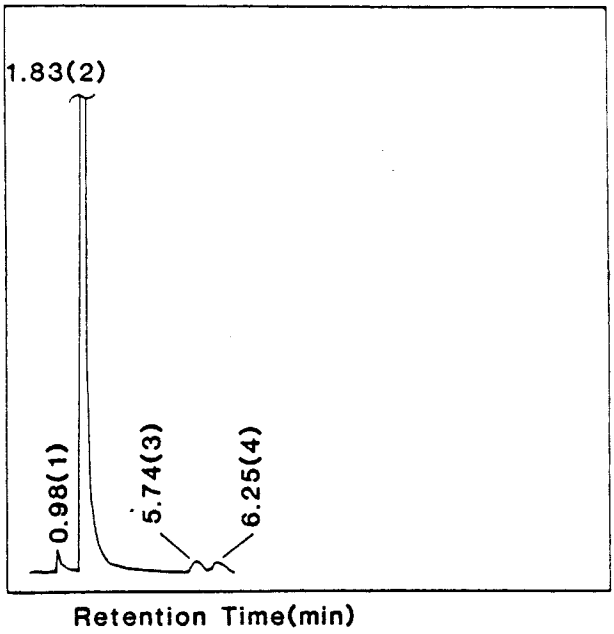


Fig. 1. Gas chromatogram of unpurified 2-hydroxypropyl methacrylate (injection volume 0.05 μL neat): (1) methacrylic acid; (2) 2-hydroxypropyl methacrylate: (3) propylene glycol dimethacrylate; (4) unknown.

Carbon (^{13}C) NMR spectra were obtained at 100.7 MHz on the same instrument.

Polymer concentrations were in the range of 5–10% in solvents which if deuterated were supplied by the Sigma Chemical Co. Polymers designated (a) and (b) (see Table I) were examined in acetone or d_6 acetone while those designated (d), (e), (f) were examined in methanol or deuterated (d_4) methanol, all at room temperature. Proton NMR resonances associated with pendant methyl groups of polymers designated (c) were best resolved in deuterated (d_6) dimethyl sulfoxide (DMSO) at 60°C; all other signals for this polymer were best resolved in deuterated (d_4) methanol at room temperature. Carbon or proton solvent signals were used as chemical shift markers.

RESULTS AND DISCUSSION

2-Hydroxypropyl Methacrylate (HPMA)

HPMA was supplied as a clear liquid with negligible polymer content (no precipitation in excess nonsolvent, no NMR signals associated with polymer). A gas chromatogram of the material is shown in Figure 1. Methacrylic acid (MAA) and propylene glycol dimethacrylate (PGDMA) are side products of the synthesis reaction in which MAA is esterified with propylene glycol (PG) or propylene oxide (PO) to produce HPMA. A proportion of HPMA is always esterified by excess PG or PO to produce PGDMA, an effective crosslinking agent. The nature of component 4 was uncertain. It does not produce an acrylate cracking pattern in the GC-MS and appeared to be a homologue

TABLE II
Composition by Gas Chromatography (GC) of 2-Hydroxypropyl Methacrylate (HPMA) Fractions at Various Stages of the Purification Procedure

	Fraction of normalized GC trace (%)			
Mixture	HPMA	Methacrylic acid (MAA)	Propylene glycol dimethacrylate (PGDMA)	Fraction 4
Unpurified HPMA	98.5	0.7	0.3	0.5
First distillation, (top fraction)	95.1	4.8	0.05	0.05
First distillation, (middle fraction)	99.1	0.6	0.2	0.06
Second distillation (middle fraction)	99.0	0.9	0.07	0.01

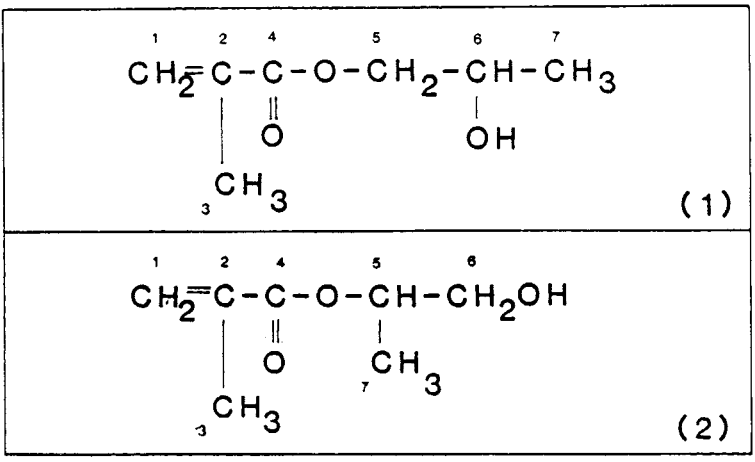
($^{+}CH_2$) of a similar fraction in 2-hydroxyethyl methacrylate (HEMA) monomer.

The composition of a representative batch of HPMA at difference stages of the purification process is given in Table II. The difference in volatility between HPMA and PGDMA/fraction 4 was sufficient to allow almost complete removal of the latter by simple distillation (compare lines 1 and 4). Methacrylic acid, on the other hand, was not removed by distillation (compare lines 1 and 4).

