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Polymer 43 (2002) 2691–2697

polymer

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Termini and main-chain composition of monomethoxy-terminated poly(ethylene glycol) studied by two-dimensional column chromatography

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Received 21 September 2001; received in revised form 14 January 2002; accepted 16 January 2002

Abstract

Samples of poly(ethylene glycol) especially those with functionalized ends have dimeric, trimeric, and tetrameric components at twice, three times, and four times as high a molecular weight (MW) as that of the main component. We used two-dimensional column chromatography to evaluate the MW and identify the terminal groups in each component. The first step is high osmotic pressure chromatography to prepare a sufficient amount of fractions that contain different percentages of the multimeric components. In the second step, each of the fractions was characterized by using regular size exclusion chromatography and high-resolution NMR. Decomposition of the chromatogram combined with isolation of the terminal methoxy peak in the NMR spectrum led to unique identification of the terminal groups. We thus found that the monomeric component is monomethoxy-terminated whereas the dimeric and other multimeric components are mostly dihydroxy-terminated. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Poly(ethylene glycol); Chain ends; Size exclusion chromatography

1. Introduction

Many different derivatives of poly(ethylene glycol) (PEG) have been developed and applied to drug delivery systems, bio-compatibilization, device fabrication, etc [1–3]. The derivatives are often triblock and diblock copolymers prepared from PEG diols and monofunctional PEG such as monomethoxy-terminated PEG (MePEG). The functions of the PEG derivatives depend on their composition homogeneity and on the length distribution of the PEG block [4,5]. Presence of components with a molecular weight (MW) twice as high as that of the main component and presence of non-stoichiometric terminal groups will cause unexpected and often undesired changes in the materials made from the PEG derivatives. In particular, presence of PEG diols in the presumably monofunctionalized PEG will lead to, upon chain growth on hydroxy terminals, a mixture of a diblock copolymer and a triblock copolymer.

The high strain of an ethylene oxide ring facilitates both anionic and cationic ring opening polymerization (ROP) [6]. PEG and MePEG with a narrow MW distribution are prepared by anionic ROP with hydroxide and methoxide as initiator. The narrow MW distribution requires a living system without chain termination or transfer reaction. To fulfill this requirement, the initiation reaction must be effectively faster than the propagation reaction. In fact, the initiation step in the polymerization of PEG and MePEG, a nucleophilic attack of ethylene oxide by OH^- and CH_3O^-, is generally faster than the step that follows.

In this report, we employ two-dimensional chromatographic separation to show that commercial MePEG samples have a substantial amount of dimeric, trimeric, and tetrameric components. The first dimension is separation of MePEG using high osmotic pressure chromatography (HOPC) [7–9]. HOPC was developed to preparatively separate a polydisperse polymer by MW. A concentrated solution of the polymer is injected in a large volume into a column packed with porous media. A high osmotic pressure in the concentrated solution will force low-MW components into the stationary phase. The partitioning of the low-MW components into the stationary phase is more efficient in HOPC than it is in size exclusion chromatography (SEC) that relies on the partitioning of each polymer chain at low concentrations. Thus, HOPC enriches high-MW components in the early eluent.

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PII: S0032-3861(02)00078-2

In the second dimension, the separated fractions with different amounts of the multimeric components were characterized by SEC and ^{1}H MNR. The average ratio of the methoxy units to the oxyethylene units in each fraction was evaluated independently from the NMR spectra and the SEC chromatogram. Comparison of the two ratios in different fractions allowed us to determine the composition of the terminals in each of the monomeric and dimeric components. We also show that the right choice of SEC columns with a specific pore size is critical in resolving the multimeric peaks.

2. Experimental

2.1. Materials

Three grades of MePEG were purchased from Aldrich and Fluka. We call them Fluka-402317/1, Aldrich-04620KU, and Aldrich-11229PG. The numbers denote the lot. All of them have a nominal MW of 5000 g/mol. Controlled pore glass (CPG75B) that has a pore size of 85 Å a pore volume of 0.59 cm^3/g and a particle size of 100/200 mesh was obtained from CPG, Inc. CPG75B was soaked in concentrated HCl (Fisher) overnight and rinsed with excess water until pH exceeded 5. HPLC-grade tetrahydrofuran was from Fisher. HPLC-grade $CHCl_3$ was from Pharmco. *d*-Chloroform and perdeuterated benzene were from Acros. Water was purified by using EasyPure (Bernstead).

