Available online at www.sciencedirect.com
SCIENCE DIRECT®
International Journal of Mass Spectrometry 238 (2004) 227–233
International Journal of Mass Spectrometry
www.elsevier.com/locate/ijms

A perspective on relative quantitation of a polydisperse polymer using chromatography and mass spectrometry

X. Michael Liu, E. Peter Maziarz*, Edmond Quinn, Yu-Chin Lai

Bausch and Lomb Inc., Research, Development, and Engineering, 1400 N. Goodman Street, Rochester, NY 14609, USA

Received 29 September 2003; accepted 6 September 2004

Abstract

High throughput analysis of polymeric materials has become increasingly important in today's medical device industry. Direct matrix-assisted laser desorption ionisation (MALDI)-TOF MS analysis of polymers has been "the method of choice" for industrial analytical chemists due to its high speed, ease of use, and soft ionization. However, using this approach we experience difficulties for the analysis of poly(dimethyl siloxane) samples containing UV curable end groups. For example we observe a considerable amount of fragment products that act as chemical noise to the peaks of interest. This makes it difficult to obtain any meaningful quantitative information about the sample. In this study, we demonstrate that this dilemma can be remedied by coupling gel permeation chromatography (GPC) with MALDI-TOF MS analysis. With this approach a true impurity in the sample is clearly detected throughout the molecular weight distribution where direct analysis provided no information due to the chemical noise of the fragment peaks. This impurity is positively identified from exact mass measurements. The content of this impurity is calculated to be 33.0% by using a multiple data point approach from both GPC and MALDI-TOF analysis.

Keywords: GPC–MALDI-TOF; Quantitative polymer analysis; UV curable PDMS; Implant device material

1. Introduction

Soft ionization mass spectrometry techniques such as electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) are becoming increasingly recognized as information rich analytical techniques for polymer analysis [1–3].

The data obtained from such analysis can be used to determine repeat unit sequence and end group chemistry [4–6]. With spatial resolution of peaks, one can also determine the existence of impurity distributions within a homopolymer [7] or sequence distributions within a copolymer [8,9]. These capabilities can be especially powerful for product development efforts if at the same time the relative quantity of the polymer composition can be determined [10–16]. One initiative would be to evaluate a series of polymer samples from iterative synthetic procedures and correlate differences in polymer composition with product behavior. With this strategy of high throughput polymer analysis it is envisioned that an ideal polymer composition can be discovered for a specific product application. After the development process the data can then be used to establish stringent compositional specifications for the polymer starting material. This would ultimately help control the quality of the established product.

High throughput MS analysis of polymer materials is a challenging task. One difficulty with this analysis is that several polymers are polydisperse and as such mass discrimination effects may accompany their analysis [17–20]. Several studies have illustrated the advantage of combining gel permeation chromatography (GPC) with MALDI [21–33] and ESI [34–37] MS for analysis of polydisperse polymer samples. Thus the analyst must determine whether the desired information can be determined from direct MS analysis or if the combination of GPC with MS is required. This is an important decision since data from direct analysis can be collected

* Corresponding author. Tel.: +1 585 338 5086; fax: +1 585 338 5875.
E-mail address: e.peter.maziarz@bausch.com (E.P. Maziarz).

1387-3806/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijms.2004.09.027

in the minute time frame while GPC–MS generally requires an hour for one sample.

Poly(siloxane) materials contain properties of special interest including thermal stability, good resistance to UV radiation, excellent release properties and surface activity, high permeability to gases, and physiological inertness. Because of these properties poly(siloxane) materials are used in a "disperse" set of applications ranging from release agents, rubber molds, adhesives, and heat transfer fluids to biomedical devices, personal care, and cosmetic products [38]. Our interest in poly(siloxane) materials derives from their use as biomedical implant devices such as continuous wear contact lens products [39,40].

In general continuous wear implant device films are made with relatively low to moderate molecular weight (2–15 kDa) poly(siloxane) polymers that contain end groups with cross-linking functionalities. The quantity of these functional end groups is vital for providing the film with the proper mechanical properties such as modulus and tear strength. Further, a large variance in mechanical properties between films, often discovered during stability testing, can be attributed to differences in the materials cross-link density. Since this is directly related to differences in elemental composition of the oligomers used to make the films, it is advantageous to use analytical techniques such as MALDI-TOF MS that can provide detailed compositional information. In this study we provide a perspective on obtaining compositional information on a candidate implantable device polymer α,ω-bis-(*t*-butylamine-fumaryl-oxy-butyl) poly(dimethyl siloxane) (BAF-PDMS). We compare results from direct and GPC hyphenated MALDI-TOF MS analysis for both qualitative and quantitative purposes.