Commercial HPMA is a mixture of 2-hydroxy-1-propyl methacrylate (isomer 1) and 1-hydroxy-2-propyl methacrylate (isomer 2) in proportions which depend upon the method of synthesis [Fig. 2(a)]. For example, isomer 1 would be the major product of esterification of MAA with propylene glycol (route 1), while isomer 2 would be the major product of esterification of MAA with propylene oxide (route 2).[11] Such a mixture is difficult to separate for analysis but easy to resolve using high-field NMR spectroscopy. The ^{1}H and ^{13}C spectra of HPMA, in the chemical shift ranges 0–1.5 ppm and 0–20 ppm, respectively, are illustrated in Figure 2(b). Appropriate NMR signal assignments are given in Table III. By this method it appears that isomer 1 was the major component (67 mol%) of the mixture.

Distilled HPMA was essentially free of crosslinking impurities yet was still unsuitable for the preparation of soluble polymers by bulk free radical polymerization in the absence of a chain transfer agent. Presumably its high viscosity (5.23 cS compared with 0.51 cS for methyl methacrylate, both at 35°C) accelerated the reaction even at zero conversion to polymer.[12]

The experimental conditions of some representative bulk polymerizations at 70°C are outlined in Table IV. In principle, the molecular weight could be reduced by increasing the temperature of polymerization in the presence or absence of initiator (the latter being termed thermal polymerization) using initiator levels above 0.1 mol% or reaction times less than 20 min. The



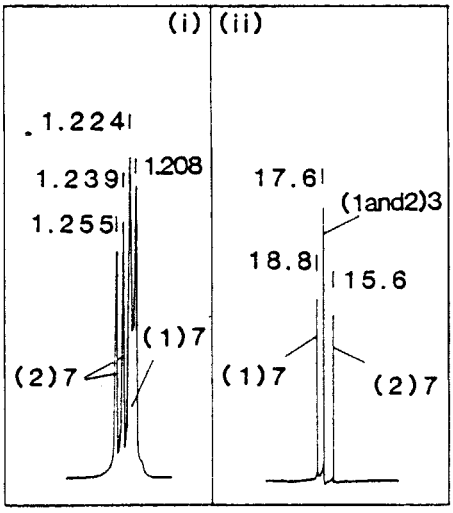


Fig. 2. (a) Isomers of commercial hydroxypropyl methacrylate: 2-hydroxy-1 propyl methacrylate (isomer 1) and 1-hydroxy-2 propyl methacrylate (isomer 2). (b) Proton ^{1}H (i) and carbon ^{13}C (ii) NMR spectra of hydroxypropyl methacrylate in the chemical shift range 0–1.5 ppm and 0-20 ppm, respectively. Isomers 1 and 2 and position 3 and 7 are identified in Figure 2(a).

TABLE III
Nuclear Magnetic Resonance (NMR) Chemical Shifts of Carbons and Protons Used to Quantify the Proportions of Isomers (1) and (2) in Commercial 2-Hydroxypropyl Methacrylate (HPMA)

Isomer[a] / nucleus	Chemical shifts (ppm from the corresponding signal of TMS)[a]						
	1	2	3	4	5	6	7
(1) / ^{1}H	6.16, 5.67	—	1.94	—	—	—	1.22 (doublet)
(1) / ^{13}C	125.2	135.6		166.9	65.0	69.0	18.8
(2) / ^{1}H	6.13, 5.64	—	1.92	—	—	—	1.25 (doublet)
(2) / ^{13}C	124.9	136.0	—	166.7	64.5	71.5	15.6

[a] Isomers (1) and (2) and positions 1–7 are identified in Figure 2(a).

TABLE IV
Bulk Polymerizations of 2-Hydroxypropyl Methacrylate (HPMA) and 2-Hydroxyethyl Methacrylate (HEMA)[a]

Reaction conditions				
Monomer (10 g)	Mole % AIBN	Temperature (±0.1 °C)	Time of reaction (min)	Nature of product
HPMA	0.01	70	90	Solid plastic
HPMA	0.01	70	20	Gel
HPMA	0.1	70	20	Solid plastic
HPMA	0	90	180	≤ 1% Yield
HEMA	0	90	180	Solid plastic

[a] No chain transfer agents.

monomer however does not appear to be susceptible to bulk thermal polymerization (Table IV, line 4). Raising the temperature of polymerization or the level of initiator would, in our opinion, produce an unstable system, while reducing the reaction time would introduce problems of temperature equilibration.

2-Hydroxyethyl Methacrylate (HEMA)

2-Hydroxyethyl methacrylate (HEMA) was supplied as a yellow liquid of viscosity 4.08 cP at 35°C, containing negligible amounts of polymer. The mixture could be clarified by passage through a silica column or by vacuum distillation. The untreated monomer undergoes rapid thermal polymerization at the temperature of distillation (about 71–75°C, 2.5 mmHg pressure) limiting the first distillate to approximately 50% of the monomer mixture. Distilled HEMA is more stable though still prone to thermal polymerization (see Table IV, line 5). Approximately 90% can be redistilled before the residue gels.

Three sets of HEMA-containing polymers were prepared, each requiring a different level of monomer purity. For example, low molecular weight polymers (series 1) were prepared with redistilled HEMA which contained a high concentration of EGDMA, using a high level of initiator (1 mol%). Moderate molecular weight polymers (series 2) were prepared with less initiator (0.1 mol%) using HEMA which had been distilled and extracted with hexane to reduce the concentration of EGDMA. High molecular weight polymers (series 3) were prepared by polymerizing monomer, which had been further purified by extraction with corn oil, in the presence of even less initiator (0.01 mol%).