2.2. High osmotic pressure chromatography

The HOPC system consists of a single-head HPLC pump (SSI, Acuflow II), a column (3.9×300 mm^2) packed with the acid-washed CPG75B, and a fraction collector (Eldex). A 50 wt% solution of MePEG in water was injected at a nominal flow rate of 0.2 ml/min until the whole column was filled with the concentrated solution. Typically, 2.7 g of the solution was injected. Then, the injection was switched to pure water. Each test tube collected five drops of the eluent in the first 10 fractions. Fractions 11 and 12 collected 50 drops each. Fraction 13 to 16 collected 100 drops each. All separations were done at room temperature.

2.3. Size exclusion chromatography

The original MePEG and the fractions separated in HOPC were analyzed by SEC. The chromatography system is composed of Waters 510 pump and a Waters 410 refractive index detector. We used primarily a set of two columns of a fixed pore size (500 Å; 10×250 mm^2; Jordi Associates, Bellingham, MA). The packing materials in these columns were not cross-linked polystyrene particles, but rather cross-linked divinylbenzene particles of diameter 5 μm. For comparison purpose only, we also used another set of two mixed-bed columns of the same dimension from the same manufacturer. The columns were thermostatted at 35 °C. The mobile phase was THF at 1 ml/min. The Jordi 500 Å columns were calibrated with PEG standards (Scientific Polymer Products; Ontario, NY) with MW from 1000 to 40,000 g/mol. The Jordi mixed-bed columns were calibrated with PEG standards with MW from 1000 to 250,000 g/mol.

The concentration of the analyte in the solution injected (10 μl) was around 0.5 wt%. We verified that the chromatograms reduced by the area above the baseline level overlapped with each other when the concentration was below 1.9 wt%. At 3.9 wt%, the peak retention time increased by 0.2% and the full width at half of the full height increased by 5%. The increases were greater at 7.8 wt%.

To dispel a suspicion about our choice of the mobile phase, we also tested the columns with chloroform mobile phase at 35 °C for MePEG. The peak retention time was shorter in $CHCl_3$ by 5% and the resolution was slightly poorer, but otherwise, the shape of the chromatogram was similar. Apparently these columns do not have specific interactions with PEG molecules in THF. For comparison, we also tested MePEG with columns packed with polystyrene–divinylbenzene particles (Phenogel, Phenomenex). The PEG with MW above 6.0×10^3 g/mol exhibited a delayed peak with a sharp rise followed by a long-time tail that extended beyond the solvent peaks. We suspect a strong interaction of PEG molecules with the packing materials. The same columns produced a normal retention curve when the solvent was chloroform. Another advantage of using the THF mobile phase in the SEC system is that THF gives a greater signal than the chloroform mobile phase does.

2.4. NMR analysis

A Bruker DPX-300 spectrometer was used to obtain proton NMR spectra for MePEG and separated fractions. The solvent was perdeuterated benzene (d_6-benzene). Aldrich-11229PG and its separated fractions were analyzed at 28 °C. Aldrich-04620KU, Fluka-402317/1, and their separated fractions were analyzed at 35 °C. In d_6-benzene, the methoxy peak at 3.24 ppm was isolated from the huge methylene peak at 3.60 ppm that corresponds to oxyethylene units. An example is shown in Fig. 1 for unfractionated Aldrich-04620KU. The integrals I_{CH_3O} at 3.27–3.19 ppm and $I_{CH_2CH_2O}$ at 3.28–3.90 ppm were calculated in each spectrum. To obtain an NMR spectrum with an adequate resolution between the two peaks the concentration of the polymer was held low (<0.2 wt%). Two hundred and fifty-six scans were used for all of the samples except for fractions 1 and 2 of Aldrich-04620KU and Fluka-402317/1. In the latter, 512 scans were used. The test tubes were spun at 20 Hz. We also tried *d*-chloroform as a solvent but the methoxy peak overlapped with the tail of the methylene peak.

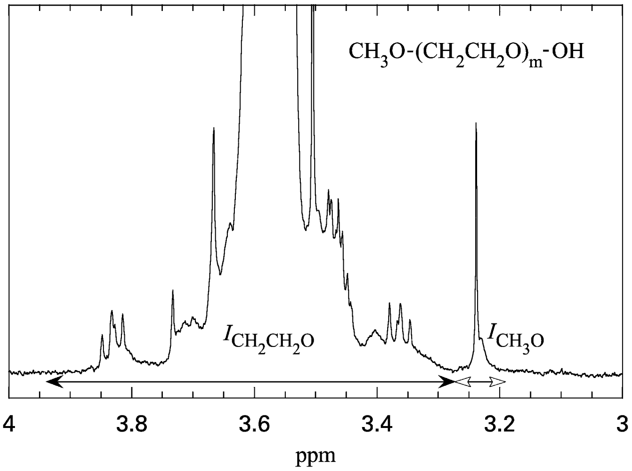

Fig. 1. ^{1}H NMR spectrum of Aldrich-04620KU in perdeuterated benzene.

