A Study on the Copolymerization Kinetics of Phenylethyl Acrylate and Phenylethyl Methacrylate

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Abstract: Copolymers of phenyl alkyl acrylates/methacrylates are used clinically as soft materials for the foldable intraocular lens (IOL) to treat cataracts. In this study, copolymers of 2-phenylethyl acrylate (PEA) and 2-phenylethyl methacrylate (PEMA) of various compositions were prepared using free radical polymerization in solution. The composition of the copolymers was determined by ^{1}H-NMR analysis. The reactivity ratios of the monomers were calculated using the conventional Fineman-Ross or Kelen-Tudos method. The reactivity ratio of PEA (r_1) and PEMA (r_2) were estimated to be 0.280 and 2.085 using the Kelen-Tudos method, respectively. These values suggest that PEMA is more reactive in copolymerization than PEA, and the copolymers will have a higher content of PEMA units. The glass transition temperature (T_g) of the copolymers increased with increasing PEMA content. The molecular weight and polydispersity indices (M_w/M_n) of the polymers were determined by GPC. Overall, these results are expected to be quite useful in applications to foldable soft IOL materials.

Keywords: 2-phenylethyl acrylate (PEA), 2-phenylethyl methacrylate (PEMA), reactivity ratios, intraocular lens (IOL).

Introduction

Cataract is the opacification of the lens due to age or other causes such as ocular trauma or inflammation which makes light rays no longer pass through the eye.[1] It is a common surgical procedure for the cataract treatment to remove the opaque natural crystalline lens and replace with an intraocular lens (IOL).

There have been many kinds of IOL materials.[2] Early IOLs were made from hard PMMA (poly(methyl methacrylate)) so that it required a big incision of 6 mm.[3] Nowadays, foldable soft IOLs are mostly used and therefore the incision is enough with 3 mm and the healing is more rapid.[4] Foldable IOLs are made from flexible polymers including hydrophobic acrylics, hydrophilic hydrogels or silicone elastomers.[5-15] Among them, silicones such as poly(dimethylsiloxanes)(PDMS) are used most commonly as they are soft and inert and their refractive index (RI) is 1.41 similar to the value of natural lens (1.42).[16] Hydrogels such as poly(hydroxyethyl methacrylate) (PHEMA) are also used and its RI is 1.44.[17] Recently, hydrophobic acrylic lenses were introduced as foldable IOLs. The representing one is based on a copolymer of 2-phenylethyl acrylate (PEA) and 2-phenylethyl methacrylate (PEMA). Its advantage is known to

have a higher RI value (1.55) to make a thinner optic.[18,19] The other advantage of this PEA/PEMA copolymer is claimed to be unfolded more slowly than silicone lenses, perhaps giving the surgeon greater intraoperative control of lens implantation.[20] Furthermore, many copolymers made of PHEMA, PMMA, PEA, or PEMA with other acrylics have been studied to modify the properties for applying to soft IOLs. All these properties are dependant on the copolymer compositions.

The composition of a copolymer is determined by the reactivity ratios of comonomers at the copolymerization. Therefore, we should define the copolymerization kinetics for the structural modification by copolymerization. In this study, a kinetic study on the copolymerization of PEA and PEMA was conducted to determine the reactivity ratios of PEA and PEMA which has not been reported to date. PEA and PEMA were copolymerized in solution and the resulting PEA/PEMA copolymers were characterized.

Experimental

Materials. PEA and PEMA (Hampford Research) were purified for the removal of *p*-methoxyphenol. They were washed three times with 5% sodium hydroxide solution and twice with distilled water. Then they were dried over anhydrous sodium sulfate overnight and distilled fractionally at

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reduced pressure under nitrogen. The middle cut of mono-mer was retained and stored at 4 °C. Benzoyl peroxide (BPO) (Sigma) was re-crystallized from a chloroform-methanol mixture. Methyl ethyl ketone (MEK) (Sigma) was used as received.

Solution Polymerization. About 0.5 g of PEA, PEMA or various mixture of PEA/PEMA was placed in a standard polymerization tube containing 2.0 mL of MEK and 1.5 mg of BPO. The mole ratio of the initiator to monomer was approximately 0.47 mol%. The reaction mixture was flushed with nitrogen for 10 min, sealed and kept in a thermostat at 70±1 °C. After the certain period of time, the polymers were precipitated into excess methanol. The polymer obtained was filtered and dried under vacuum. For the copolymeriza-tion to determine the reactivity ratio the conversion was limited to less than 10%. Five copolymers of PEA and PEMA (abbreviated as PPEAX-MA, where X indicated the mole fraction of PEA) having different mole fraction of the monomers in the feed ranging from 0.15 to 0.85 were pre-pared.