A GC separation of the components of untreated HEMA is shown in Figure 3. The composition of representative HEMA fractions at various stages of the purification process are listed in Table V. Methacrylic acid (MAA) was probably esterified with ethylene glycol (EG) to produce HEMA, some of which was esterified by excess MAA to produce ethylene glycol dimethacrylate (EGDMA). The latter (EGDMA) was less efficiently removed and MAA/EG more efficiently removed by distillation than similar fractions in HPMA (compare Table II with Table V) as HEMA was less volatile than HPMA while EGDMA was more volatile than PGDMA. The unknown

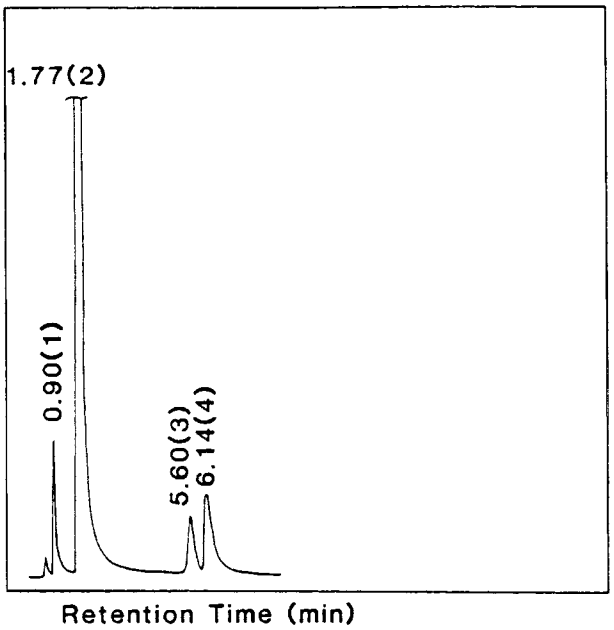


Fig. 3. Gas chromatogram of unpurified 2-hydroxyethyl methacrylate (injection volume: 0.05 μL neat): (1) methacrylic acid (80%), ethylene glycol (20%); (2) 2-hydroxyethyl methacrylate; (3) ethylene glycol dimethacrylate; (4) unknown.

fraction 4 has been discussed in the context of similar material in HPMA (Table II, Fig. 1). Extraction with corn oil and/or hexane removed EGDMA but did not remove MAA from the monomer mixture. The effect of MAA on the final polymer properties is discussed below.

Solution Polymerizations

Polymerizations were performed in dilute solution to minimize the viscosity of the reaction medium and the degree of crosslinking associated with residual dimethacrylate. Series 1 and 3 polymers were performed at (70 ± 0.05°C) using azobisisobutyronitrile (AIBN) as initiator. Series 2 polymers were prepared using azobismethylisobutyrate (AMIB) as initiator. Polymerizations using AMIB were performed at approximately 75°C in refluxing solvent to in part compensate for its lower activity (30% less than that of AIBN at 80°C).[13] Reaction conditions are summarized, and polymers identified in Table I.

Polymer yields are summarized in Table VI. Conversions ranged from 70–80% for series 1 polymers, from 30–60% for series 2 polymers, and from 12–20% for series 3 polymers. Conversions increased across each series from (a) to (e) and (f), indicating that HEMA and HPMA polymerize more rapidly than MMA in dilute solution.

Copolymer compositions were obtained, using high resolution proton NMR spectroscopy, by ratioing the integrated signal intensities produced by the methyl ester protons of MMA repeat units, to those produced by the hydroxyethyl ester protons of HEMA repeat units (Table VII). A typical spectrum is shown in Figure 4. Copolymer compositions were all very similar to the monomer feed ratios indicating that HEMA and MMA randomly copo-

TABLE V
Composition by Gas Chromatography of 2-Hydroxyethyl Methacrylate (HEMA) Fractions at Various Stages of the Purification Procedure

	Fraction of normalized GC trace (%)			
Mixture	Hydroxyethyl methacrylate	Methacrylic acid and ethylene glycol	Ethylene glycol dimethacrylate	Fraction 4
Purified HEMA	93.3	1.6	1.7	3.3
First distillation, (top fraction)	93.5 (97.7)[a]	5.6 (1.5)[a]	0.9 (0.8)[a]	≤ 0.01
First distillation, (middle fraction)	96.3	1.0	1.7	1.0
Second distillation, (top fraction)	93.6	4.7	1.1	0.7
Second distillation, (middle fraction) (series 1)	97.3	0.7	1.6	0.4
Extracted with hexane (series 2)[b]	97.5	0.7	1.2	0.3
Extracted with corn oil and hexane (series 3)[b]	97.7	0.7	0.8	0.3

[a]Value in brackets is that obtained when distilled from sodium bicarbonate.
[b]Normalized to account for hexane content of HEMA phase (approximately 29% of the mixture).

