

Determination of Mean Molecular Weight of Polyethylene Glycols by Several Physical Methods

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Synopsis

Several physical methods were used for the determination of the mean molecular weight of polyethylene glycols (PEG). Gas chromatography proved to be the best method to obtain a molecular weight of PEG lower than 600 by using Tenax as a stationary phase. Reverse gas chromatography was long but valid for PEG between 400 and 3000. Viscosity measurements gave more suitable values by taking different Mark-Houwink constants according to the molecular weight of PEG. Gel permeation chromatography using the universal calibration method was shown reliable, and by means of three μ -Styragel phases (100, 500, and 10^4 Å) the molecular weight range between 200 and 20,000 was covered. Infrared measurements were related to the molecular weight by taking the OH absorbing band, and a result for PEG of 5000 or less was obtained. Vapor pressure measurements as made in tonometry were an accurate and sensitive method.

INTRODUCTION

The molecular weights of polyethylene glycol (PEG) differ according to the manufacturing process. The ethylene oxide polymerization by using ethylene glycol as an initiator provides PEG mixtures whose molecular weight may vary between 400 and 100,000. Of course, identification and analysis of PEG mixtures, as well as the molecular weight determination, are of importance. This difficult problem requires the use of several different analysis methods, such as chemical and physical methods. These methods differ in suitability according to the molecular weight for PEG. In general, chemical methods consist of measuring the number of functional groups such as terminal hydroxyl (OH).

We attempted to show the efficiency and the sensitivity of different physical methods for the determination of molecular weight of PEG mixtures: gas phase chromatography as a direct method and as a "reverse" method; viscosity and gel permeation chromatography; vapor pressure measurements as in tonometry; and IR and NMR studies.

IDENTIFICATION AND ANALYSIS OF PEG BY GAS CHROMATOGRAPHY

Gas chromatography has been often used for the analysis of PEG of molecular weight below 400. PEG has been injected either as pure^{1,2} or as silylation after derivatization.³⁻⁵

We attempted to improve this work by using a more recent stationary phase,⁶ made of a porous polymer based on 2,6-diphenyl-*p*-phenylene oxide, called Tenax (AKZO, Holland). We verified first the interesting fact that the peaks are sharper for pure PEG than for their silyl ether derivatives.

Identification of PEG by Isothermal Chromatography

Under isothermal conditions, the retention time of any solute is defined by⁷

$$\frac{t_r - t_g}{t_g} = A \exp \frac{\overline{\Delta H}_{\text{des}}^0}{RT} \quad (1)$$

where A is a constant characterizing the solute, $\overline{\Delta H}_{\text{des}}^0$ is the standard molar enthalpy of desorption for the solute, at temperature T , and R is the ideal gas constant. By working with different temperatures, it was possible to obtain $\overline{\Delta H}_{\text{des}}^0$ values for several PEGs (Table I).

Identification and Analysis of PEG by Programmed Temperature Chromatography

Operational conditions were as follows: Heating rate $b = 8^\circ\text{C}/\text{min}$; initial column temperature $T_0 = 423\text{ K}$. PEG 200 and 300, 1 m long; Tenax, 0.65 g; t_g , 38 sec. PEG 400, 0.5 m long; Tenax, 0.32 g; t_g , 21 sec.

Retention temperatures T_r were calculated by using the known relation⁷

$$bt_g = \sum_{T_0}^{T_r} \left[1 + A \exp \frac{\overline{\Delta H}_{\text{des}}^0}{RT} \right]^{-1} \Delta T \quad (2)$$

where ΔT is the temperature increment (1°C). This calculation and the A and $\overline{\Delta H}_{\text{des}}^0$ values shown in Table I as well were achieved by using a pocket computer. The measured values for retention temperatures and the corresponding calculated values were in good agreement.

Relative response factors k were measured for pure PEG, as well as for DEG 106, TEG 150, TAG 194, by using the third solute, TAG 194, as an internal standard. For these solutes, we observed a linear variation for relative response factors against the molecular weight. For higher molecular weight PEG members, the values were extrapolated according to that law.

The average weight percent values found for different polyethylene glycols in commercial samples of PEG 200, 300, and 400 (FLUKA) are shown in Table II.

The mean molecular weights \overline{M}_n and \overline{M}_p calculated for commercial PEG are shown in Table III.