Analytical Measurements. ¹H-NMR spectra of the copoly-mers were recorded on JNM-LA 300WB FT-NMR (JEOL) at 300 MHz at around 25 °C. CDCl₃ was used as solvent and tetramethylsilane served as an internal standard. Differential scanning calorimetry (DSC) was analyzed by TA series DSC 2010 instrument under nitrogen atmosphere at a heating rate of 10 °C/min. Molecular weights (MW) and polydispersity index (M_w/M_n) of the polymers were determined using a Waters M 77251, M510 gel permeation chromatography (GPC) equipped with four Styragel columns (HR0.5, HR1, HR3, and HR4) at 40 °C using tetrahydrofuran (HPLC grade) as an eluent at a flow rate of 1 mL/min and calibrated relative to polystyrene standards.

Results and Discussion

PPEA or PPEMA Homopolymers. Figure 1 and Figure 2 showed the ¹H-NMR spectra of PPEA[poly(2-phenylethyl acrylate)] or PPEMA[poly(2-phenylethyl methacrylate)],
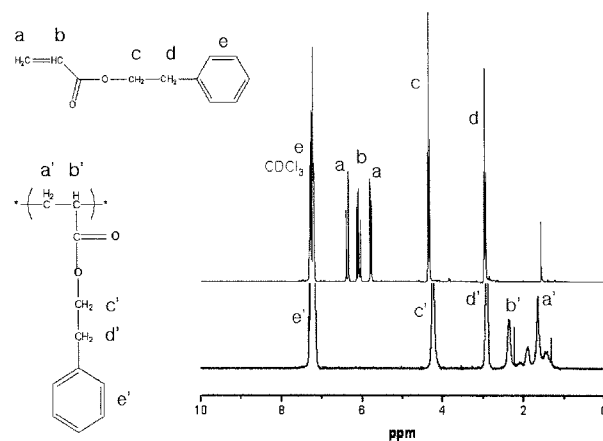

Figure 1. ¹H-NMR spectrum of PEA monomer (top) and PPEA homopolymer (bottom).
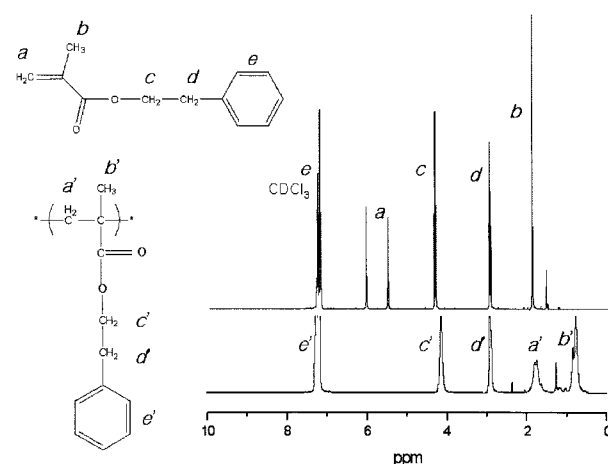

Figure 2. ¹H-NMR spectra of PEMA monomer (top) and PPEMA homopolymer (bottom).

respectively. These homopolymers were reacted for 24 h at 70 °C. In the Table I, all the peaks were assigned. It was confirmed that the vinyl protons (at 6.41 and 5.81 ppm) of PEA were disappeared and new peaks at 1.65 (-CH₂) and

Table I. ¹H-NMR Peaks of PEA, PPEA, PEMA and PPEMA

PEA System				PEMA System			
Peak	PEA (ppm)	Peak	PPEA (ppm)	Peak	PEMA (ppm)	Peak	PPEMA (ppm)
e	7.26	e'	7.24	e	7.26	e'	7.3
a	6.41			a	6.07		
b	6.1			a	5.53		
a	5.81			c	4.35	c'	4.18
c	4.37	c'	4.25	d	2.98	d'	2.95
d	2.98	d'	2.91			a'	1.81
		b'	2.36	b	1.91	b'	0.83
		a'	1.65				

