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Electrohydrodynamic Ionization Mass Spectrometry of Poly(ethylene glycols)

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ABSTRACT: Electrohydrodynamic ionization mass spectrometry was applied to the analysis of poly(ethylene glycols) of number-average molecular weights 406, 605, 1041, and 1396 (determined by end-group titration). Spectra were obtained from glycerol solutions of each polymer, using NaI as supporting electrolyte. Singly, doubly, and triply charged ion series were detected, corresponding to attachment of one, two, or three sodium ions to oligomer molecules. Ions of low intensity attributable to protonated oligomers were also detected in the lighter samples. No evidence of significant fragmentation was obtained. Molecular weight distributions calculated from mass spectra could be used to obtain estimates of number-average molecular weights in excellent agreement with end-group-titration determinations. In addition to molecular weight information, the spectra also provided estimates of the level of vinyl, methylene, and propylene impurities in the sample.

Both average molecular weight and molecular weight distribution are among the physical properties which determine whether a given polymer is suitable for a certain application. Sensitivity of bulk behavior to these parameters, and also to the presence of low-level impurities, can be extreme. The resultant need for characterization of the degree of polymerization in many systems has promoted the development of a variety of analytical techniques for determining polymer molecular weights.

End-group titration is probably the most reliable method for absolute determination of number-average molecular weight, $\bar{M}_n$

$$\bar{M}_n = \sum N_i M_i / \sum N_i \qquad (1)$$

In eq 1 N_i is the number of moles of molecules of molecular weight M_i contained in a polymer sample. Titrations give no information about molecular weight distributions. Furthermore, the measured average can be spuriously lowered for branched polymers with multiple end groups.

The only common technique which routinely provides both weight-average and weight-distribution information is gel permeation chromatography (GPC). Recent developments in "high-performance" GPC (see, for example, ref 1 and 2) have extended its applicability to relatively low-molecular-weight samples. However, resolution falls quickly with increasing molecular weight, requiring multiple-column, time-consuming experiments for characterization of a broadly distributed sample. In addition, molecular weight standards of near monodispersity are usually required for good quantitation. Even when such standards are available, morphological differences between samples and standards (e.g., different branching or conformation) may shift molecular weight calibration. The need for calibration standards can be relieved by use of low-angle laser light scattering (LALLS) detection of the GPC effluent.[3] However, this technique measures instantaneous average effluent molecular weight and requires efficient chromatographic separation for accurate determination of molecular weight distributions. Furthermore, calculation of molecular weights from scattering data requires prior knowledge of sample virial coefficients and "refractive increments" (dependence of refractive index on concentration). These parameters are not always precisely known. Clearly, an absolute measure of molecular mass (such as that obtained in mass spectrometry) would greatly facilitate characterization of these important polymer properties.

The thermal lability and low ambient volatility of most polymers have severely limited their analysis by conventional mass spectrometry. Some approaches to polymer mass spectrometry involve preliminary pyrolysis,[4] severely altering polymer composition prior to analysis. Even very "soft" ionization techniques, such as field desorption,[5] require sample heating to increase volatility and therefore may promote fragmentation. Nevertheless, recent field-desorption experiments[6-8] have appreciably extended the range of compounds amenable to mass spectral analysis. In at least one instance,[8] ions beyond 10 000 amu have been detected.

Electrohydrodynamic (EH) ionization[9] offers a simple and extremely soft ionization mechanism for ionic or polar samples soluble in solvents of low volatility, such as glycerol. Ionization occurs at ambient temperature via salt dissociation or ion attachment in solution. Ions are subsequently extracted from solution by an applied electric field. Sample solution is contained in a syringe and is continuously replenished at the emission site, avoiding some of the sampling uncertainties arising from depletion in conventional field-desorption mass spectrometry.[10] The work described here involves an investigation of the applicability of EH mass spectrometry for determining the molecular weight average and distribution of each of a series of poly(ethylene glycols) (PEG's). Values obtained for $\bar{M}_n$ by EH mass spectrometry are compared with manufacturer's estimates and with results of ASTM end-group determinations.[11] Estimates of low-level impurity concentrations are also obtained from mass spectral data.