TABLE VI
Yields of Polymers Prepared by Solution Polymerization (Weight %)

		Poly HEMA-MMA				
Series	Poly MMA a	b	c	d	Poly HEMA e	Poly HPMA f
1	71.4	70.2	57.1	69.0	80.4	78.5
2	29.0	30.1	35.0	33.8	52.6	57.7
3	12.0	15.1	16.4	16.2	20.3	22.7

lymerize in dilute solution even at high conversions to polymer. This is consistent with the reported reactivity ratios.[7]

Chain Transfer to Corn Oil

In the purification of HEMA by extraction with corn oil, it or the trace impurities in the corn oil may be carried over into the polymerization. For this reason, we tested the effect of corn oil as a chain transfer agent on the

TABLE VII
Composition of Copolymers of 2-Hydroxyethyl Methacrylate (HEMA) with Methyl Methacrylate (MMA)[a]

Series	b	c	d
1[b]	24	51	73
2[b]	26	49	79
3[b]	27	51	79
Monomer feed[b]	25	50	75

[a]By proton nuclear magnetic resonance (NMR) spectroscopy.
[b]Mole % HEMA in copolymer (mole % MMA by difference).

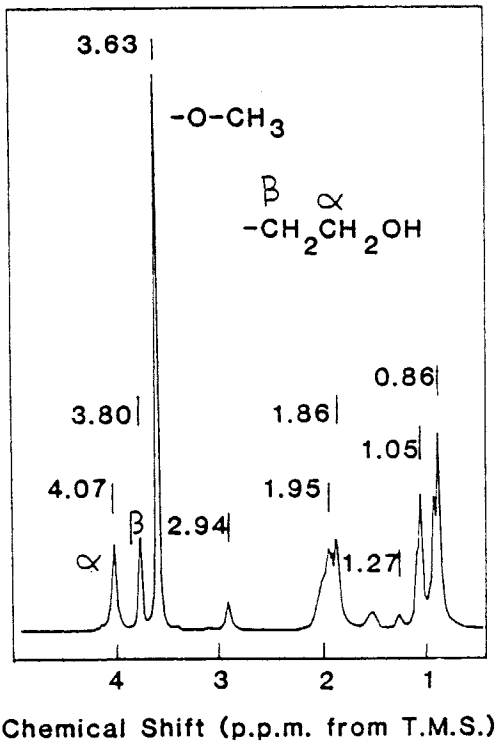


Fig. 4. Proton NMR spectrum of polymer 3 b, a high molecular weight copolymer of methyl methacrylate (73 mol %) and 2-hydroxyethyl methacrylate (27 mol%).

molecular weight and yields of bulk-polymerized poly(methyl methacrylate) (PMMA). We also prepared PMMA in the absence of any corn oil and in the presence of 95% ethanol (the polymerization solvent) and hexane (another impurity introduced by the purification procedure); neither of the latter two are active chain transfer agents. Polymers were prepared at 70°C at conversions close to the gel point[14] to emphasize changes in molecular weight and yield of polymer. Our results, summarized in Table VIII, indicate that corn oil had little effect on the yield and molecular weight of bulk-polymerized poly(methyl methacrylate) and therefore, does not appear to be either an efficient chain transfer agent or a retarder of polymerization of methacrylate monomers.

TABLE VIII
The Effect of Selected Additives on the Molecular Weight and Conversion to Polymer of Bulk Polymerized Polymethyl Methacrylate[a]

Additive (wt %)	Polymer yield	$\bar{M}_w \times 10^{6}$ [b]	C_s of additive at 70°C ($\times 10^{-4}$)
None	13.8	1.46	—
95% Ethanol (1%)	14.6	1.37	~ 0.5 (Ref. 15)
Hexane (1%)	14.4	1.25	~ 2–3 (Ref. 16)
Corn oil (1%)	14.2	1.07	—

[a] Prepared by reaction at 70°C for 90 min in the presence of 0.01 mol% AIBN.
[b] From equation (2).
C_s = chain transfer constant.

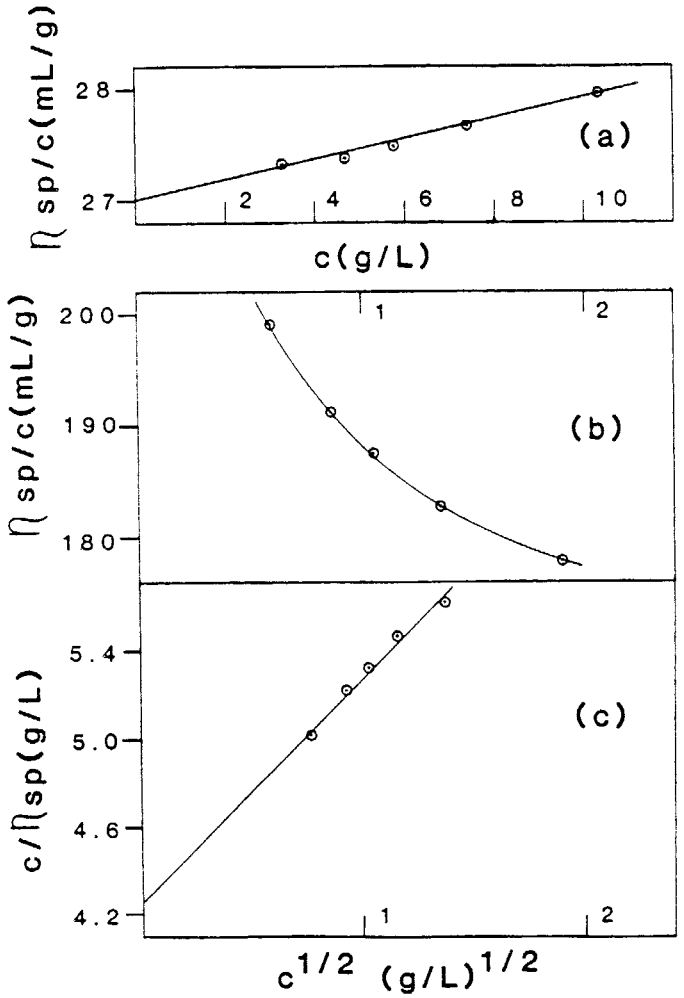


Fig. 5. Limiting viscosity plots for poly HPMA; (a), (b) η_{sp}/c against c for polymers 1f and 3f, respectively; (c) c/η_{sp} against $c^{1/2}$ for polymer 3f.