2. Experimental

2.1. Polymer samples and chemicals

The sample α,ω-bis(*t*-butylamine-fumaryl-oxy-butyl) poly(dimethylsiloxane) was synthesized in house and the general synthesis procedure has been described previously [40,41]. Sodium nitrate and dithranol were obtained from Aldrich (Milwaukee, WI). HPLC grade tetrahydrofuran (THF) was purchased from Fisher Scientific (Fairlawn, NJ). All chemicals and solvents were used as-received.

2.2. Gel permeation chromatography

The GPC system was equipped with a Waters Alliance 2690 Separation Module (Waters Corporation, Milford, MA). One hundred microliters of 0.1% (w/v) sample solution was injected onto the GPC system. The separation was performed on a set of two Waters Styragel columns having pore size diameters of 10^3 and 100 Å. The column dimensions were 300 mm × 7.8 mm i.d. and the average particle size of the packing materials was 5 μm diameter. The column temperature was set at 35 °C. HPLC grade tetrahydrofuran (Fisher Scientific, Fair Lawn, NJ) was used as the mobile phase at a flow rate of 1.0 mL/min. A series of narrow polystyrene (Polymer Laboratories, Amherst, MA) molecular weight standards (ranging from 30,000 to 500 Da) were used to calibrate the GPC system. A Waters 2410 refractive index detector (Waters Corporation) was used to monitor the GPC effluent. The internal temperature of the refractive index detector was set at 35 °C. All GPC data collection and manipulation was performed on the Millennium software (Waters Corporation, Milford, MA).

2.3. GPC data analysis

The molecular weights and molecular weight distributions of a polymer were calculated by the following formulae:

$$M_n = \frac{\sum N_i \times M_i}{\sum M_i} \quad (1)$$

$$M_w = \frac{\sum N_i \times M_i^2}{\sum N_i \times M_i} \quad (2)$$

$$M_z = \frac{\sum N_i \times M_i^3}{\sum N_i \times M_i^2} \quad (3)$$

$$\mathrm{PD} = \frac{M_w}{M_n} \quad (4)$$

where M_n, M_w, and M_z represent number-average, weight-average, and *z*-average molecular mass, respectively and where N_i is the number of polymer molecules at molecular mass M_i. PD is the polydispersity index or molecular weight distribution. These average mass values were determined from GRAMS 32 (Galactic Industries, Salem, NH) and Millennium 32 software (Waters Corporation, Milford, MA). Based on the calibration curve generated from a series of narrow polystyrene standards, the polystyrene-equivalent average number-average (M_n) and weight-average (M_w) molecular weight values are determined to be 2500 and 4250 Da, respectively. A PD of 1.7 was calculated from these average mass values.

2.4. LC-transform (GPC–MALDI-TOF MS interface)

The automated GPC–MALDI MS employed an LC-Transform 500 Series (Lab Connections Inc., Northborough, MA). This system was modified for a matrix co-deposition mechanism with GPC effluent and has been previously described [33]. Dithranol was used as the matrix and was prepared as 15 mg/mL in HPLC grade THF with the addition of 2% by volume saturated sodium nitrate in THF. The matrix solution flow rate was 0.2 mL/min and it was directed towards a Valco tee where mixing with GPC effluent occurred prior to deposition on the MALDI sample plate. The nozzle temperature was set at 183 °C and the nitrogen sheath gas was adjusted to a pressure of 10 psi. While evaporating most of the solvent,

the uniform micro-co-crystals between sample molecules and matrix were formed due to the well-controlled experimental conditions. After the GPC experiment, the MALDI sample plate was subjected to MALDI-TOF MS analysis.