Experimental Section

Mass spectra were obtained with a double-focusing mass spectrometer (AEI MS902) equipped with an EH ion source. Source geometry and operation have been described elsewhere.[12,13] Source emitter potential was varied from +4.5 to +8.5 kV (giving ions of roughly 4-8-kV energy[13]), lower potentials being used to improve instrument transmission of heavy ions. Source extractor potential was varied from -3 to -1.5 kV in order to maintain a potential difference between the emitter and extractor of about 7-9 kV. This resulted in a more or less constant electric field at the emission site and ensured the maintenance of acceptable emission current. Source collector potential was fixed at ground.

For all spectra, exact emitter potential and spectrometer electric sector potential were empirically matched, thus accepting only ions that had not undergone any metastable evaporative loss of solvating glycerol molecules prior to the electric sector.[10] Spectrometer resolution of about 600 was employed. At this resolution, the sensitivity at m/z 569.3 ($[HO(CH_2CH_2O)_{12}H + Na]^+$, the most intense ion of sample B, described below) was roughly 5×10^{-14} coulomb/μg of PEG (estimated in a manner similar to that suggested by Olson et al.;[14] the average electron multiplier anode signal was roughly 1×10^{-9} A; the electron multiplier voltage was -2.73 kV, giving a gain of roughly 1.8×10^5). Because this ion comprised about 10% of the total PEG ion intensity, an overall

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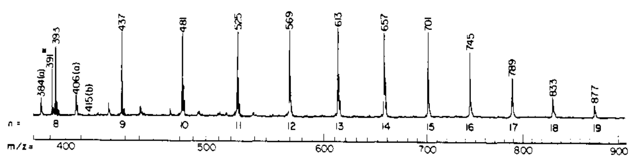

Figure 1. Portion of an oscillographic recording of the EH mass spectrum of sample B. The abscissa is shown both as mass-to-charge ratio (m/z) and as n in the structure $[HO(CH_2CH_2O)_nH + Na]^+$. The ion at m/z 391 (marked by an asterisk) is due to glycerol solvent and has the structure $[(HOCH_2CHOHCH_2OH)_4 + Na]^+$. Two series of ions attributable to intrachain vinyl and methylene impurities are visible (but not labeled, for clarity) at m/z ratios 2 and 14 mass units, respectively, below the principal peaks. Additional identified ion series have the following probable structures: (a) $[HO(CH_2CH_2O)_nH + 2Na]^{2+}$ (first two visible members are labeled (a) and correspond to $n = 16$ and $n = 17$); (b) $[HO(CH_2CH_2O)_nH + H]^+$ (first visible member is labeled (b) and corresponds to $n = 9$).

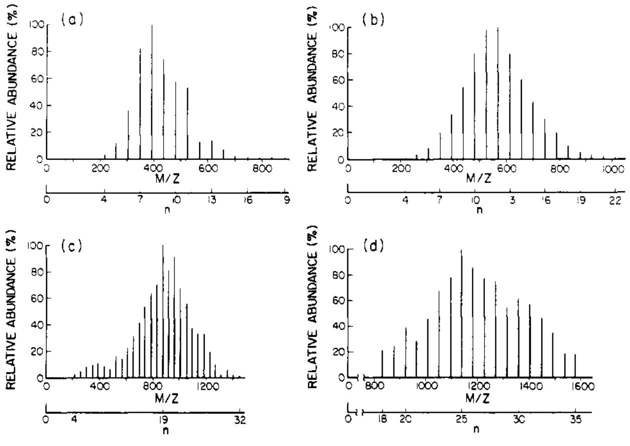

Figure 2. Relative abundances of $[HO(CH_2CH_2O)_nH + Na]^+$ ions vs. m/z for samples (a) A, (b) B, (c) C, and (d) D. For each sample, intensities are relative to the most intense $[HO(CH_2CH_2O)_nH + Na]^+$ ion (100%).

sensitivity of about 5×10^{-13} coulomb/μg may be estimated from these data.