Chromatograms are shown in Figure 1 for PEG 200 and PEG 300. Gas chromatography is the best method for identification and measurement for PEG mixtures, and these chromatograms showed its limitations. A column with Tenax in it can work for PEG 300 and PEG 400 as usual. But PEG 600 needed too high a temperature, and not all the components of the mixture appeared in our chromatograms.

TABLE I
Desorption Thermodynamic Characteristics of PEG

	DEG	TEG	TAG	PAG	HEG	HAG	OEG	NEG	DAG
M	106	150	194	238	282	326	370	414	458
$\overline{\Delta H}_{\text{des}}^0$, kcal/mole	12.1	13.5	15.2	16.2	17.4	18.7	20	21.3 ^a	22.6 ^a
$A \times 10^7$	46	41	25	17	11	6	4	2.9 ^a	1.9 ^a

^a Extrapolated values.

TABLE II
Quantitative Analysis and Retention Temperature for Commercial PEG

Solutes	DEG	TEG	TAG	PAG	HEG	HAG	OEG	NEG	DAG	UDEG	DDEG	TDEG
<i>M</i>	106	150	194	238	282	326	370	414	458	502	546	590
<i>k</i>	0.8	0.9	1	1.1 ^a	1.2 ^a	1.3 ^a	1.4 ^a	1.5 ^a	1.6 ^a	1.7 ^a	1.8 ^a	1.9 ^a
PEG 200												
wt %	4.3	22.6	31	25.7	16.4							
<i>T_r</i> , K	453	481	511	538	564							
PEG 300												
wt %		3.2	10.9	19.8	24.1	26.7	15.3					
<i>T_r</i> , K		481	511	538	564	587	616					
PEG 400												
wt %			1.6	4	8.9	16.2	20.2	20.8	17.2	11.1		
<i>T_r</i> , K			456	481	501	520	538	556	572	588		

TABLE III
 \bar{M}_n and \bar{M}_p for Commercial PEG

	PEG 200	PEG 300	PEG 400
\bar{M}_n	193.5	272	371
\bar{M}_p	206	285	386

IDENTIFICATION OF PEG BY REVERSE GAS CHROMATOGRAPHY

Several PEG mixtures were studied by "reverse gas chromatography." This method consists in taking every PEG mixture as a stationary liquid and using these columns to chromatograph some paraffins and alcohols.

Variation of Relative Retention Time for Alcohols with Mean Molecular Weight of PEG

The variation of relative retention time for some paraffins and alcohols as a function of the mean molecular weight of PEG used as stationary liquid is shown in Figure 2. We can see a retention time increase for paraffin and a decreasing one for alcohols with increasing molecular weight of PEG. But there is an asymptotic tendency for alcohol retention time when the molecular weight of PEG reaches 4,000.

This variation of relative retention time for alcohols as a function of the mean molecular weight of PEG can be expressed in several equations. The first is

$$\frac{t_r - t_g}{t_g} = A \cdot \bar{M}_n^a \quad (3)$$

where A and a are two constants characterizing a solute such as alcohol.

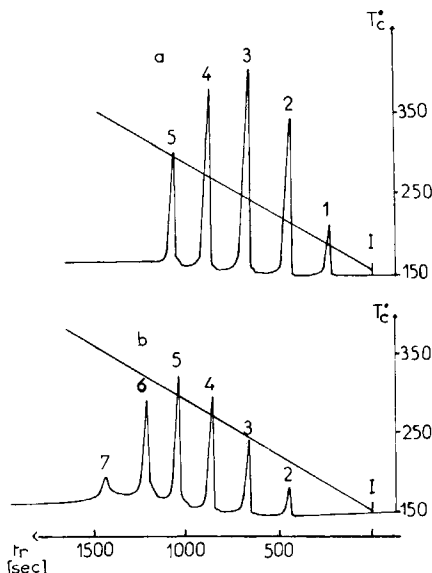


Fig. 1. (a) Chromatogram of PEG 200; $T_0 = 423$ K, $L = 1$ m. (b) Chromatogram of PEG 300; $T_0 = 423$ K, $L = 1$ m. $t_g = 38$ sec; Tenax as stationary phase.