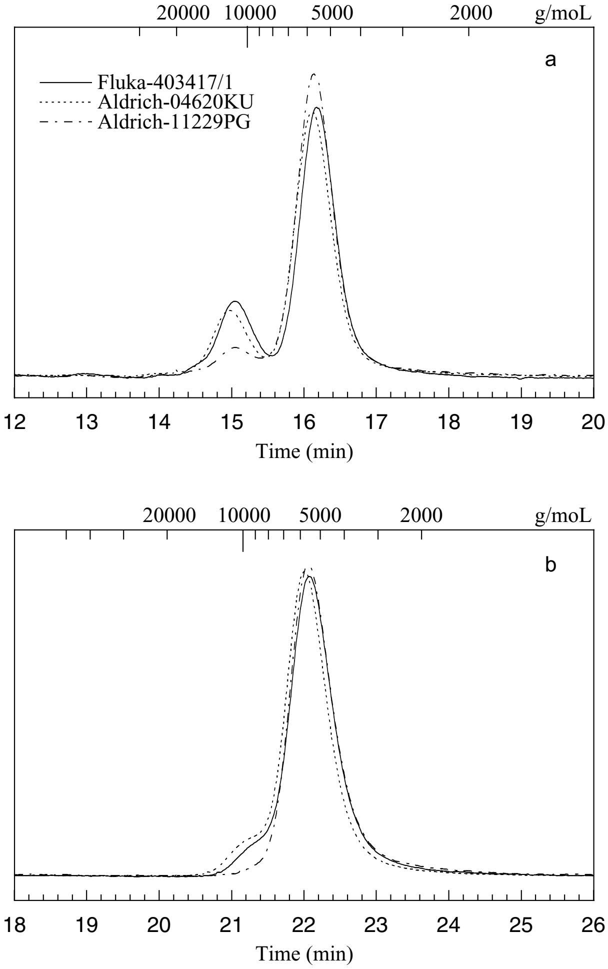

Fig. 2. SEC chromatograms for three grades of MePEG obtained with (a) 500 Å columns and (b) mixed-bed columns. The upper axis shows the MW (PEG).

3. Results and discussion

3.1. Comparison of two sets of SEC columns

Two parts of Fig. 2 compare the chromatograms obtained for the three original samples of MePEG. Each curve is normalized by the area under the peak. Part (a) was obtained with the 500 Å columns, and part (b) with the mixed-bed columns (also applies to Fig. 3). It is apparent in (a) that MePEG has a dimeric component at twice as high a MW as that of the main peak. The samples have a low-MW tail as well. In contrast, the dimeric component shows up only as a shoulder in (b), even for the sample with the largest percentage of the dimeric peak. In the sample with the smallest dimeric peak, the shoulder is almost absent in (b). Compared at the same total column length the mixed-bed columns lack the number of plates needed to resolve the two components, making us believe that the MePEG samples are nearly monodisperse. Table 1 lists M_n, M_w and the polydispersity M_w/M_n, where M_w and M_n are the weight-average MW and number-average MW, respectively. The mixed-bed columns report an artificially low polydispersity for the first two samples of MePEG that have a more dimeric component than the last sample.

We did preparative separation of MePEG by HOPC. HOPC produced early fractions enriched with high-MW components. Enrichment was different from fraction to fraction. The separated fractions were then characterized by off-line SEC with the two sets of columns. Fig. 3 compares the results for fractions 2, 3, and 4 obtained from 04620KU. The difference between the two sets of columns is more obvious compared with that in Fig. 2.

In addition to the two peaks with the peak retention time t_R at 16.1 (main component) and 15.0 min in the chromatogram of the unfractionated MePEG (Fig. 2(a)), we observe in Fig. 3(a) two more components to the left of the dimeric peak. One has a distinct peak at 14.1 min in fractions 2 and 3 and the other appears as a shoulder between the two components. Although HOPC separated MePEG by MW the peak positions barely moved from fraction to fraction. Instead, the relative heights changed.