PEG samples were obtained from J. T. Baker and were dissolved in glycerol (Fisher Scientific) solutions containing 6 mol % NaI (i.e., 6 mol of NaI/100 mol of glycerol solvent). NaI was supplied by Mallinckrodt. Solutions of PEG's of nominal molecular weights 380–420 (sample A), 580–630 (sample B), and 950–1050 (sample C) were each prepared at 1 mol %. PEG of nominal molecular weight 1300–1600 was not soluble at this level; a 0.2 mol % solution of this sample was used instead (sample D). All solutions were degassed[12,13] to $\lesssim 1 \times 10^{-2}$ torr before analysis.

End-group analysis for determination of $\bar{M}_n$ was performed for each sample. The procedure outlined by ASTM was employed.[11] Because PEG is a linear polymer, end-group-analysis error due to branching should not be significant.

Results and Discussion

Figure 1 is a portion of an oscillographic recording of the EH mass spectrum of sample B. The trace shown was obtained at medium recorder gain; sensitivity 1 order of magnitude higher was available to facilitate quantitation of low-abundance ions. Dominant ions arise from single sodium ion attachment to oligomers and belong to the series $[HO(CH_2CH_2O)_nH + Na]^+$. A schematic representation of this series as measured for each of the four polymer samples is presented in Figure 2. Isotope peaks due to ^{13}C, ^2H, and ^{18}O have been deleted from Figure 2 (and subsequent figures) for clarity. Each spectrum is the result of a single spectral scan. While repeated scans were subject to statistical fluctuations and variations in emission current of perhaps as much as a few percent, the overall shape of the curves was reproducible.

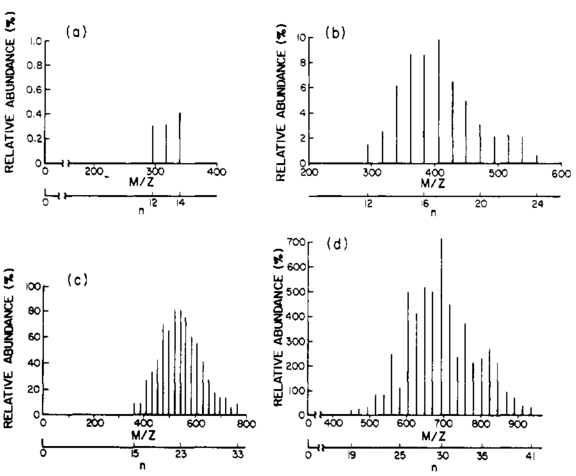

Figure 3. Relative abundances of $[HO(CH_2CH_2O)_nH + 2Na]^{2+}$ ions vs. m/z for samples (a) A, (b) B, (c) C, and (d) D. For each sample, intensities are relative to the most intense $[HO(CH_2CH_2O)_nH + Na]^+$ ion (100%).

Each spectrum in Figure 2 has roughly the normal distribution which would be expected for the degree of polymerization of a given sample. However, even if ions of all oligomers were formed and sampled with equal efficiency, the distributions of Figure 2 would need to be adjusted for isotopic contributions before attempting to derive molecular weight distributions from intensities. To understand why this is so, consider the peaks of equal intensity at nominal mass-to-charge ratio (m/z) 261 and 921 in the spectrum of sample B (Figure 2b). These m/z ratios correspond to the "base peaks" for $[HO(CH_2CH_2O)_5H + Na]^+$ and $[HO(CH_2CH_2O)_{20}H + Na]^+$, respectively; i.e., they correspond to molecules comprised exclusively of ^{12}C, ^1H, ^{16}O, and ^{23}Na. Considering only these base peaks, it might appear as if the corresponding species were of equal concentration in the glycerol solution. However, if one considers the contribution of ^{13}C to the "M + 1" peak (i.e., to m/z 262 and 922, respectively), the intensity at m/z 922 would be 4 times that at m/z 262; one is more likely to incorporate a ^{13}C atom in a molecule with 40 carbons than in one with only 10. If the sum of intensities at m/z 261 and 262 ($i_{261} + i_{262}$) is used to estimate the total intensity of the 5-unit polymer, while $i_{921} + i_{922}$ is attributed to the 20-unit chain, the resulting estimate of the latter intensity will exceed the former by a factor of about 1.44/1.11, or by almost 30%. In fact, if intensities of all significant isotopic peaks (exceeding ~0.05% of the associated base-peak intensity) are calculated from the known isotopic abundances of ^{13}C, ^2H, and ^{18}O, the corrected total intensities for the species with base peaks at m/z 921 and 261 are in the ratio 1.66:1.13. This stands in sharp contrast to the equal intensities of the base peaks.