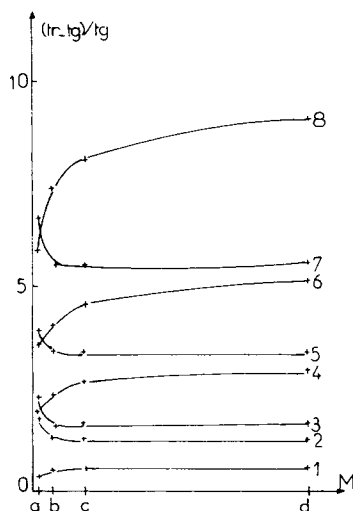


Fig. 2. Variation of $(t_r - t_g)/t_g$ for paraffins and alcohols against mean molecular weight of PEG, $T = 1000^\circ\text{C}$: (a) 400; (b) 1500; (c) 4000; (d) 20,000. Legend: 1, heptane; 2, methanol; 3, ethanol; 4, decane; 5, propanol; 6, undecane; 7, butanol; 8, dodecane.

The second equation was studied in an early paper⁸:

$$\frac{t_r - t_g}{t_g} = B_0 n_O + C_{OH} n_{OH} \quad (4)$$

where B_0 and C_{OH} are two constants characterizing a solute such as an alcohol, and n_O and n_{OH} are the number of O and OH groups in the polymer, respectively.

The third equation is

$$\frac{t_r - t_g}{t_g} = a \ln \bar{M}_n + b \quad (5)$$

where a and b are constants characterizing a solute such as a paraffin.

The values for the constants in these three equations are shown in Tables IV and V.

TABLE IV
Relative Retention Time Against \bar{M}_n or PEG According to Equation (3)^a

	Methanol	Ethanol	<i>n</i> -Propanol	<i>n</i> -Butanol
<i>a</i>	-0.33	-0.32	-0.27	-0.22
<i>A</i>	64.4	82.3	114.4	181.2
Calculated \bar{M}_n Values				
DEG 106	99	108	101	108
TEG 150	132	152	135	150
PEG 400	410	428	405	385
PEG 1500	1274	1527	1394	1510

^a At 60°C . The \bar{M}_n values were calculated with the help of eq. (3) and by using a and A values for the four different alcohols. It seems that *n*-butanol provides the best results for \bar{M}_n .

TABLE V
Constant Values Obtained for PEG According to Equation (5)^a

	<i>n</i> -Octane	<i>n</i> -Nonane	<i>n</i> -Decane
<i>a</i>	1.09	2.42	4.86
<i>b</i>	-3.73	-8.32	-16.2
<i>r</i> ²	0.99	0.99	0.99

^a At 60°C. The \bar{M}_n values calculated by using eqs. (4) and (5) are as follows: DEG 106 = 106 ± 4; PEG 400 = 438 ± 30; TEG 150 = 144 ± 8; PEG 1500 = 1457 ± 60.

Determination of Mean Molecular Weight of PEG by Using Retention Indexes of Alcohols

According to McReynolds,⁹ the retention index of a solute varies with the chemical function number. For PEG, this relationship is as follows:

$$I = I_m + \alpha \cdot n_{OH} \quad (6)$$

Where *I* is the retention index for a solute eluted with a PEG 4000 as a stationary liquid and *I_m* is the retention index for the same solute eluted with a high PEG molecular weight (about 20,000).

The values we found for the retention index of the four alcohols methanol, ethanol, propanol, and *n*-butanol at two temperatures (60 and 100°C) are similar to the values given in an earlier work⁹ (Table VI).

The calculated values of mean molecular weight \bar{M}_n for PEG 400 and PEG 1500 are in good agreement with the results obtained by the other methods. However, the methods using "reverse gas chromatography" have some disadvantages. They require a very long working time and moreover, they are ineffective when the PEG molecular weight is higher than 3000.

MOLECULAR WEIGHT DETERMINATION BY VISCOSIMETRY

Viscosimetry has been used for the determination of the mean molecular weight \bar{M}_v of PEG mixtures.^{10,11} Our work was done with an Ostwald viscosimeter (capillary diameter 0.4 mm) and with chloroform as solvent, at 20°C. The intrinsic viscosity was extrapolated for zero concentration from both the

TABLE VI

	Methanol		Ethanol		<i>n</i> -Propanol		<i>n</i> -Butanol	
	60°C	100°C	60°C	100°C	60°C	100°C	60°C	100°C
α	943	1000	991	1047	957	1017	920	1,035
<i>I_m</i>	880	874	914	909	1015	1015	1118	1,121
PEG 1500	1668 ± 176		1739 ± 122		1516 + 60		1542 ± 40	
PEG 400	397 ± 6		405 ± 5		405 ± 5		403 ± 4	

TABLE VII
Viscosimetry Determination

PEG	20,000	10,000	4000	1500	600	400	300	200
$10^3 \times [\eta], \text{l./g}^a$	64	48	20	9	5.4	4.2	3.8	3.2

^a $[\eta] = K \cdot \bar{M}_v^\alpha$.