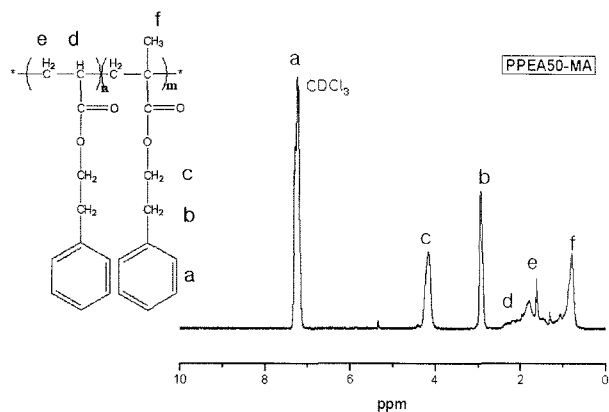**Figure 3.** ^{1}H-NMR spectrum of the PPEA50-MA copolymer.

Figure 4. ^{1}H-NMR spectra of the PPEA-MA copolymers.

2.36 ppm (-CH) were formed after the polymerization. The similar change of peaks was observed also for PEMA.

PEA-PEMA Copolymers (PPEA-MA) and the Composition. For studying the copolymerization behavior of PEA and PEMA, five copolymers of PPEA-MA having different mole fraction of the monomers in the feed ranging from 0.15 to 0.85 were synthesized by a radical polymerization in MEK where the copolymer conversion was limited to less than 10%.

The ^{1}H-NMR spectrum of a representing copolymer, PPEA50-MA made from PEA 50: PEMA 50 mol% in feed, was shown in Figure 3. The aromatic protons (Ar-H, 5H) were shown at 7.29 ppm. The peak at 4.18 ppm should be assigned to the methyleneoxy protons (-CH$_2$-O, 2H) and the other at 2.94 ppm to the methylene protons (-CH$_2$-Ar, 2H) coupled to a phenyl group. The broad resonance signals observed at 2.42-1.20 ppm were for the backbone methylene groups (CH$_2$-, 2H) and methylidene groups (CH-, 1H). The α-methyl groups (-CH$_3$, 3H) were shown at 0.83 ppm. Methylene, methylidene or, especially, α-methyl groups were further divided into several peaks, which would be resulted from the monomer sequence and tacticity distribution of PEMA units.

The Figure 4 illustrated the NMR spectra of PPEA-MA copolymers of various compositions. Methyl protons (3H) at 1.05-0.55 ppm were well separated from other peaks in the spectra, and the intensity was well corresponded with
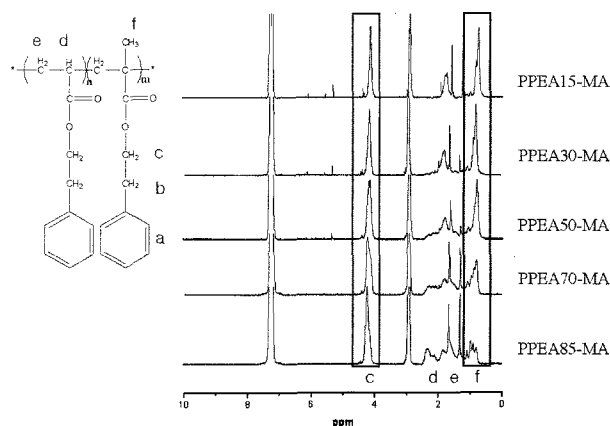
the mol fraction of PEMA in the feed. On the other way, the -OCH$_2$ (2H) protons at 4.18 ppm indicated the same intensity as both PEA and PEMA units possess the same groups. Therefore, the ratio of the methyl protons to the -OCH$_2$ was compared to calculate the mole fraction of PEMA in the PPEA-MA copolymers. The calculated composition of each copolymer was summarized in Table II.

Determination of Monomer Reactivity Ratios. The monomer reactivity ratios (r) are defined whether the growing chain end monomer carrying an active center prefers to add its own monomer or combine with a different monomer. Thus, the type of copolymer formed and the composition will be best predicted from the value of reactivity ratio of the comonomers. As the compositions in the feed and resulting copolymers are known, the reactivity ratios are able to be calculated from the well known copolymerization equation;

$$\frac{[m_1]}{[m_2]} = \frac{[M_1]k_{11}[M_1 \cdot] + k_{21}[M_2 \cdot][M_1]}{[M_2]k_{12}[M_1 \cdot] + k_{21}[M_2 \cdot][M_2]} \tag{1}$$

$$\frac{[m_1]}{[m_2]} = \frac{1 + r_1\dfrac{[M_1]}{[M_2]}}{1 + r_2\dfrac{[M_2]}{[M_1]}} \tag{2}$$

$$r_1 = \frac{k_{11}}{k_{12}}, \quad r_2 = \frac{k_{22}}{k_{21}} \tag{3}$$

Table II. Compositions and Fineman-Ross or Kelen-Tudos Parameters of the PPEA-MA Copolymers