Using the numerical analysis method that we will describe later we can find t_R for each of the four components. We thus estimated the degrees of polymerization (DP) of the four components with reference to PEG standards as 523, 397, 273, and 130, respectively. Their ratio is 4.01:3.05:2.09:1. The four components correspond

Table 1
Average molecular weights of three grades of MePEG

Sample	Columns	M_n (g/mol)	M_w (g/mol)	M_w/M_n
Fluka-402317/1	500 Å	5.9×10^3	6.7×10^3	1.15
	Mixed-bed	4.9×10^3	5.5×10^3	1.12
Aldrich-04620KU	500 Å	6.0×10^3	6.8×10^3	1.14
	Mixed-bed	5.3×10^3	5.9×10^3	1.12
Aldrich-11229PG	500 Å	5.4×10^3	6.0×10^3	1.12
	Mixed-bed	4.7×10^3	5.3×10^3	1.12

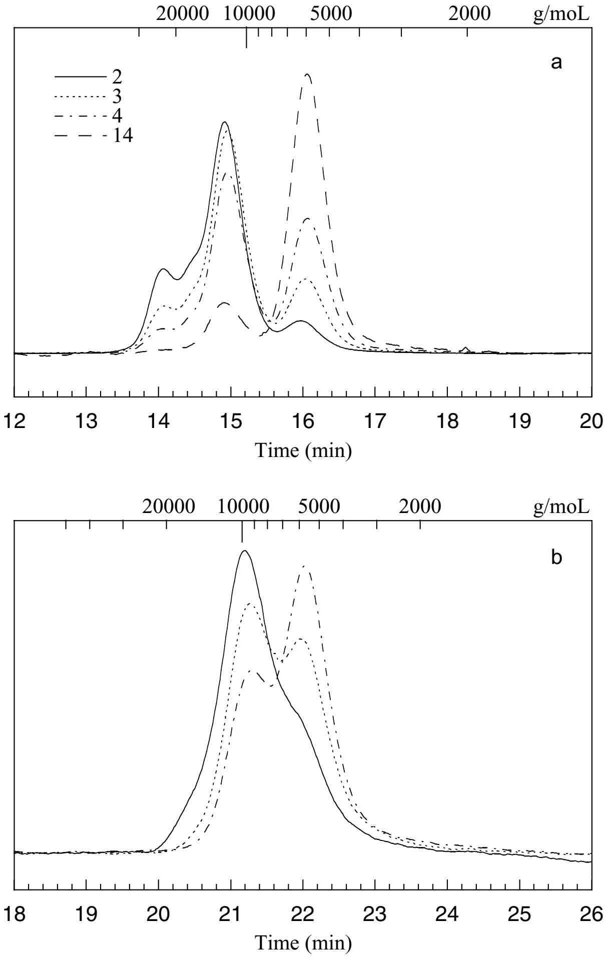

Fig. 3. SEC chromatograms obtained with (a) 500 Å columns and (b) mixed-bed columns for some of the fractions separated from Aldrich-04620KU by HOPC. The numbers in the legend denote the fraction number. The upper axis shows the MW (PEG).

to tetrameric, trimeric, dimeric, and monomeric components. The DP of the tetrameric, trimeric, and dimeric components were obtained from the average t_R of fractions 2 to 6. The DP of the monomeric component was obtained from t_R of the original sample.

In Fig. 3(a), we also present the chromatogram of fraction 14 as a long-dashed line. Compared with the early fractions the monomeric component is more significant and the low-MW tail is greater. The trimeric and tetrameric peaks are almost absent.

In the chromatograms obtained by using the Jordi mixed-bed columns (Fig. 3(b)), however, the trimeric and tetrameric components are not observed as distinct peaks even in the early fractions. Moreover, transition in the relative heights of the dimeric and main peaks from fraction to fraction is obscured.

We thus find that using columns with a fixed pore size is imperative to avoid a false conclusion on the MW distribution of the MePEG samples. The following analysis was performed solely with the 500 Å-pore columns.

3.2. Decomposition of chromatograms

We decomposed each chromatogram into four components. Thus we could estimate MW the peak broadness and the area of each component.

3.2.1. Molecular weights of individual components

We explain here how we estimated MW of the main component and the other multimers through numerical analysis of the SEC chromatograms. The procedure is explained for unfractionated 04620KU and its fraction 3 obtained in HOPC. Their SEC chromatograms are presented as solid lines in Figs. 4 and 5, respectively. As we will learn later the four major components were identified in these samples. We label them as components 4 to 1 in the elution order.