2.5. MALDI-TOF mass spectrometry

The MALDI-TOF MS data was obtained with an Applied Biosystems DE-STR TOF mass spectrometer, operating in either linear or reflector mode. Ions were formed by laser desorption at 337 nm (N_2 laser, 3 ns pulse width, 10^6 W/cm^2, 100 μm diameter spot), accelerated to 20 kV and detected as positive ions. During the ionization process, a delay time of 125–175 ns was applied before acceleration for ion focusing. The grid and guide wire voltages were set at 85.0 and 0.050% of the applied acceleration voltage, respectively to focus the beam of ions. For the high-resolution analysis the grid and guide wire voltages were set at 65 and 0.001%, respectively. Each spectrum was the average of 256 laser shots. Dithranol (Aldrich Chemical Company, Milwaukee, WI) was used as the sample matrix and was prepared as 15 mg/mL with the addition of 1% by volume $NaNO_3$. For direct analysis matrix solution and samples were mixed 10:1 and 1 μL of this mixture was manually spotted on the sample plate and dried under ambient conditions. For direct analysis the mass scale was calibrated externally with a well-characterized methyl-terminated PDMS sample. For the high-resolution analysis the BAF-PDMS monoistopic peaks were used as an internal standard to determine the accurate mass of the unknown distribution. Data was acquired with a Tektronix digitizing oscilloscope and transferred to a data analysis station equipped with GRAMS/386 software (Galactic Industries, Salem, NH).

3. Results and discussion

3.1. Direct MALDI-TOF MS analysis

The structure of the polymer BAF-PDMS used in this study is illustrated in Fig. 1. This structure contains end groups with a carbon–carbon double bond used for cross-linking the BAF-PDMS oligomers into a film. The direct MALDI-TOF mass spectrum of (BAF-PDMS) material prepared by the dried drop method is illustrated in Fig. 2. Plenty of qualitative information is provided by this analysis. Three series of mass distributions each containing oligomers separated by 74 Da are observed. This suggests the mass distributions contain dimethyl siloxane (C_2H_6SiO; M_w = 74 Da)

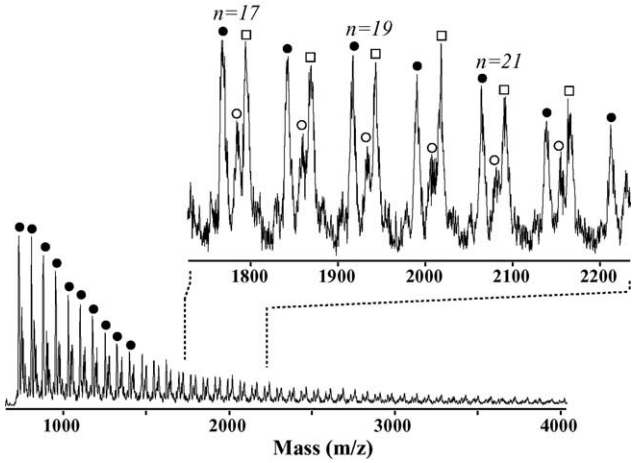

Fig. 2. Direct MALDI-TOF MS analysis of BAF-PDMS. Three PDMS distributions are observed and denoted as closed circle, open circle, and open square. The distribution denoted by open square is the sodiated BAF-PDMS oligomers. The inset provides an expanded view for a relative comparison of the distribution peaks.

repeat units and they differ in their end group chemistry. The peak masses in the distribution denoted by open square in Fig. 2 correlate with that of intact sodiated BAF-PDMS oligomers. The simple expression (74n + 510 + 23 Da) can be used to describe the mass of these peaks where n is the number of repeat units, 510 is the total mass of the end groups for BAF-PDMS and 23 is the mass of Na charge agent. The end group composition of the other two distributions, denoted as filled circle and open circle, need to be determined since films made from this PDMS material requires end groups with cross-link functionalities that provide specific mechanical properties. After the unexpected end groups are identified the next desired information is to determine their quantity relative to the target BAF-PDMS distribution. This information is of paramount importance for determining the impact these impurities have on product performance. Ultimately this is what determines the amount of effort that will be put forth in modifying the synthetic procedure to prevent the impurities from forming. A relative comparison of the peaks in Fig. 2 indicates that the filled circle distribution is the most intense in the low molecular weight range (500–1600 Da). The oligomer peaks in the open circle distribution are more intense than the BAF-PDMS oligomers up to approximately 1000 Da. The inset in Fig. 2 indicates that the oligomer peak intensities of the closed circle and open square (BAF-PDMS) distributions are approximately equal at 1900 Da. With increasing mass the BAF-PDMS oligomers are slightly more intense than the closed circle oligomers.