Copolymer	$M_1{}^a$	$m_1{}^b$	$F=M_1/M_2$	$f=m_1/m_2$	$G = F(f\text{-}1)/f$	$H = F^2/f$	$\eta = G/(\alpha + H)$	$\xi = H/(\alpha + H)$
PPEA15-MA	0.15	0.08	0.1765	0.0823	-1.969	0.3786	-0.7000	0.1346
PPEA30-MA	0.30	0.09	0.4286	0.0989	-3.905	1.857	-0.9099	0.4328
PPEA50-MA	0.50	0.30	1.000	0.4245	-1.356	2.356	-0.2830	0.4918
PPEA70-MA	0.70	0.44	2.333	0.7905	-0.6183	6.887	-0.06634	0.7389
PPEA85-MA	0.85	0.67	5.667	2.052	2.905	15.65	0.1606	0.8654

$\alpha = (H_{max} \times H_{min})^{1/2}$. $^a M_1$ is the mol fraction of PEA in the feed. $^b m_1$ is the mol fraction of PEA in the copolymer analyzed by NMR.

where M_1 and M_2 denote the mole fraction of the monomer 1 (PEA in this study) and monomer 2 (PEMA) in the feed, m_1 and m_2 represent the mole fraction of the monomer 1 and monomer 2 in the copolymer, r_1 (PEA) and r_2 (PEMA) are the reactivity ratios of each monomer.

Usually, the reactivity ratio is determined by a graphical method such as by Fineman-Ross[21] or Kelen-Tudos[22] method.

Fineman-Ross (F-R) equation:

$$G = (F^2/f)r_1 - r_2 \qquad (4)$$

where $G = \dfrac{F(f-1)}{f}$ and $F = \dfrac{M_1}{M_2}$, $f = \dfrac{m_1}{m_2}$

G was plotted against (F^2/f) according to eq. (4), r_1 being the slope and r_2 the intercept at the origin.

Kelen-Tudos (K-T) equation:

$$\eta = \left(r_1 + \frac{r_2}{\alpha}\right)\zeta - \frac{r_2}{\alpha} \qquad (5)$$

where η and ξ are mathematical functions of the comonomers molar fractions in the feed and in the copolymer, respectively:

$$\eta = \frac{G}{\alpha + (F^2/f)} \text{ and } \zeta = \frac{(F^2/f)}{\alpha + (F^2/f)} \text{, with}$$

$$\alpha = \sqrt{(F^2/f)_m (F^2/f)_M}$$

$(F^2/f)_m$ and $(F^2/f)_M$ are, respectively, the lowest and the highest values of (F^2/f).

The value of r_1 and r_2 were obtained from the plots of η as function of ξ, r_1 being the intercept at $\xi = 1$ and $(-r_2/\alpha)$ the intercept at $\xi = 0$.[23]

The parameters obtained by the F-R and K-T methods were listed in Table II. And the plot of G against H after the F-R equation was provided in Figure 5 for various copolymers, while the plot of η against ξ after the K-T method was
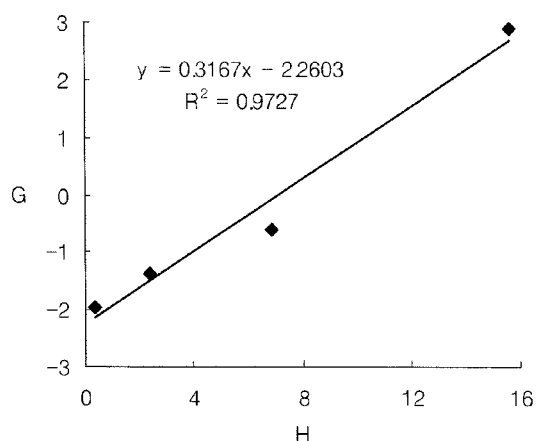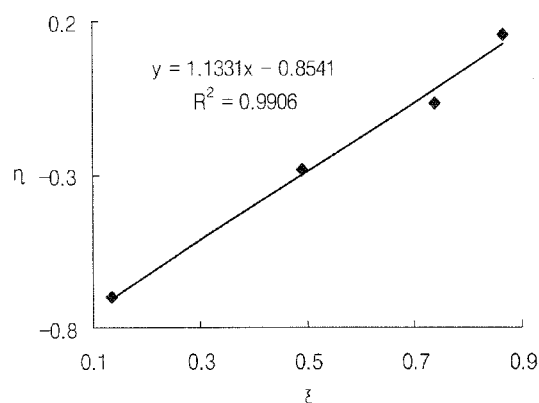

Figure 6. Kelen-Tudos plot for PPEA-MA.