TABLE VIII
Viscometry Determination

	α	K	r^2
200 < PEG < 1500	0.57	15×10^{-5}	0.99
1500 < PEG < 20,000	0.75	4.3×10^{-5}	0.99
200 < PEG < 20,000	0.69	7.3×10^{-5}	0.98
200 < PEG < 20,000	0.74	3.75×10^{-5}	ref. 12
200 < PEG < 1500	0.5	20×10^{-5}	ref. 10

reduced viscosity and the logarithmic viscosity (Tables VII and VIII). Our values are in good agreement with the earlier values,¹⁰ the difference between them being not more than 10%. The coefficients K and α in the Mark-Houwink relationship were calculated by using the method of least squares.

The values of earlier workers¹² were quite different from those of others.¹⁰ The explanation of these differences is obvious by considering the variation of the Mark-Houwink parameters against the molecular weight, as shown in Figure 3.

The importance of the variation of the Mark-Houwink coefficients is pointed out by tabulating the \bar{M}_v values corresponding to different polymers in Table IX.

MOLECULAR WEIGHT DETERMINATION OF PEG BY GEL PERMEATION CHROMATOGRAPHY

Gel permeation chromatography (GPC) has been accepted as a relatively rapid and reliable technique for determining the molecular weight distribution of polymers, but the columns used for PEG had a low efficiency.¹³

The model 440 gel permeation chromatograph (Waters Associates) was operated at 20°C using chloroform as the solvent at a flow rate of 1.10 ml/min. Three μ -Sytragel columns of 100, 500, and 10^4 Å (nominal porosity) were used

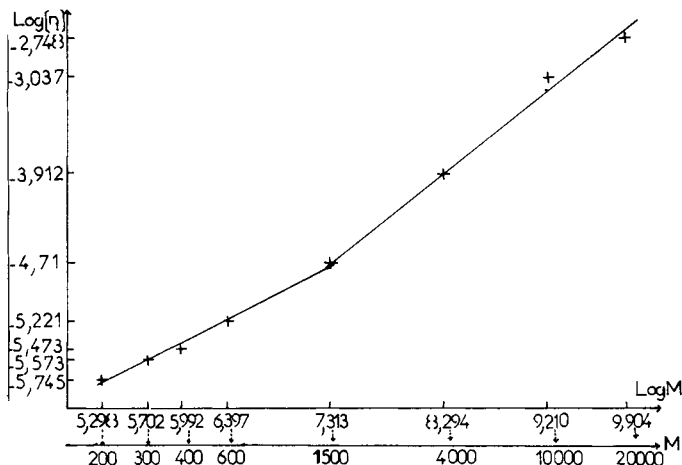


Fig. 3. Log-log plot of intrinsic viscosity η as function of mean molecular weight of PEG.

TABLE IX
 \bar{M}_v Variation with Mark-Houwink Coefficient Values^a

$10^3 \times [\eta], \text{l./g}$	Reference 10	Reference 12	Our values
4.2 ± 0.2	441 ± 40	587 ± 40	450 ± 30
9 ± 0.45	2025 ± 200	1646 ± 200	1317 ± 120
20 ± 1	$10,000 \pm 1000$	4840 ± 300	3600 ± 250

^a Two different errors were made in \bar{M}_v values: the first one due to the error in the $[\eta]$ measurement, and the second due to the choice for the Mark-Houwink coefficients.

in turn, separately. They were 30 cm long. The μ -Styragel recently described¹⁴ has a mean particle diameter of about $9 \mu\text{m}$, and the diameter range is very narrow.

The variation of $\ln M[\eta]$ against the retention time is shown in Figure 4 (curve c for 100 \AA μ -Styragel, curve b for 500 \AA μ -Styragel, and curve a for 10^4 \AA μ -Styragel).¹⁵ For each of these three curves, we can see a linear part¹⁶⁻¹⁹ the equations of which are respectively

$$\begin{aligned}
 100 \text{ \AA } \mu\text{-Styragel, } 150 < \text{PEG} < 800 & \quad \ln M[\eta] = -0.0092t_r + 3.2 \\
 500 \text{ \AA } \mu\text{-Styragel, } 200 < \text{PEG} < 5000 & \quad \ln M[\eta] = -0.027t_r + 15.38 \\
 10^4 \text{ \AA } \mu\text{-Styragel, } 200 < \text{PEG} < 110,000 & \quad \ln M[\eta] = -0.04t_r + 28.5 \\
 & \quad r^2 = 0.99
 \end{aligned} \quad (7)$$

These columns were calibrated with polystyrene standards for 10^4 \AA μ -Styragel and with pure polyethylene glycols (TEG 150, TAG 194, and PEG 238) for 100 \AA μ -Styragel. The theoretical plate number was about 3000, and the theoretical effective plate number reached 500.