It should be pointed out that the dynamic range of the MS902 was sufficient (~5 orders of magnitude) to allow direct measurement of isotope peaks such as those at m/z 262 or 922. However, in these experiments instrument resolution was too low (~600) to resolve these ions from their respective base peaks, especially for heavy ions. Low resolution was necessary to ensure sensitivity to low-abundance species. Thus, all species' intensities were adjusted by calculation of isotopic contributions, as outlined above.

Single-cation attachment was not the only mode of oligomer ionization. Figures 3 and 4 present spectra for doubly and triply charged oligomers, arising from attachment of 2 and 3 sodium ions. All intensities in these samples are relative to the most intense *singly* charged ion

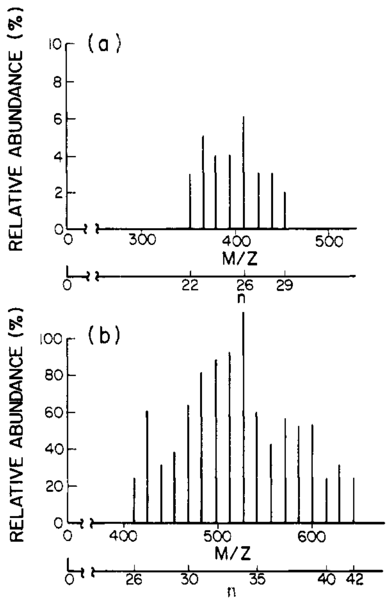

Figure 4. Relative abundances of $[HO(CH_2CH_2O)_nH + 3Na]^{3+}$ ions vs. m/z for samples (a) C and (b) D. For each sample, intensities are relative to the most intense $[HO(CH_2CH_2O)_nH + Na]^+$ ion (100%).

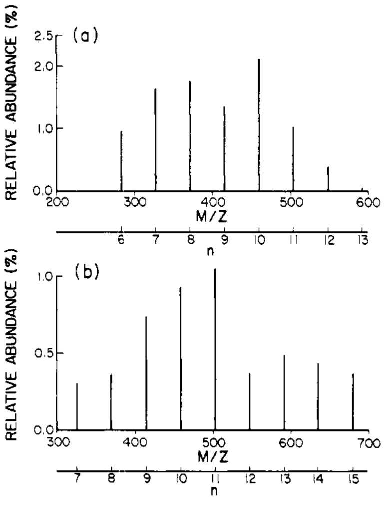

Figure 5. Relative abundances of $[HO(CH_2CH_2O)_nH + H]^+$ ions vs. m/z for samples (a) A and (b) B. For each sample, intensities are relative to the most intense $[HO(CH_2CH_2O)_nH + Na]^+$ ion (100%).