TABLE IX
Limiting Viscosity Numbers of Polymers Prepared by Solution Polymerization

Series	Poly MMA a	Poly HEMA-MMA b	c	d	Poly HEMA e	Poly HPMA f
1	12.7[a] (37,200)	18.6[a]	22.7[a]	23.5[a]	31.9[a]	27.0[a]
2	22.6[a] (82,900)	32.7[a]	65.4[a]	71.5[b]	124.5[b]	87.0[b]
3	72.6[a] (419,000)	107.3[a]	162.6[b]	439[b]	1124[b]	235.3[b]

[a] $[\eta]$ in mL/g.
[b] A in mL/g.
Values in brackets for poly MMA are molecular weights calculated using eq. (2).

Limiting Viscosity Numbers

Series 1 polymers and other solution-polymerized materials which contained a high proportion of methyl methacrylate obeyed the Huggins' equation in dilute solution in dimethylformamide (DMF) at 35°C giving straight line plots, with positive gradient, of reduced specific viscosity (η_{sp}/c) against concentration (C). These were extrapolated to zero concentration to yield values of $[\eta]$, the intrinsic viscosity of the polymer [Fig. 5(a)].[17] Higher molecular weight polymers which contained a high proportion of hydrophilic monomer gave nonlinear Huggins' plots with a negative gradient [Fig. 5(b)]. In contrast, plots of C/η_{sp} against $c^{1/2}$ [Eq. (1)] were linear with a positive gradient, indicating that these polymers behaved as polyelectrolytes in DMF [Fig. 5(c)]:[18]

$$c/\eta_{sp} = 1/A + KC^{1/2} \tag{1}$$

Limiting viscosity numbers for uncharged ($[\eta]$) and polyelectrolyte (A) polymers are reported in Table IX. Weight average ($\bar{M}_w$) molecular weights for PMMA polymers (listed in parentheses) were obtained from the relationship.[19]

$$[\eta]^{35°C}_{DMF} = 6.50 \times 10^{-3}\bar{M}_w^{0.72} \tag{2}$$

Because of differences in polymer composition, comparisons of molecular weight across a series were not possible. Even so, the PMMA polymers which were prepared in the absence of any crosslinking agent were assumed to possess the lowest molecular weight of each series. The limiting viscosity numbers of polymers with similar compositions (for example of polymers 1c, 2c, and 3c) were compared directly and show (albeit indirectly) that the three series of polymers cover a wide range of molecular weights.

Polyhydroxyethyl methacrylate polymers have been shown to obey the Huggins equation in DMF over a wide range of molecular weights.[20] The polyelectrolyte character of the more hydrophilic higher molecular weight polymers is, therefore, not an intrinsic property of hydroxyalkyl methacrylate

polymers. The effect is probably due to small amounts of copolymerized methacrylic acid. The increasing polyelectrolyte character of polymers across a series from (a) to (e) and (f) was presumably due to an increasing content of MAA, which accompanies the HEMA and HPMA monomers but not the MMA monomer. The decreasing polyelectrolyte character of polymers from series 3 to 1 was presumably due to the reduction in polymer molecular weight. In statistical terms, the lower molecular weight polymer may not contain enough MAA per chain to induce the observed chain expansion on dilution.

IR Spectra

We attempted to use infrared spectroscopy to determine the proportions of methyl methacrylate and 2-hydroxyethyl methacrylate in polymers (b), (c),