The MW of component 1 was evaluated from the normalized chromatogram $y(t)$ ($\int y(t)\mathrm{d}t = 1$; t is the retention time) in Fig. 4. We fitted the main peak with a Gaussian peak $A_1 f(t; t_1, \sigma_1)$, where A_i is the area, and $f(t; t_i, \sigma_i)$ is a normalized Gaussian profile with a mean t_i and a standard deviation σ_i for component i. We chose the lower and upper limits, τ and τ' in the curve fitting to represent a good part of the main peak as indicated by the two slant lines in Fig. 4 and minimized the residual error by adjusting τ and τ'. Typically, τ was close to the local minimum on the left of the main peak and τ' was close to the point where the tailing of the main peak becomes obvious. The optimal fitting (dashed line) resulted in $t_1 = 16.124$ min and $\sigma_1 = 0.245$ min. The DP at the peak MW (M_p) is thus calculated as 130. The dash-dotted line in the figure is the residual, $y(t) - A_1 f(t; t_1, \sigma_1)$.

The low-MW tail of MePEG has a broad and skewed peak in the residual curve. We obtained M_n of component 1 with the tail portion included as 5395 g/mol, slightly lower than M_p of component 1. This M_n gives DP = 123.

The MW of components 2 to 4 were evaluated as illustrated in Fig. 5. We first fitted the peak on the left of

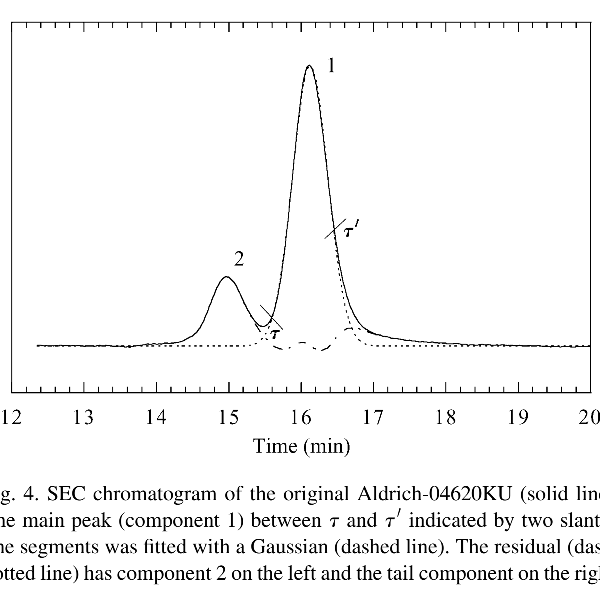

Fig. 4. SEC chromatogram of the original Aldrich-04620KU (solid line). The main peak (component 1) between τ and τ' indicated by two slanted line segments was fitted with a Gaussian (dashed line). The residual (dash-dotted line) has component 2 on the left and the tail component on the right.

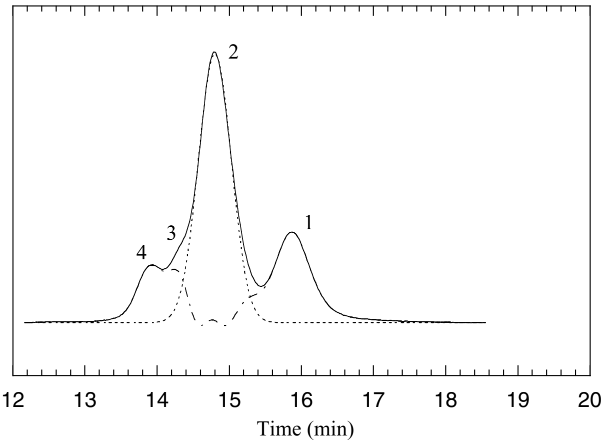

Fig. 5. SEC chromatogram of fraction 3 obtained by HOPC from Aldrich-04620KU (solid line). The dimeric peak (component 2) was fitted with a Gaussian (dashed line). The residual (dash-dotted line) has two components on the left.

component 1 by a Gaussian profile $A_2f(t;t_2,\sigma_2)$ and obtained $t_2 = 14.962$ min and $\sigma_2 = 0.228$ min (dashed line). The residual, $y(t) - A_2f(t;t_2,\sigma_2)$, displayed as a dash-dotted line has two peaks (components 4 and 3) on the left of the first zero. We fitted this bimodal peak with $A_3f(t;t_3,\sigma_3) + A_4f(t;t_4,\sigma_4)$ and obtained $t_3 = 14.450$ min, $\sigma_3 = 0.117$ min; $t_4 = 14.080$ min, $\sigma_4 = 0.203$ min. There is at least one more peak to the left of component 1 but its area is small.