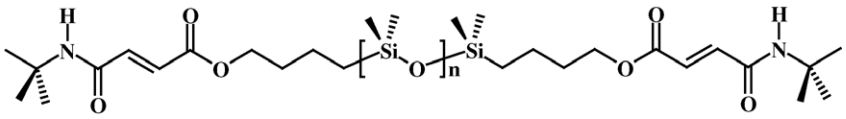

Fig. 1. Representative structure for the polymer target compound BAF-PDMS. Molecular formula is $C_{26}H_{46}N_2O_6Si[C_2H_6OSi]_n$.

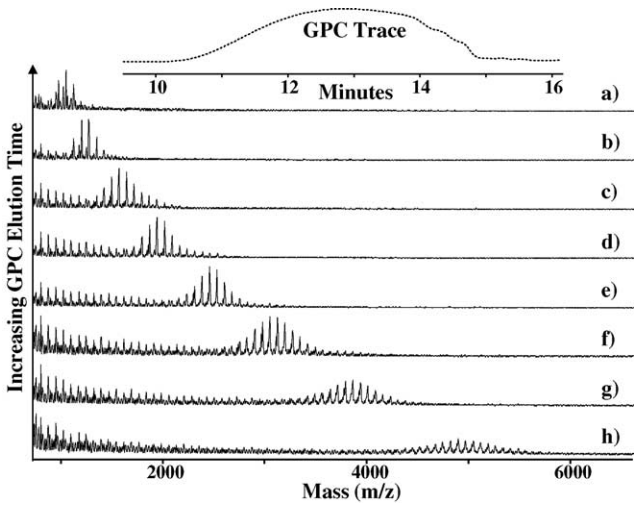

Fig. 3. Mass spectra from the automated GPC–MALDI-TOF MS analysis of BAF-PDMS. In each fractionated sample a continuous series of low mass peaks separated by 74 Da are observed. The elution time for each fractionated spectrum is: (a) 14.5 min; (b) 14.2 min; (c) 13.9 min; (d) 13.5 min; (e) 13.2 min; (f) 12.9 min; (g) 12.5 min; (h) 12.2 min. The inset provides the RI chromatogram from the GPC analysis.

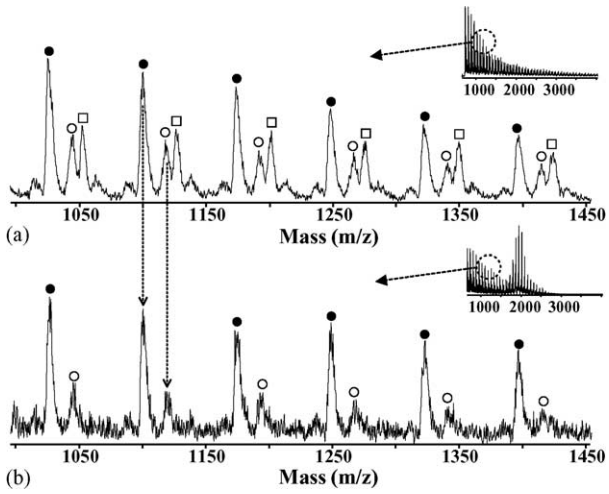

Fig. 4. Comparison of the same mass range from (a) direct MALDI-TOF MS to a (b) low mass portion of a fractionated spectrum from GPC–MALDI-TOF MS analysis. Existence of the closed circle and open circle distributions are confirmed to be fragment products in the direct MALDI-TOF MS analysis.

These relative comparisons from direct analysis provide a rapid approximation of the components contained within this sample.