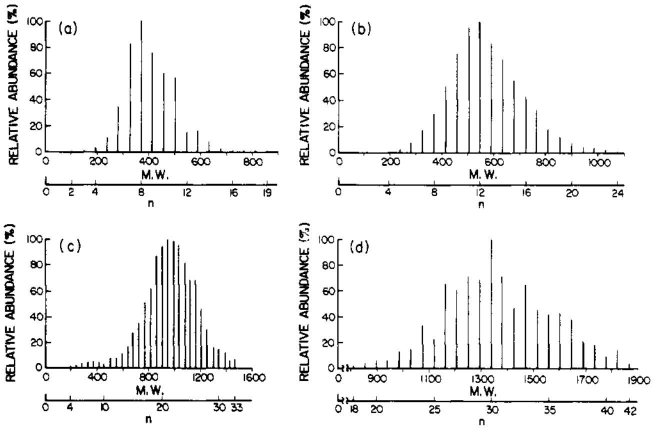

Figure 6. Molecular weight distributions calculated from total EH mass spectral ion intensities (corrected for isotopic contributions) for samples (a) A, (b) B, (c) C, and (d) D.

Table I
Various Estimates of Average Molecular Weight ($\overline{M}_n$) and Degree of Polymerization ($\overline{X}_n$) of PEG Samples A-D

sample	$\overline{M}_n$ manufacturer's spec	$\overline{M}_n$ end-group titration	EHMS estimates: isotopic contrib incl $\overline{M}_n$	$\overline{X}_n$	EHMS estimates: isotopic contrib ignored $\overline{M}_n$	$\overline{X}_n$
A	380-420	406	406	8.8	401	8.7
B	570-630	605	572	12.6	561	12.3
C	950-1050	1041	962	21.5	938	20.9
D	1300-1600	1396	1365	30.6	1342	30.1

from the corresponding sample in Figure 2. It is interesting to note that intensities of multiply charged ions are greatest for the heaviest ions. In fact, doubly charged ions of sample D are generally more intense than their singly charged counterparts (compare Figures 2d and 3d). Furthermore, intensity distributions are shifted toward higher mass in the spectra of multiply charged ions, compared with distributions of corresponding oligomers with lower charge. Should this tendency toward higher charge on heavier oligomers prove to be general, the applicability of EH mass spectrometry to polymer analysis may be extended appreciably, because high charge values will lower measured m/z ratios of heavy ions.

One further set of ions attributable to PEG oligomers was detected for the lighter samples (A and B; see Figure 5). The m/z for these series corresponded to protonated oligomers, $[HO(CH_2CH_2O)_nH + H]^+$. A similar ion series was reported by Lee and Sedgwick in their electron-impact experiment.[15] They believed these ions to be the products of double-McLafferty-type rearrangements. While this explanation is probably correct for their data, the low energy input in EH ionization virtually precludes such fragmentations here. A more likely explanation for the ion series in the EH spectra is proton transfer from glycerol solvent to PEG. This explanation is supported by the observed disappearance of the $[HO(CH_2CH_2O)_nH + H]^+$ series when a base stronger than PEG (e.g., sodium acetate) is added to the glycerol solutions.

Thus, four kinds of ions can be generated from each oligomer in a given sample, arising from attachment of either a proton or 1–3 sodium ions. Figure 6 shows the molecular weight distributions obtained for each sample when all contributions to a given oligomer are added, after correcting intensities for isotopic contributions. These distributions compare quite favorably with those claimed by the manufacturer, as summarized in Table I.

Also listed in Table I are values for $\overline{M}_n$ (see eq 1) and $\overline{X}_n$ (the number-average degree of polymerization) determined from the data of Figure 6. $\overline{X}_n$ is defined by eq 2,

$$\overline{X}_n = \sum xN_x / \sum N_x \qquad (2)$$

where N_x is the number of moles of molecules containing a chain of x monomer units. The values of $\overline{M}_n$ and $\overline{X}_n$ in Table I were calculated by using the total corrected intensities of Figure 6 as estimates for N_i and N_x in eq 1 and 2, respectively. For comparison, Table I also shows values of $\overline{X}_n$ and $\overline{M}_n$ obtained from the uncorrected intensities of Figures 2–4. Finally, Table I lists values of $\overline{M}_n$ determined by an ASTM end-group-determination method.[11] Agreement between the end-group determinations and the values derived from the data of Figure 6 is quite good. The effect of ignoring isotopic contributions is not negligible but is small. The evident trend toward low estimates of $\overline{X}_n$ and $\overline{M}_n$ by EH mass spectrometry (compared with end-group titration) may suggest some mass discrimination in favor of lighter species in the sampling or ionization