We repeated the analysis for fractions 2, 4, 5, and 6. The M_p of the components 4, 3, and 2 obtained from the average of the peak retention times for the five fractions and the corresponding DP are listed in Table 2. From the values of DP we can identify the four peaks as tetrameric (PEG_4), trimeric (PEG_3), dimeric (PEG_2), and monomeric (PEG_1) components. Because fraction 1 had only a small amount (0.2 mg) we neglected it in the analysis.

The peak retention time was identical within experimental errors from fractions 2 to 6. The fraction-to-fraction variation of t_2 is typically 0.03 min, which is the largest among the four components. This fact indicates that each component of MePEG has a narrow MW distribution; HOPC's resolution was consumed in separating different components rather than separating different MW components within the narrow peak.

The higher-MW components have a smaller σ_i. The distribution is ascribed to the band broadening in SEC and the MW distribution. We cannot say which of the two factors has a greater contribution to σ_i; they have a similar MW dependence.

Table 2
Peak molecular weights and DP of the four components in 04620KU

Component	Symbol	M_p (g/mol)	DP	Ratio
1	PEG_1	5734	130	1
2	PEG_2	11,993	273	2.09
3	PEG_3	17,470	397	3.05
4	PEG_4	23,018	523	4.01

3.2.2. Areas of individual components

We evaluated the area of each component in three-step decomposition of the chromatogram. First, the PEG_1 peak was fitted with a Gaussian to estimate A_1. The area A_{1t} of the low-MW tail was evaluated as the residual of the fitting to the right of the last zero point. Then, the PEG_2 peak in the original chromatogram was fitted with a Gaussian to estimate A_2. Finally, A_3 and A_4 were evaluated in the curve fitting of $y(t) - A_2f(t;t_2,\sigma_2)$. We performed this analysis for the original 04620KU and its fractions 2 to 6. In the decomposition of unfractionated MePEG which has a small $A_3 + A_4$, we did not decompose the left part of $y(t) - A_2f(t;t_2,\sigma_2)$.

In Fig. 5, we notice that the dash-dotted line (residual) has a hump on the left of component 1 peak. We ascribe it to the low-MW tail of component 2 that was not included in the Gaussian fitting. Its area A_{2t} was evaluated by subtracting $A_1 + A_{1t}$ from the area in the residual curve to the right of the last zero. We combine A_1 and A_{1t} for PEG_1 and A_2 and A_{2t} for PEG_2. Table 3 lists the area of each component in the original 04620KU and its fractions. The total area, $A_{total} = (A_1 + A_{1t}) + (A_2 + A_{2t}) + A_3 + A_4$ is close to unity for all the fractions.

3.3. Terminal chemistry of individual components

We characterized original 04620KU and separated fractions by NMR. The results from the NMR analysis and the area analysis of the SEC chromatograms were used to determine the terminal chemistry in each component.

In the NMR spectrum, we evaluate the number of methoxy units per oxyethylene unit, x_{NMR} by

$$x_{NMR} = \frac{I_{CH_3O}/3}{I_{CH_2CH_2O}/4} \qquad (1)$$

Table 3 lists x_{NMR} for 04620KU and its separated fractions. Because I_{CH_3O} of fraction 2 is too low to obtain the accurate value, we do not list it. It is removed from the following analysis as well.

From the SEC chromatogram and the Gaussian fitting, we have another estimate of the same quantity. We assume that

Table 3
Areas of the four components in the original 04620KU and its fractions 2 to 6

	$A_1 + A_{1t}$	$A_2 + A_{2t}$	A_3	A_4	A_{total}	x_{NMR}
Fraction 2	0.115	0.633	0.070	0.181	0.999	
Fraction 3	0.238	0.604	0.045	0.111	0.997	0.00220
Fraction 4	0.422	0.491	0.027	0.061	1.000	0.00360
Fraction 5	0.563	0.384	0.017	0.038	1.002	0.00482
Fraction 6	0.681	0.292	0.009	0.019	1.001	0.00573
Original	0.815	0.177	0.008	0.008	1.000	0.00669

Table 4
Average of $n = x_{\mathrm{SEC}}/x_{\mathrm{NMR}}$ in fractions 3 to 6 and original 04620KU

$p_2 \backslash p_1$	0.8	0.9	1	1.1
0	93.0	105	116	128
0.1	98.9	111	122	134
0.2	105	116	128	139
0.3	110	122	134	145

Table 5
Standard deviation of $n = x_{\mathrm{SEC}}/x_{\mathrm{NMR}}$ in fractions 3 to 6 and original 04620KU