By using these calibration curves, while the response factor was equal to 1 for every compound, it was possible to determine the molecular weight distribution for every mixture and the mean molecular weight, \bar{M}_n and \bar{M}_p (Table X), of each.

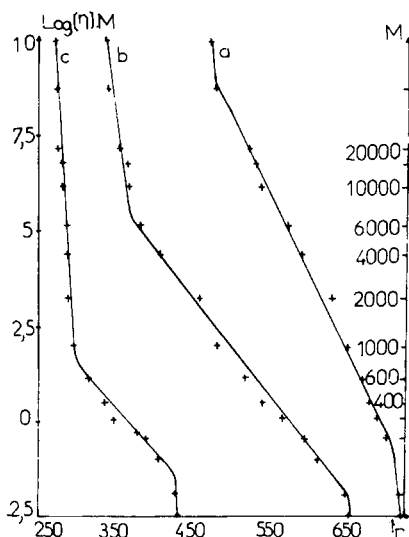


Fig. 4. Log plot of $M(n)$ versus retention time for PEG: (a) 10^4 \AA ; (b) 500 \AA ; (c) 100 \AA μ -Styragel.

TABLE X
 \bar{M}_n and \bar{M}_p Values by GPC

Commercial PEG	\bar{M}_n	\bar{M}_p	\bar{M}_n/\bar{M}_p
PEG 600	454	564	1.24
PEG 1000	700	970	1.39
PEG 2000	1400	1800	1.30
PEG 4000	3050	3900	1.26
PEG 6000	4600	6100	1.33
PEG 10,000	8900	11,300	1.30

MOLECULAR WEIGHT DETERMINATION OF PEG BY VAPOR PRESSURE MEASUREMENTS (TONOMETRY)

We used a vapor pressure osmometer (A.I.S.) working according to the vapor pressure measurement called tonometry. These measurements are differential measurements, and the sensitivity is so high that this apparatus is able to measure a molecular weight of about 20,000. Toluene was used as solvent, and temperature was 34.5°C.

The instrument was calibrated with three pure PEG samples (diethylene glycol 106, triethylene glycol 150, and tetraethylene glycol 194) and with four polybutadiene samples ($M = 1900, 2100, 3100, \text{ and } 3400$).

The well-known eq. (8) was used:

$$(P_A^0 - P_A)/P_A^0 = K \text{ PEG } W/\text{PEG } \bar{M}_n \quad (8)$$

where P_A^0 and P_A are the vapor pressure for pure solvent and for solvent into the PEG solution, respectively; PEG W is the PEG weight in the solution, and PEG \bar{M}_n is the mean molecular weight of PEG.

As shown in Table XI, there is a little variation between the \bar{M}_n values measured according to the chosen samples for calibration. With PEG samples used for calibration, \bar{M}_n values for PEG are lower than the others, and the ratio for both of them is obviously equal to K_2/K_1 .

The K constant as a function of the apparatus and the operational conditions was determined by the calibration with the above defined solutes.

MOLECULAR WEIGHT DETERMINATION OF PEG BY IR AND NMR MEASUREMENTS

The infrared (IR) method was used for the characterization of PEG.^{20,21} A model 457 double-beam infrared spectrometer (Perkin-Elmer) with a 1-mm-wide cell was used. The solvent was chloroform. The concentration was chosen to be 2% for PEG with a molecular weight below 1000 and 4% for PEG with a molecular weight above 1000.

TABLE XI
 \bar{M}_n Values by Tonometry^a

PEG	106	150	194	600	1000	2000	6000	10,000
K_1				625	1020	1990	6130	9570
K_2	106	150	194	580	945	1840	5670	8860

^a $K_1 = 153.17 \times 10^4$ with polybutadiene samples; $K_2 = 141.8 \times 10^4$ with DEG samples.