Table III. Reactivity Ratios of PEA and PEMA Calculated by Fineman-Ross or Kelen-Tudos Method

Method	r_1 (PEA)	r_2 (PEMA)	$r_1 r_2$
Fineman-Ross	0.3171 ± 0.041	2.264 ± 0.200	0.72
Kelen-Tudos	0.2800 ± 0.038	2.085 ± 0.185	0.58

shown in Figure 6. The r_1 and r_2 values calculated by the F-R or K-T plot were reported in Table III. The r_1 (PEA) and r_2 (PEMA) values by the F-R method were 0.3171 ± 0.041 and 2.264 ± 0.200 and those by the K-T plot 0.2800 ± 0.038 and 2.085 ± 0.185, respectively. The reactivity ratios calculated by the two methods were not so much different. The coefficient of determination, R^2, is a statistical measure of how well a regression line approximates the real data points. A R^2 value of 1.0 indicates that the regression line perfectly fits the data.[24] The R^2 value was 0.9727 for F-R plot (Figure 5) and 0.9906 for K-T method (Figure 6), thus the K-T method seemed to be more reasonable in this study.

The reactivity ratio values shown in Table III provided a relationship between the PEA content in the feed (M_1) and in the copolymer (m_1) as shown in Figure 7. Since the value of r_1 (PEA) is less than 1 and r_2 (PEMA) is greater than 1, the growing radicals with PEA end will be added preferably by PEMA monomer rather than by PEA monomer. Moreover, the radicals with PEMA end will be added preferably by the same PEMA monomer at a higher rate than by PEA monomer. Therefore, in this copolymerization system of PEA and PEMA, PEMA showed a higher copolymerization rate than PEA did so that the resulting copolymer had always the higher content of PEMA units or lower content of PEA than in the feed. However, the product of r_1 and r_2 is less than 1, which clearly indicated that the system forms a random copolymer with longer sequence of PEMA units in the copolymer chain. However, in our previous homopolymerization study of PEA or PEMA we observed that the homopolymerization rate of PEMA was not faster than PEA did, actually PEA seemed to be rather faster than PEMA.
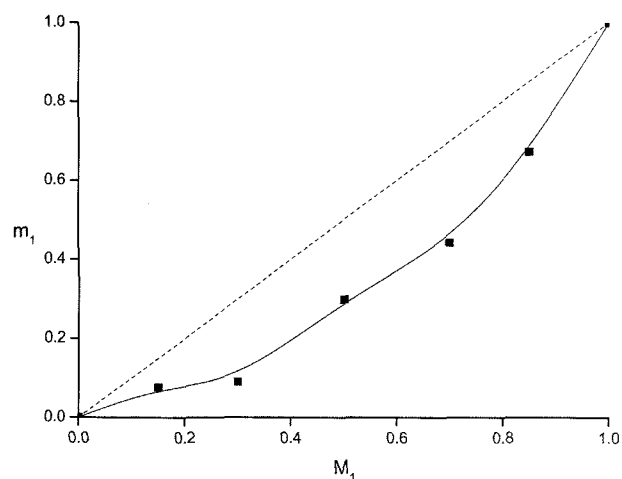

Figure 5. Fineman-Ross plot for PPEA-MA.

Figure 7. PEA composition in the copolymer (m_1) versus in the feed (M_1).

Figure 8. T_g of the PPEA-MA copolymers depending on the compositions.

Such a behavior of PEMA to show a slow homopolymerization rate but higher copolymerization rate was not rare as reported for other monomers too. Relative stability and steric effect of polymerizing radicals determine such a different reactivity in homo- or copolymerization. The reactivity ratios of some alkyl acrylates-methacrylates comonomers were reported in the literature; ethyl acrylate $(r_1=0.22)$-methyl methacrylate $(r_2=2.04)$[25] and methyl acrylate $(r_1=0.40)$-methyl methacrylate.[26] Those values are very similar to the values for PEA $(r_1=0.28)$-PEMA $(r_2=2.085)$ in our study.