$p_2 \backslash p_1$	0.8	0.9	1	1.1
0	3.61	4.06	4.51	4.96
0.1	1.40	1.25	1.26	1.42
0.2	5.52	5.12	4.73	4.35
0.3	9.93	9.51	9.10	8.69

DP for components 1, 2, 3, and 4 are n, $2n$, $3n$, and $4n$, respectively, where n is DP of PEG$_1$. Let p_i ($0 \le p_i \le 2$) be the number of methoxy terminals per chain in component i. Then, x_{SEC} defined as

$$x_{\mathrm{SEC}} = \frac{p_1(A_1 + A_{1\mathrm{t}}) + p_2(A_2 + A_{2\mathrm{t}})/2 + p_3A_3/3 + p_4A_4/4}{(A_1 + A_{1\mathrm{t}}) + (A_2 + A_{2\mathrm{t}}) + A_3 + A_4} \tag{2}$$

gives the average number of methoxy terminals per n oxyethylene units in a given sample. Note that x_{SEC} relies on p_1 through p_4 for the estimate of the number of methoxy terminals whereas x_{NMR} gives it directly. The following relationship should hold:

$$x_{\mathrm{SEC}} = n \times x_{\mathrm{NMR}} \tag{3}$$

Except for those of fraction 2 excluded from the analysis, A_3 and A_4 are small. The effect of these areas on x_{SEC} is further reduced by a factor of 3 or 4. Therefore, x_{SEC} is insensitive to p_3 and p_4. We arbitrarily set p_3 and p_4 to 0 when estimating p_1 and p_2.

With different combinations of p_1 and p_2, we evaluated $n = x_{\mathrm{SEC}}/x_{\mathrm{NMR}}$ for the original 04620KU and each of fractions 3 to 6. Tables 4 and 5 list the average and the standard deviation of n in these five estimates for some values of p_1 and p_2. The best choice of p_1 and p_2 should give the average of n close to the number-average DP of component 1 (123, including the tail portion) and the smallest standard deviation of n. These criteria lead to $p_1 = 1$ and $p_2 = 0.1$.

We also did the same analysis for the other two samples of MePEG. The results for the optimal p_1 and p_2 are listed in Table 6. In Fig. 6, we plot x_{SEC} thus obtained as a function of x_{NMR} for the original MePEG and its separated fractions. For each sample of MePEG the data are fitted by a straight line through the origin. The slope of the line gives n the DP of PEG$_1$. The good fitting indicates that the values of p_1 and p_2 thus estimated are sound.

Table 6
Results of p_1 and p_2 analysis for three grades of MePEG

MePEG	n (SEC)	$n = x_{\mathrm{SEC}}/x_{\mathrm{NMR}}$	p_2	p_1
Aldrich-04620KU	123	122	0.1	1
Aldrich-11229PG	123	122	0	1
Fluka-403417/1	119	117	0	1

To determine the terminal groups of PEG$_3$ and PEG$_4$, we need a fraction that contains as little PEG$_1$ as possible. We employed preparative SEC on the early fractions of HOPC separated from 04620KU. HOPC cannot be used to separate these fractions because it would require a much greater amount of the polymer for injection. In the preparative SEC, we prepared an 8.9 wt% solution in THF by dissolving the first 8.8 mg of MePEG obtained in HOPC and injected 50 μl of the solution into the Jordi 500 Å columns the same as those used in the analytical SEC. When the polymer was detected, we collected the eluent into different test tubes. The test tube was changed every minute. We collected seven test tubes. The first two test tubes did not have a polymer. The polymer in the next two test tubes was combined to make fraction I. The rest are fractions II to IV. Another batch of preparative SEC was conducted for an 8.5 wt% solution prepared from the first 10.6 mg of MePEG from HOPC. The purpose was to obtain another fraction I. Two fractions I were combined to make a sufficient amount for further analysis.