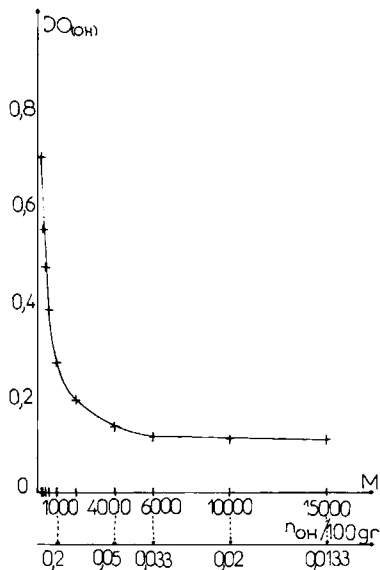


Fig. 5. Absorbance vs. mean molecular weight of PEG in solution in chloroform. IR band: 3400 cm^{-1} .

The absorption bands considered were 3400 cm^{-1} for the OH band and 2850 cm^{-1} for the CH_2 band. We found that the absorbance varies linearly with the PEG concentration in solution when the concentration is taken between 0 and 4%.

The variation of OH absorbance is shown in Figure 5 against the molecular weight for PEG and the OH function number calculated into a 100-g weight of PEG mixture. We can appreciate in this figure the sensitivity provided by this method. Because the OH absorbance band from H_2O is near that for OH from PEG, it is not possible to distinguish between them. Our PEG mixtures were selectively dehydrated by using molecular sieves of type A. Titration by the Karl Fisher method showed it did not remain any water more than 0.1%. Figure 6 shows a linear variation of the ratio of absorbances for OH and CH_2 against the number ratio of OH and CH_2 groups for PEG.

NMR method based on ^{13}C was used as well²² for the mean molecular weight determination of PEG. As for the IR method, this last method provides the \bar{M}_n value. But it has some disadvantages. First is the higher cost of analysis due to the great number of cumulated spectra. The second disadvantage is more critical because of the low sensitivity of the method which does not permit an accurate measurement for a PEG molecular weight higher than 1500.

The results provided by using these two methods are much the same for PEG lower than 1500.

CONCLUSION

Since a physical method may have a better efficiency for a particular PEG molecular weight than for another, the results obtained by these methods are complementary. Gas chromatography, as the usual direct method, provided a very valuable information for PEG of low molecular weight. All the components were identified and measured for PEG of 400 or lower, by using a solid

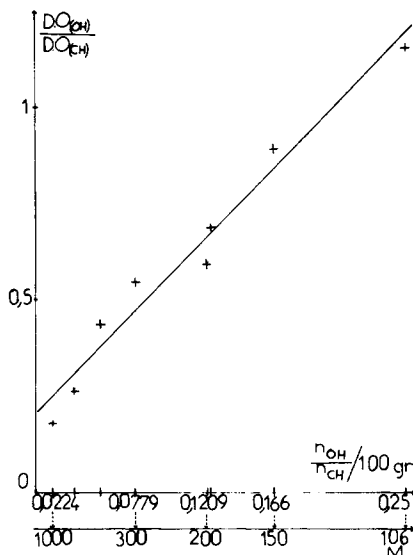


Fig. 6. Ratio of OH and CH_2 absorbances vs. ratio of n_{OH} and n_{CH_2} number.

support such as Tenax and by injecting water solutions of PEG without a derivatization. The precision was about 5%.

Gas chromatography as a "reverse" method, used with PEG as the stationary liquid and alcohols or paraffins as the solutes, is a long-acting method, but it gave some valuable information about the mean molecular weight \bar{M}_n in the range between 400 and 2000. It seemed that the precision was not better than 10%.

Viscometry measurements were better in that respect. We found that the accuracy was better by considering a variation of the Mark-Houwink constants against the molecular weight values of PEG; in that case, the precision for \bar{M}_v was of about 7%.

Gel permeation chromatography was a reliable technique for determining the molecular weight distribution of PEG. The universal calibration method has been confirmed as suitable for linear PEG between 150 and 20,000 by using three μ -Styragel stationary phases with a porosity of 100, 500, and 10^4 Å. The precision was between 5 and 10%. The vapor pressure tonometric measurements was found to be an accurate method for \bar{M}_n determination of PEG mixtures. The precision was not better than 10%, and a systematic error for calibration appeared to be 8%.

Molecular weight determinations based upon infrared measurements were made by taking the OH absorbance band. It is an interesting method for polymer identification; its sensitivity decreases as the molecular weight increases, and this method yielded results only for PEG 4000.

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