3.2. GPC–MALDI-TOF MS analysis

In order to further verify the results obtained from the direct MALDI-TOF MS analysis and to get higher S/N of the higher mass products often under represented by direct analysis of polydisperse polymers [17–20] we hyphenated GPC to the analysis via an automated GPC–MALDI device previously described [33]. MALDI-TOF mass spectra were obtained as a function of time throughout the molecular weight distribution as shown in Fig. 3a–h. Surprisingly, we observed continuous low mass peaks in each GPC–MALDI-TOF mass spectrum of Fig. 3a–h. This continuum of peaks is uncharacteristic of the GPC size separation mechanism. Our initial prediction for these peaks is that they occurred as fragment products from the intact parent oligomers contained within the well-defined Gaussian-like distributions of Fig. 3a–h. However in order to eliminate the possibilities of deteriorated GPC column set or mobile phase contamination from the automated GPC–MALDI experiment, we evaluated a well-characterized methyl terminated PDMS material with similar nominal molecular weights under the same experimental conditions. Well-defined Gaussian-like distributions were obtained from this analysis (data not shown) without the presence of continuous low mass peaks. Therefore, the GPC column set is confirmed to be functioning properly, the THF mobile phase proved to be free of contamination, and we conclude that the low mass peaks in the spectra of Fig. 3 occur from fragmentation. Fig. 4a and b illustrates a comparison, in the mass range of 1000–1450 Da, of the direct MALDI-TOF mass spectrum, and the continuous low mass peaks from a GPC fractionated mass spectrum respectively. From this comparison it is observed that the peaks from the closed circle and open circle distributions in Fig. 4a occur at the same mass as the fragment peaks in Fig. 4b. Thus we conclude that the closed circle and open circle distributions observed from the direct MALDI-TOF analysis of this polymer sample are actually fragment products. It is important not to consider these peaks within the quantitative analysis as they do not reflect the true composition of the condensed phase sample. This finding illustrates the importance of hyphenated technologies, namely that of GPC with MS for the quantitative assessment of polydisperse polymers. It is noteworthy to mention that tandem mass spectrometry or PSD experiments could also confirm that these peaks occur from fragmentation of the expected molecular species.

Fig. 5 illustrates an expanded view of a GPC fractionated mass spectrum from the BAF-PDMS sample. Another

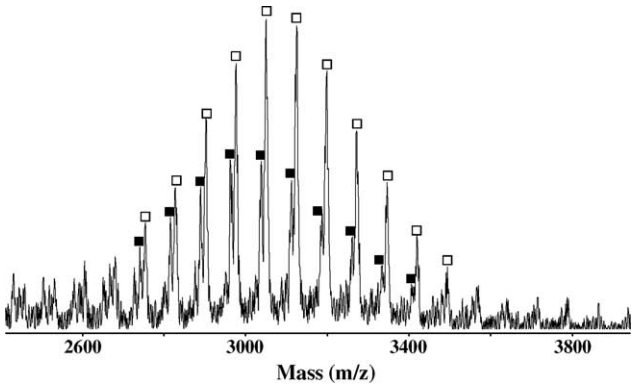

Fig. 5. Expansion of the GPC–MALDI-TOF mass spectrum of the 12.9 min eluting fraction (Fig. 3f). The distribution denoted by closed square is an impurity not observed from direct MALDI-TOF analysis. The open square distribution is the target BAF-PDMS oligomers.

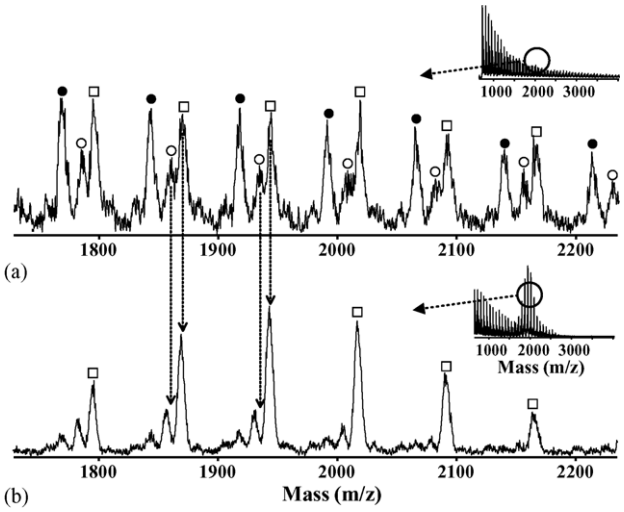

Fig. 6. Comparison of the same mass range from (a) direct MALDI-TOF MS to the (b) high mass portion of a fractionated spectrum from GPC–MALDI-TOF MS analysis. This comparison is made to verify that the open circle peaks are not the same as the closed square peaks from Fig. 5.