Glass Transition Temperatures of PPEA-MA Copolymers. The soft IOL materials are basically soft and flexible polymers or gels. The glass transition temperature, T_g, of materials represents the chain mobility and therefore flexibility. So, the IOL materials should exhibit low T_g. However, if the T_g is too low, the dimension of IOLs can be easily changed to cause the visual problems.

The T_g of the homopolymers and copolymers polymerized for 24 h were determined using DSC. Table IV and Figure 8 summarized the T_g value and molecular weight of the copolymers. All the copolymers showed a single T_g indicating a homogeneous structure. The T_g of PPEA homopolymer was 2 °C and that of PPEMA was 38 °C. The T_g values of the copolymers were decreased proportionally with increase in the mol fraction of PEA in the copolymer. The
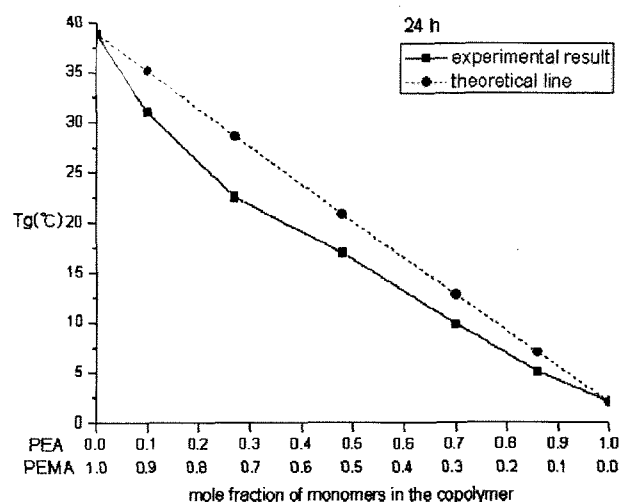
values were a little deviated from the theoretical line defined by the Fox equation.[27]

The weight (M_w) and number-average (M_n) molecular weights and polydispersity index (M_w/M_n) of PPEA, PPEMA homopolymer and PPEA-MA copolymers were determined by GPC as presented in Table IV. The M_w/M_n of these polymers were > 2. The theoretical values of M_w/M_n for polymers produced via radical recombination or radical disproportionation are reported as 1.5 or 2.0 respectively.[28] Methacrylates generally undergo termination by disproportionation $(M_w/M_n=2)$.[29,30] The polydispersity values of PPEA and PPEMA suggested that the tendency for chain termination by disproportionation is greater for PEMA than PEA.

Conclusions

The copolymers of PEA and PEMA having various compositions were synthesized by a free radical solution polymerization at low conversion to investigate copolymerization kinetics of PEA and PEMA. The compositions of copolymers were determined by ^{1}H-NMR analysis. The reactivity ratios of PEA (r_1) and PEMA (r_2) calculated by the Fineman-Ross or Kelen-Tudos method were $r_1=0.3171$ (F-R) or 0.2800 (K-T) and $r_2=2.264$ (F-R) or 2.085 (K-T),

Table IV. The Glass Transition Temperature (T_g) and Molecular Weight of PPEA-MA Copolymers, Polymerized for 24 h

	PEA : PEMA in feed	PEA : PEMA in copolymer	T_g	M_w $\times 10^{-4}$	M_n $\times 10^{-4}$	M_w/M_n
PPEMA	0 : 100	0 : 100	39	9.5	4.4	2.2
PPEA30-MA	30 : 70	27 : 73	23	9.8	4.2	2.4
PPEA50-MA	50 : 50	48 : 52	17	10	3.9	2.6
PPEA70-MA	70 : 30	70 : 30	10	9.9	3.9	2.6
PPEA	100 : 0	100 : 0	2	12	4.8	2.5

respectively. That r_1 is less than 1 and r_2 is larger than 1 indicates that PEMA is more reactive than PEA and the copolymer will be always richer in PEMA units than that provided in the feed. The product value of r_1 and r_2 is less than 1, clearly indicates that the system forms a random copolymer with longer sequence distribution of PEMA units in the copolymer chain. The molecular weight of the polymers were in the range of 10^4-10^5. The T_g of the copolymers increased proportionally with increase of PEMA content. These results would be very useful for the application to foldable soft IOL material.

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