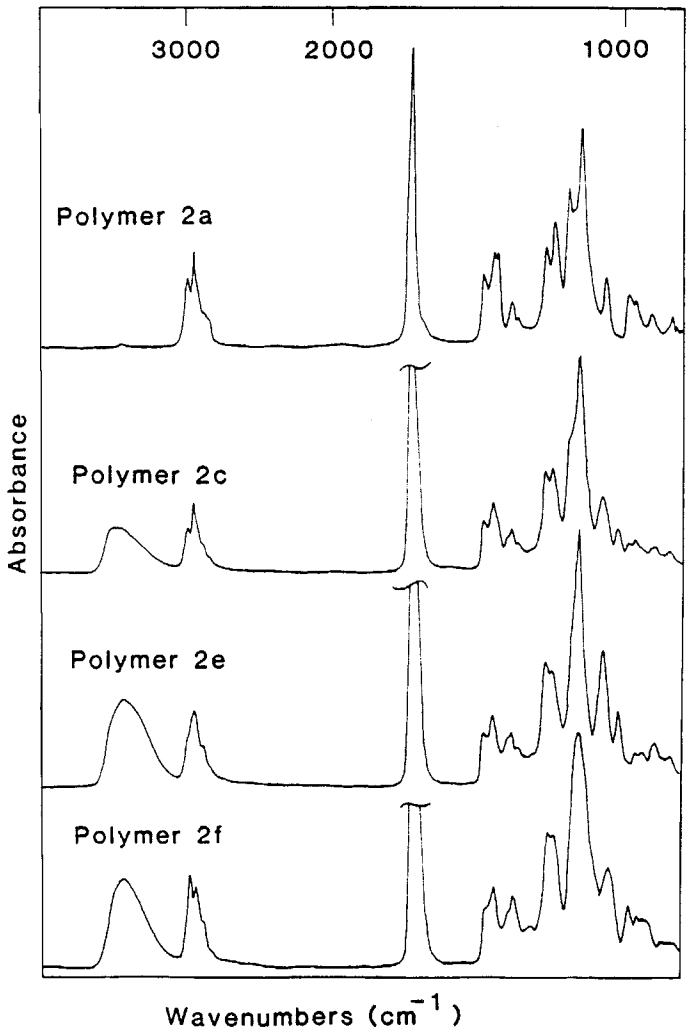


Fig. 6. Infrared spectra of intermediate molecular weight polymers (series 2) as thin films on NaCl disks. Polymers are identified in Table I.

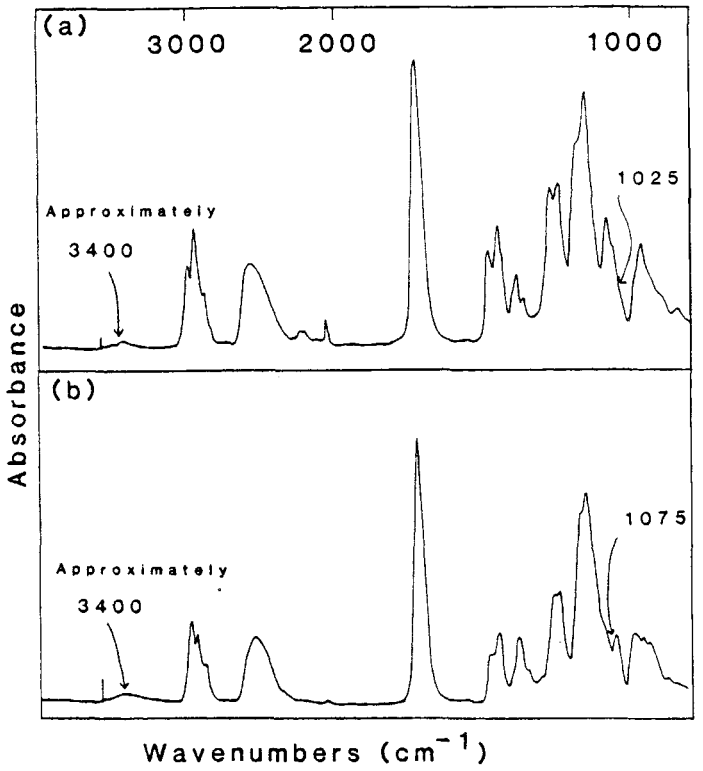


Fig. 7. Infrared spectra of (a) poly-HEMA and (b) poly HPMA, (polymers 1e and 3f respectively) after exposure to deuterated (d_4) methanol vapour. Arrows denote major peaks removed by deuteration.

and (d). In this we were unsuccessful. The mid IR region from 4000 cm^{-1} to 600 cm^{-1} did not contain any well resolved absorbances which could be attributed to either monomer unit. We were, however, able to make some band assignments which are reported here.

As expected, the IR spectra of corresponding series 1, 2, and 3 polymers were identical. The infrared spectra of some series 2 polymers are reproduced in Figure 6. Moving from polymer 2(a) (PMMA) to polymer 2(e) (PHEMA) and 2(f) (PHPMA) a gradual appearance of hydroxylic material (approximately 3400 cm^{-1}) is seen. Changes in the symmetric and antisymmetric C-H deformation modes in the region 1500-1300 cm^{-1} also appear, presumably associated with the introduction to the polymer of pendant hydroxyethyl and hydroxypropyl groups. The PMMA C-C skeletal vibration at 1200 cm^{-1} weakens while the other skeletal modes at 1270 cm^{-1} and 1240cm^{-1} become broader and suffer an intensity reversal.

Deuterium exchange experiments (Fig. 7) show that the in-chain C-C skeletal vibration of PMMA at 1070 cm^{-1} associated with atactic polymer[21] has an analogue in PHEMA (1080 cm^{-1}) and PHPMA (1060 cm^{-1}). Spectral subtraction after deuteration revealed the primary alcohol C-O stretch of PHEMA (1025 cm^{-1}) and the secondary alcohol C-O stretch of PHPMA (1075 cm^{-1}).