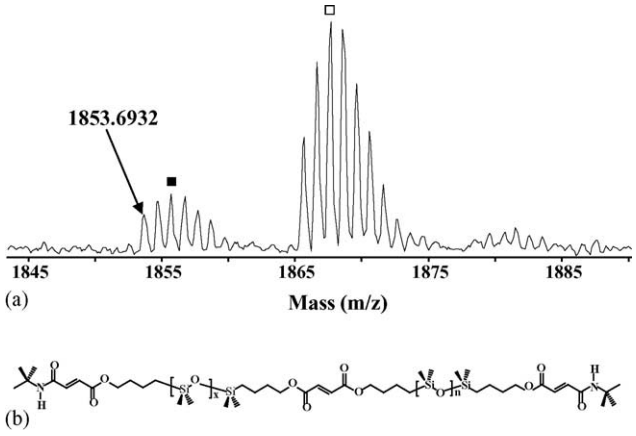

Fig. 7. (a) Expanded view from the high resolution MALDI-TOF MS analysis of the fractionated BAF-PDMS sample eluting at 13.9 min. The monoisotopic peak mass is obtained for an oligomer in the closed square distribution. (b) Proposed structure for the oligomers in the closed square distribution. Molecular formula is $C_{40}H_{70}N_2O_{10}Si_2[C_2H_6OSi]_n[C_2H_6OSi]_x$.

distribution of peaks approximately 12 Da away from each respective target BAF-PDMS oligomer is observed. This unknown distribution of peaks denoted as closed square has a Gaussian-like distribution. With this characteristic these peaks resemble products that have been size separated by GPC and thus they would be likely to represent the condensed phase sample. However, it was noted that the peaks in the closed square distribution had similar mass to that of the open circle distribution (from direct analyis) determined to be fragment peaks. To further verify these products as being different the direct MALDI-TOF mass spectrum and the higher mass region from a GPC fractionated mass spectrum were compared and illustrated in Fig. 6a and b, respectively. Indeed from close inspection the open circle distribution of peaks in Fig. 6a do not overlap with the peaks from the newly determined closed square distribution in Fig. 6b. Therefore, the hyphenation of GPC with MS for the analysis of this sample has allowed us to detect a true impurity that would have otherwise gone undetected by direct MALDI-TOF MS analysis.

Since it is now clear that the peaks within the closed square distribution are true impurities it is timely to qualitatively determine the composition of these peaks. Fig. 7a illustrates an expanded view from a high resolution MALDI-TOF mass spectrum of a GPC fraction of BAF-PDMS. The isotopic peaks of the oligomers are nearly baseline resolved. For this mass determination the 18mer and the 19mer of BAF-PDMS were used as internal standards that bracketed the isotopic distribution pattern of the unknown oligomer. From knowledge of the synthetic chemists and deduction of elemental compositions provided by the data analysis software we propose the structure illustrated in Fig. 7b as the identity of the oligomers in the closed square distribution. Consistent with the target BAF-PDMS oligomers, the proposed impurity structure contains the desired end groups with the proper cross-link functionalities (C=C). However the impurity structure also contains a middle group with cross-link potential. The monoisotopic mass of the oligomer representing the closed square distribution in Fig. 7a is 1853.6932 Da. This mass would correlate to the structure in Fig. 7b having a total number of 14 dimethyl siloxane repeat units. Including the end groups, the middle group, and the Na charge agent the elemental composition for this oligomer would be $C_{68}H_{154}O_{24}Si_{16}N_2Na$. This elemental composition has a theoretical mass of 1853.7092 and thus an error of 8.6 ppm from the experimental mass. A series of the closed square monoisotopic peaks were evaluated in the same manner and an average error of 7.3 ppm was determined.

For this relatively low average mass polymer system the extra cross-link functionality contained within this impurity may have an impact on the cross-link density of the final film. As such, it is important to know how much of this impurity occurs in the batch-to-batch synthesis of this sample. With this understanding fluctuations in the mechanical properties can be controlled from incorporation of higher material specifications.

3.3. Relative quantification of the impurity distribution

Since GPC was not able to separate the impurity from the target compound and MALDI-TOF MS alone provides erroneous information, we combined the results from both instruments. Initially we attempted to sum all the mass spectra from the GPC–MALDI-TOF MS analysis to obtain percent composition of the impurity. The attempt failed because of interferences from the low mass fragment peaks. Alternatively the impurity content was calculated using Eq. (5):

$$\%\,\text{Impurity} = \frac{\sum \text{RI}_i \times \text{IP}_i}{\sum \text{RI}_i} \times 100 \quad (5)$$