Fig. 7 shows the SEC chromatograms for fractions I to IV. Fraction I does not have a distinct peak for PEG$_1$ as expected. $I_{\mathrm{CH_3O}}$ in its NMR spectrum (not shown) is close to the noise level. The small $I_{\mathrm{CH_3O}}$ can be ascribed to PEG$_2$ ($p_2 = 0.1$). We therefore can conclude that PEG$_3$ and PEG$_4$ are almost free of methoxy terminals. Our

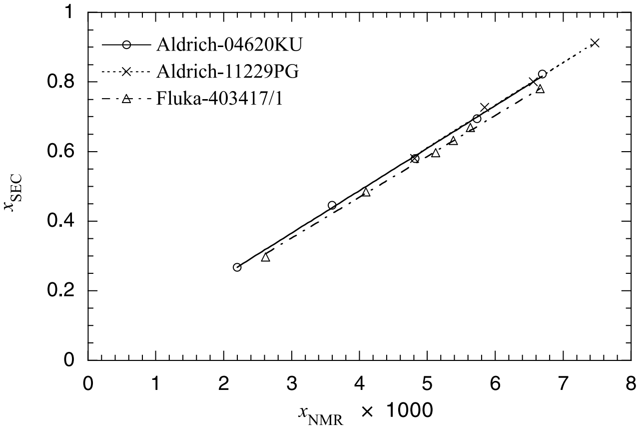

Fig. 6. Comparison of composition analysis by NMR and SEC. The abscissa x_{NMR} is the number of methoxy units per oxyethylene unit evaluated from the NMR spectrum. The ordinate x_{SEC} is the number of methoxy units per n oxyethylene units of PEG$_1$ evaluated from the SEC chromatogram. Circles, crosses, and triangles correspond to the original sample and separated fractions for Aldrich-04620KU, Aldrich-11229PG, and Fluka-403417/1, respectively. The points were fitted by a straight line through the origin.

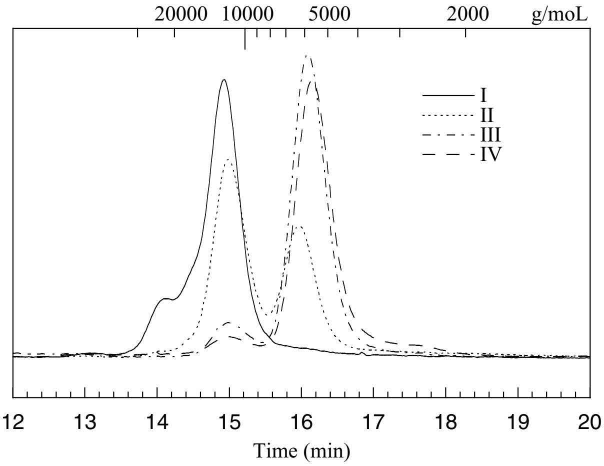

Fig. 7. SEC chromatograms of fractions I to IV obtained in preparative SEC for the early fractions of HOPC separation of Aldrich-04620KU. The upper axis shows the MW (PEG).

assumption of $p_3 = p_4 = 0$ in estimating p_1 and p_2 is thus substantiated.

In Fig. 7, the peak position of each component shifts to a longer time for later fractions in stark contrast to almost no change in Fig. 3(a). The difference suggests a difference in the separation mechanism of HOPC and SEC. When it is necessary to separate different MW components in a given polymer sample that is often multimodal, HOPC can readily separate each component without being complicated by the separation within each component. In the separation of poly(vinyl pyrrolidone), a similar trend was observed [10]. Also note a difference in the processing capacity. Loading of the solid polymer was 1.35 g in HOPC as opposed to 3.6 mg in preparative SEC although the column volume in the latter was about eleven times as large.

Most chains in PEG_2 have OH terminals at both ends (HO–PEG_2–OH). The diol termination of PEG_2 suggests presence of H_2O in the polymerization of MePEG. Water would initiate the polymerization on both sides of the oxygen atom resulting in a component twice as high in MW compared with the one that starts with CH_3O^-. We speculate that PEG_4 was produced in coupling of two molecules of PEG_2 and therefore free of methoxy. The origin of PEG_3 representing a smaller amount of the sample is not clear.

Our analysis does not distinguish 100% pure Me–PEG–OH from a 50–50 mixture of Me–PEG–Me and HO–PEG–OH for instance. It is, however, highly unlikely that PEG_1 contains Me–PEG–Me.

4. Conclusion

We established an analytical method to characterize multiple components in a given polymer sample. The MWs of individual components and their terminal chemistry can be determined. The multimers are likely present in polymers prepared by ROP because of imperfect control of reaction conditions such as the initiators. Our method can be applied to a broad range of polymers made by ROP. The information may shed light on the polymerization mechanism.

HOPC adopted in the present study was optimized for enriching multimeric components in the early fractions. A separate study is under way to remove the multimeric components and obtain pure $MePEG_1$ in late fractions.

Acknowledgements

We appreciate financial support from NSF-DMR 9876360. We thank Professor Y. Kimura at Kyoto Institute of Technology for illuminating discussion and Jordi Associates for some of the SEC columns.

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