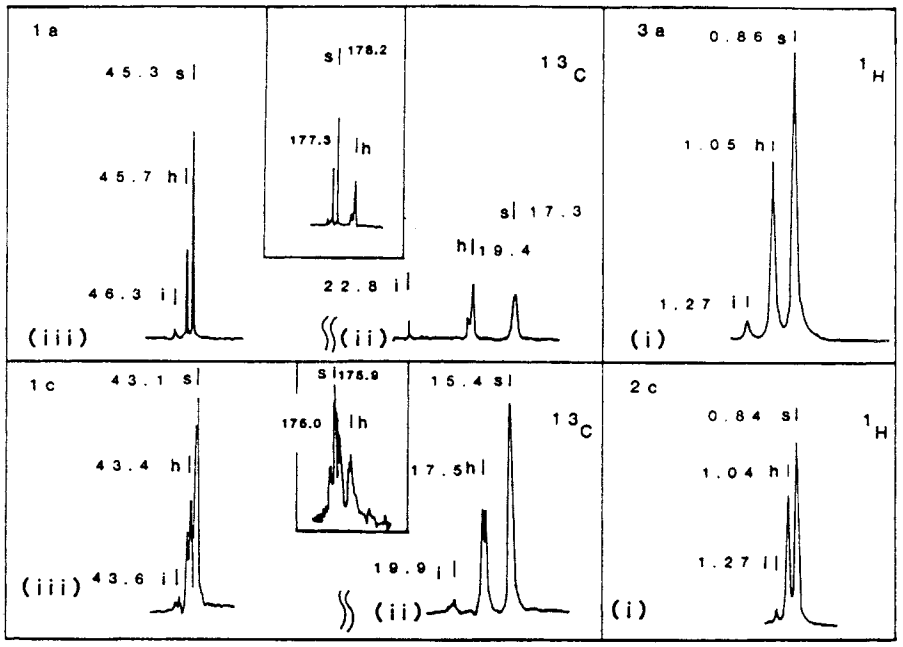


Fig. 8. NMR signals used to calculate tacticity distribution (i) pendant methyl ^{1}H resonance, (ii) pendant methyl ^{13}C resonance, (iii) tertiary chain ^{13}C resonances. Insert shows corresponding ^{13}C carbonyl resonances. Peak position referred to TMS. Upper panel: Poly MMA; lower panel: poly MMA-HEMA (50-50).

NMR Spectra

It has been shown that the tacticity of crosslinked HEMA-containing polymers can influence glass transition temperature[22] and equilibrium water uptakes,[23] the latter being an important factor in soft tissue compatibility and solute permeability. The tacticity distributions of methacrylate polymers are most easily determined by nuclear magnetic resonance (NMR) spectroscopy. Modern high-field instruments have detected triad splitting of the pendant methyl ^{13}C and ^{1}H signals of PMMA,[24] the pendant methyl ^{13}C signals of crosslinked PHEMA,[23] and pentad splitting of the ester carbonyl ^{13}C signal of PMMA.[25] We have, in addition, observed here the triad splitting of the pendant methyl ^{1}H signal of PHPMA, PHEMA, and copolymers of the latter with MMA; the triad splitting of the in-chain tertiary carbon ^{13}C signal of PMMA, PHEMA, and copolymers of the two; as well as pentad splitting of the carbonyl ^{13}C signal of PHPMA and PHEMA. Carbon ^{13}C and proton ^{1}H signal line widths were not appreciably molecular weight dependant, with the result that the NMR spectra of polymers and copolymers with similar composition, for example of polymers 1(b), 2(b), and 3(b), were almost identical.

Pendant methyl ^{1}H resonances of some representative polymers are shown in Figures 8 and 9(i). The spectra of polymers (a), (b), (d), and (e) (MMA and all but one HEMA-MMA copolymer) were sufficiently well resolved to allow the proportions of isotactic (i), heterotactic (h), and syndiotactic (s) material to be measured. The spectra of the three (c) polymers (50-50 HEMA/MMA)

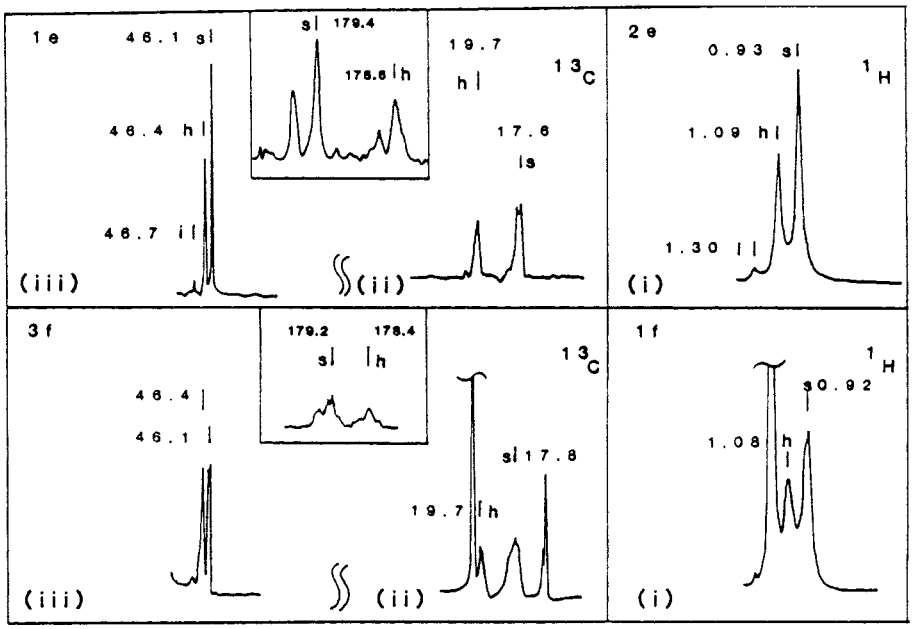


Fig. 9. Same as Fig. 8. Upper panel: Poly HEMA; lower panel: PolyHPMA.

were broad and ill defined when obtained in d_4 methanol at room temperature, but were well defined when obtained in d_6 dimethylsulfoxide at 60°C. Pendant methyl ^1H resonances of PHPMA polymers coincided with a signal at 1.22 ppm attributable to protons of the methyl groups of the two isomeric hydroxypropyl substituents in the polymer [Fig. 2(b)].