Table 1
Measurements of eight GPC fractions of BAF-PDMS using GPC–MALDI-TOF MS

GPC fraction	Elution volume (mL)	% Impurity determined by MS ($IP_i \times 100$)	RI intensities by GPC	% Relative RI intensities
1	12.2	48.0	90.1	13.56
2	12.5	42.2	96.8	14.57
3	12.9	38.5	100.0	15.05
4	13.2	30.5	97.5	14.67
5	13.5	27.3	93.5	14.07
6	13.9	23.2	83.7	12.60
7	14.2	22.6	60.1	9.05
8	14.5	19.4	42.7	6.43

where the percent impurity is the estimated impurity of the whole sample. RI_i is the refractive index intensity at elution volume i and IP_i is the impurity content at elution volume i. The value IP_i is obtained by dividing the summation of impurity peaks by the summation of the total peaks (impurity and BAF-PDMS peaks) within the mass spectrum of elution volume i. This equation effectively eliminates the concentration effect. This measurement included eight data points each containing a MALDI mass spectrum of a fractionated mass across the GPC distribution as summarized in Table 1. The impurity content for the whole sample based on this calculation was determined to be 33.0%. Triplicate analysis was performed to evaluate the precision of the measurements and a relative standard deviation of ±6.1% was determined.

The composition of a polymer containing homogeneous mass distributions can be reasonably represented at the most concentrated area of the molecular weight distribution (Mp). For comparison purposes, we measured the impurity content from a single IP_i determination that represented the most probable location in the GPC chromatogram. The impurity content calculated from this one mass fraction was determined to be 38.5%. This is quite comparable to the value obtained from the eight-point average (33.0%) determined by Eq. (5). This suggests that we can reasonably estimate the impurity of this polymer at the center fraction of the GPC distribution. However, it must first be determined that the mass distributions are homogeneous throughout the sample. This rapid approach would compliment high throughput polymer GPC–MS demands. The increasing quantity of impurity at higher molecular weight (as shown in Table 1) supports the proposed impurity in Fig. 7b where each oligomer contains two siloxane chains. As such this impurity is expected to have a higher average molecular weight than that of the target polymer.

4. Conclusions

The results presented in this report demonstrate some difficulties that can arise from direct MALDI-TOF analysis of a polymer containing reactive end groups with cross-linking functionalities. We predict that the fragment peaks observed in this analysis occurs from the end groups absorbing UV radiation from the nitrogen laser. These fragment products masked the peaks of interest and made the quantitative analysis of this material difficult. By means of hyphenated GPC with MALDI-TOF MS, we were able to differentiate the target compound from the fragmented products. Also the GPC–MALDI-TOF analysis we observed a true impurity that was otherwise masked from the fragment products in the direct analysis. From exact mass measurements the impurity was positively identified to be a recombinant BAF-PDMS with three cross-link functionalities. The content of this impurity was determined to be 33.0% using data from eight GPC fractions across the molecular weight distribution. By using only the most concentrated GPC data point the impurity content was determined to be 38.5%. We believe the 5.5% deviation between these methods is acceptable. Further the more rapid one-point approach complements our high throughput polymer analysis process. However, precaution must be exercised when dealing with more complex heterogeneous polymer samples.

Acknowledgement

The authors thank Bausch and Lomb Inc., for its support of this research and for granting permission for its publication.

References

[1] S.D. Hanton, Chem. Rev. 101 (2001) 527.
[2] J.H. Scrivens, A.T. Jackson, Int. J. Mass Spectrom. 200 (2000) 261.
[3] G. Montaudo, R.P. Lattimer (Eds.), Mass Spectrometry of Polymers, CRC Press, New York, 2002.
[4] G. Montaudo, M.S. Montaudo, C. Puglisi, F. Samperi, Macromolecules 28 (1995) 4562.
[5] D.R. Maloney, K.H. Hunt, P.M. Lloyd, A.V.G. Muir, S.N. Richards, P.J. Derrick, D.M. Haddleton, J. Chem. Soc. Chem. Commun. (1995) 561.
[6] A.T. Jackson, H.T. Yates, C.I. Lindsay, Y. Didier, J.A. Segal, J.H. Scrivens, G. Critchley, J. Brown, Rapid Commun. Mass Spectrom. 11 (1997) 520.
[7] C.M. Guttman, W.R. Blair, P.O. Danis, J. Polym. Sci., Part B: Polym. Phys. 35 (1997) 2409.
[8] G. Montaudo, M.S. Montaudo, F. Samperi, in: G. Montaudo, R.P. Lattimer (Eds.), Mass Spectrometry of Polymers, CRC Press, New York, 2002, p. 476.
[9] S.D.H. Shi, C.L. Hendrickson, A.G. Marshall, W.J. Simonsick, D.J. Aaserud, Anal. Chem. 70 (1998) 3220.