Table II
Estimates of Total Vinyl, Methylene, and Propylene Impurities within the Polymer Chains of PEG Sample A

impurity	% of tot (cor) intens	impurity	% of tot (cor) intens
one vinyl	0.81	two methylenes	0.87
one methylene	1.32	two propylenes	0.41
one propylene	0.39		

steps and will receive additional attention. However, the accuracy of the data obtained is probably suitable for a number of applications, and the ease of the determination suggests that it may be extremely useful for determinations of molecular weight distributions and averages.

The EH mass spectral data provided one further kind of information. Ion series were detected which could be attributed to trace impurities *within the polymer chain.* For example, in the spectrum of sample A, members of ion series 2, 14, and 28 mass units lower than the ions of Figure 2a were observed, as were series 14 and 28 mass units higher than the ions of Figure 2a. These series could be attributed to chains incorporating, respectively, 1 vinyl, 1 methylene, 2 methylene, 1 propylene, or 2 propylene groups in the chain. Table II lists ratios of total impurity ion intensity for each series in sample A (corrected for isotopic contributions) to total (corrected) ion intensity for that sample. These ratios should provide some quantitative indication of the level of each impurity in the polymer chain. To our knowledge, this information is not readily available from other analysis techniques.

Conclusions

EH mass spectrometry provides a simple and convenient probe for characterization of oligomer molecular weight averages and distributions. The technique is sufficiently sensitive to detect oligomers with impurities in their polymer chains at a level of 1% or less. The evident tendency of heavy oligomers to carry multiple charge offers a possibility of extending the molecular weight range of a given mass spectrometer, because multiple charges lower detected mass-to-charge ratios. For example, the heaviest singly charged ions detected in this study had nominal m/z ratios around 1582, near the instrument's rated high-mass limit at the 4.0-kV energy employed (rated $m/z \lesssim 1600$) but well within the overall instrument specifications ($m/z \le 6400$ at 1 kV; the feasibility of EH ionization at potentials this low has not yet been assessed). However, because the heaviest detected ion (derived from oligomer of molecular weight ~ 1867) was triply charged, its m/z (~645) was easily within instrument specifications even at 4.0 kV. In fact, instead of spectrometer span, it appears more likely that the present need to introduce polymers as glycerol solutions may pose a fundamental limitation on the analytical applicability of the technique. The heaviest sample employed in this study ($\bar{M}_n = 1396$) was only slightly soluble in NaI-doped glycerol (0.2 mol %). Even for the more soluble samples, ions at m/z ratios corresponding to glycerol solvation of protonated or cationated oligomers were not abundant. In fact, ions with the structure $[\mathrm{HO(CH_2CH_2O)}_n\mathrm{H} + \mathrm{Na} + \mathrm{glycerol}]^+$ were detected only in sample A and only for values of n between 2 and 5, inclusive. Such solvated ions are much more abundant in other systems and have been interpreted to indicate favorable interaction between solute and glycerol solvent.[9]

The tendency toward greater proton and glycerol attachment to lighter ions contrasts markedly with the tendency toward multiple sodium ion attachment to heavy oligomers. The data suggest distinct attachment mechanisms and/or sites for sodium ions and protons and may even carry implications concerning intramolecular hydrogen bonding of large oligomers (if, for example, such bonding blocks attachment of glycerol or protons to hydroxyl end groups of larger oligomers). Studies are presently under way investigating these hypotheses and the possible roles of solvents other than glycerol in extending the applicability of EH mass spectrometry of polymers.

Finally, the agreement between $\bar{M}_n$ values obtained from EH mass spectrometry data and by end-group determinations seems to support a hypothesis that oligomer ions are formed and sampled with roughly equal total efficiencies, regardless of oligomer mass (although, as mentioned above, heavier oligomer ions have a greater tendency to be multiply charged). Experiments are presently being designed to further test this hypothesis.

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