Pendant methyl ^{13}C resonances of the same polymers are shown in Figures 8 and 9(ii). The spectra of polymers (a), (b), (c), and (d) (PMMA and HEMA-MMA copolymers) were well enough resolved to allow isotactic (i), heterotactic (h), and syndiotactic (s) contents to be measured. The heterotactic and syndiotactic resonances of PHPMA were sandwiched between resonances attributable to methyl groups of the two isomeric hydroxypropyl substituents in the polymer [Fig. 2(b)]. In common with other authors,[22] we were unable to isolate a signal attributable to isotactic triads in PHEMA.

Tertiary in-chain carbon ^{13}C resonances are shown in Figures 8 and 9(iii). Signals produced by polymer (a)–(e) (PHMA, PHEMA, and copolymers) were well enough resolved to allow the proportions of syndiotactic, heterotactic, and isotactic material to be measured. We could not positively interpret the signal-splitting pattern of the tertiary in-chain carbon ^{13}C resonance of PHPMA (f).

Carbonyl ^{13}C resonances are shown as inserts in Figures 8 and 9. Signals attributable to (a) and (e) polymers show well resolved pentad fine structure. The associated resonances of PHPMA show poorly resolved pentad splitting (possibly as a result of its copolymer character) while those of copolymers of MMA with HEMA [polymers (b), (c), and (d)] could not be positively interpreted.

The isotactic (i), heterotactic (h), and syndiotactic (s) contents of all polymers designated (a)–(e) were obtained by integrating and normalizing

TABLE X
Tacticity Distributions, by Nuclear Magnetic Resonance Spectroscopy, of Polymers Prepared in Solution

Series	Poly MMA a[a]	Poly HEMA-MMA b[a]	Poly HEMA-MMA c[a]	Poly HEMA-MMA d[a]	Poly HEMA e[a]	Poly HPMA f[b]
1	63,31,6	61,33,6	64,33,3	59,32,9	57,37,4	71,29
2	62,33,5	62,34,4	64,33,3	60,34,6	63,33,4	68,32
3	63,33,4	61,36,3	60,37,3	64,31,5	60,32,8	71,29

[a] Normalized mole percentages of (syndiotactic, heterotactic, and isotactic) material.
[b] Normalized mole percentages of (syndiotactic and heterotactic) material.

proton signals produced by the respective triads in the polymer. The normalized heterotactic and syndiotactic contents of polymers designated (f) were obtained by integrating and normalizing pendant methyl ^{13}C signals associated with the two types of material in this polymer. Tacticity distributions determined by these procedures are shown in Table X. On average, polymers (a)–(e) (PMMA, PHEMA, and copolymers) were composed of 61.5 mol% syndiotactic material, 33.5 mol% heterotactic material, and 5.0 mol% isotactic material, a distribution which is entirely consistent with the product of a propagation reaction which conforms to simple Bernouillian statistics. In other words, the mode of addition of the incoming monomer unit is influenced by steric repulsion with the chain end substituent, but not by the stereochemistry of the penultimate repeat unit of the macroradial.[26] The ratios of syndiotactic to heterotactic material in PHPMA were close to those of polymers (a)–(e), indicating a similar mode of propagation.

Further Improvements

We have noted that very small amounts of copolymerized methacrylic acid (MAA), present as an impurity in HEMA monomers, can substantially increase the equilibrium water uptake of HEMA- and HPMA-containing polymers when ionized at physiological pH.[27] As an impurity, its concentration will vary from batch to batch introducing uncertainties into the composition and behavior of the final product. Methacrylic acid is efficiently removed by simple distillation with sodium bicarbonate added to the still pot (Table IV, line 2). We, therefore, suggest that improved products would result from the polymerization of HPMA which had been double distilled from sodium bicarbonate, and by the polymerization of HEMA which had been distilled from sodium bicarbonate, extracted with corn oil ($\times 2$) and hexane ($\times 2$), then redistilled from sodium bicarbonate before use. In subsequent work we have also learned that the corn oil need not be purified prior to its use as an extraction solvent.

Subsequent to the preparation and characterization of the polymers described here, we have found that addition of copper turnings (Aldrich) to the HEMA still pot and sidearm, results in a polymer with a lower solution viscosity than before. This has been attributed to the inhibitory effect of the copper on HEMA dimerization with consequent reduction in crosslinking/branching during polymerization. These polymers appear to be superior for

microencapsulation given the operational restrictions on polymer solution viscosity in our microencapsulation system.

CONCLUSIONS

Vacuum distillation and various solvent extractions have been found to be sufficient to purify hydroxyalkyl methacrylate monomers (HEMA and HPMA) sufficient to prepare soluble polymers, even at low initiator concentrations by solution polymerization. The purified monomers and the resulting polymers have been characterized by a number of techniques in order to understand the polymerization process. Some of these polymers are now being investigated further as mammalian cell immobilization matrices for the preparation of an artificial pancreas and other metabolic prostheses.

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