[10] S.M. Hunt, M.R. Binns, M.M. Sheil, J. Appl. Polym. Sci. 56 (1995) 1589.
[11] H.J. Rader, J. Spickermann, K. Mullen, Macromol. Chem. Phys. 196 (1995) 3967.
[12] G. Wilczek-Vera, P.O. Danis, A. Eisenberg, Macromolecules 29 (1996) 4036.
[13] M.S. Montaudo, F. Samperi, Eur. Mass. Spectrom. 4 (1999) 459.
[14] S. Yoshida, S. Yamamoto, T. Takamatsu, Rapid Commun. Mass Spectrom. 12 (1998) 535.
[15] J. Liu, R.S. Loewe, R.D. McCullough, Macromolecules 32 (1999) 5777.
[16] B.S. Prebyl, J.D. Johnson, A.A. Tuinman, S. Zhou, K.D. Cook, J. Am. Soc. Mass Spectrom. 13 (2002) 921.
[17] J. Axelsson, E. Scrivener, D.M. Haddleton, P.J. Derrick, Macromolecules 29 (1996) 8875.
[18] K. Martin, J. Spickermann, H.J. Rader, K. Mullen, Rapid Commun. Mass Spectrom. 10 (1996) 1471.
[19] D.C. Schriemer, L. Li, Anal. Chem. 69 (1997) 4169.
[20] D.C. Schriemer, L. Li, Anal. Chem. 69 (1997) 4176.
[21] G. Montaudo, D. Garozzo, M.S. Montaudo, C. Puglisi, F. Samperi, Macromolecules 28 (1995) 7983.
[22] J. Dwyer, D. Botten, Am. Lab. 28 (1996) 51.
[23] C.E. Kassis, J.M. DeSimone, R.W. Linton, E.E. Remsen, G.W. Lange, R.M. Friedman, Rapid Commun. Mass Spectrom. 11 (1997) 1134.
[24] M.S. Montaudo, C. Puglisi, F. Samperi, G. Montaudo, Macromolecules 31 (1998) 3839.
[25] M.W.F. Nielen, Anal. Chem. 70 (1998) 1563.
[26] M.S. Montaudo, G. Montaudo, Macromolecules 32 (1999) 7015.
[27] X.W. Lou, J.L.J. van Dongen, J. Mass Spectrom. 35 (2000) 1308.
[28] X.W. Lou, J.L.J. van Dongen, E.W. Meijer, J. Chromatogr. A 896 (2000) 19.
[29] S.D. Hanton, X.M. Liu, Anal. Chem. 72 (2000) 4550.
[30] O. Laine, H. Ostreholm, M. Selantaus, H. Jarvinen, P. Vainiotalo, Rapid Commun. Mass Spectrom. 15 (2001) 1931.
[31] X.M. Liu, E.P. Maziarz, F. Price, D.J. Heiler, G.L. Grobe, Eur. J. Mass Spectrom. 7 (2001) 473.
[32] E.P. Maziarz, X.M. Liu, E.T. Quinn, Y.C. Lai, D.M. Ammon, G.L. Grobe, J. Am. Soc. Mass Spectrom. 13 (2002) 170.
[33] E.P. Maziarz, X.M. Liu, Eur. J. Mass Spectrom. 8 (2002) 397.
[34] W.J. Simonsick, L. Prokai, Adv. Chem. Ser. 247 (1995) 41.
[35] M.W.F. Nielen, S. Malucha, Rapid Commun. Mass Spectrom. 11 (1997) 1194.
[36] D.J. Aaserud, L. Prokai, W.J. Simonsick, Anal. Chem. 71 (1999) 4793.
[37] L. Prokai, D.J. Aaserud, W.J. Simonsick, J. Chromatogr. A 835 (1999) 121.
[38] A.C.M. Kuo, Polymer Data Handbook, Oxford University Press Inc., 1999, p. 411.
[39] J.F. Kunzler, TRIP 4 (1996) 52.
[40] Y.C. Lai, E.T. Quinn, R.E. Bambury, Proc. ACS Div. Polym. Mater.: Sci. Eng. 76 (1997) 38.
[41] Y.C. Lai, R.E. Bambury, U.S. patent 5,420,324.