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ANALYSIS OF POLYLACTIDE GLYCOLIDE BY COUPLED GPC/MALDI-MS

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Presented at ASMS, Montréal, Canada, 8th-12th June 2003

OVERVIEW

Poly-(DL-Lactide-co-glycolide) (PLG) polymers are biocompatible and biodegradable polyesters used in drug delivery. Molecular weight data for these polymers is of importance as it relates to performance characteristics.

PLG polymers are usually highly polydisperse (P_d>1.5), thus presents a challenge for MALDI analysis.

GPC fractionation and MALDI-MS are coupled for the study of dispersed PLG.

INTRODUCTION

PLG polymers often have large polydispersities (P_d>1.5).

Although (MALDI-MS) has been used extensively to provide molecular weight, structural and compositional information of synthetic polymers, it often fails to provide correct molecular weight values for polydisperse (P_d>1.2) polymers.

The combination of GPC and MALDI-MS is used as a method for the characterization of polydisperse PLG by fractionation of the polymer into narrower molecular weight fractions before analysis by MALDI.

The polydispersity of the selected PLG sample is given as 5,000 to 15,000 Daltons by the manufacturer (Aldrich, Milwaukee, WI).

The GPC analytes (fractions) are deposited onto a matrix (Dithranol) pre-coated foil for subsequent MALDI analysis utilizing a LC-Transform® 600 instrument.

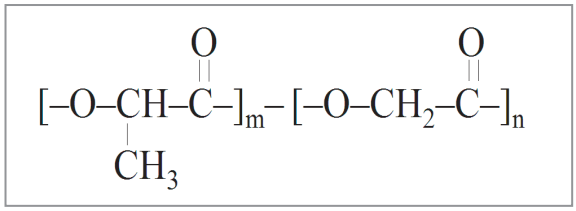

Figure 1. Poly-(DL-Lactide-co-glycolide) (PLG).

PLG is a copolymer of lactide and glycolide. As a result even low molecular weight oligomers exist as a complex mixture of molecular weights.

Lactide Glycolide Copolymer	MW: acid	MW: mer
Lactic acid: $C_3O_3H_6$	90	72
Glycolic acid: $C_2O_3H_4$	76	58

Table 1: PLG Copolymer repeating units information.

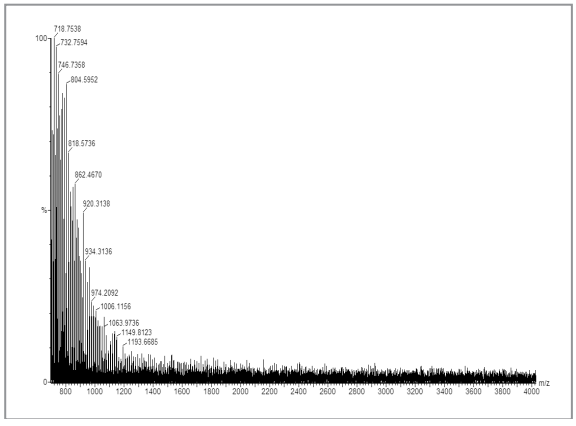

Figure 2. MALDI spectrum of PLG prior to GPC.

METHODS

Gel Permeation Chromatography (GPC)

Column:	Waters Styragel® HR2 4.6 x 300 mm at 25˚C
HPLC Pump:	Waters 616 pump with 600S controller
Detector:	Waters 2410 Refractive Index detector and 2996 Photodiode Array (PDA) detector
Flow rate:	Isocratic gradient of tetrahydrofuran (THF) at 0.3 mL/min for 60 min
Injection volume:	20 mL

LC-Transform Sample Collection Conditions

Sample concentration:	10 mg/mL
Sheath gas temperature:	125°C
Sheath gas flow:	30
Nebulizer gas flow:	25
Foil:	Dithranol 1-Time®/with sodium salt
Moving rate of collection	
Stage:	5 mm/min

MALDI-MS

Instrument:	Waters MALDI LR
Source Voltage:	15 KV
Delay time:	500 ns
Laser:	337 nm Nitrogen Laser from LSI (Franklin, MA)
Laser Rate:	10 Hz
Mode:	Positive ions in Reflectron mode
Detector:	MCP

RESULTS

GPC PDA spectrum

The GPC UV spectrum (Figure 3) shows that the polymer sample peak is between 10 min and 20 min.

The small peak close to the end of the run was not identified; no useful MALDI mass spectrum could be obtained from this fraction.

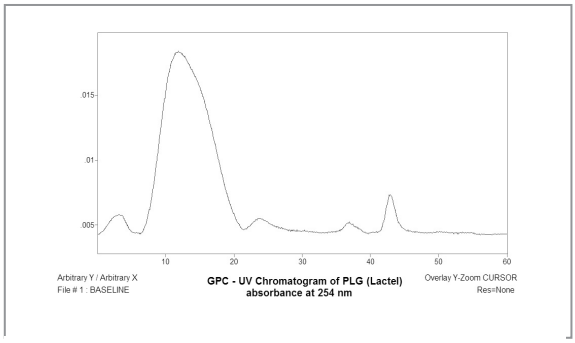

Figure 3. GPC PDA spectrum of the selected PLG co-polymer at UV wavelength of 254 nm.

MALDI-MS Spectra

Figure 4 shows a nice polymer distribution centered at about m/z=2,000, which indicates the GPC has separated the polydispersed PLG into narrow fractions. This is an example of one fraction.

Figure 5 is an expanded spectrum from Figure 4, which shows that the mass difference between the spectrum peak clusters is 14 amu, which is the mass difference between the monomers of Lactide [$OCH(CH_3)C(O)$] and Glycolide [$OCH_2C(O)$].

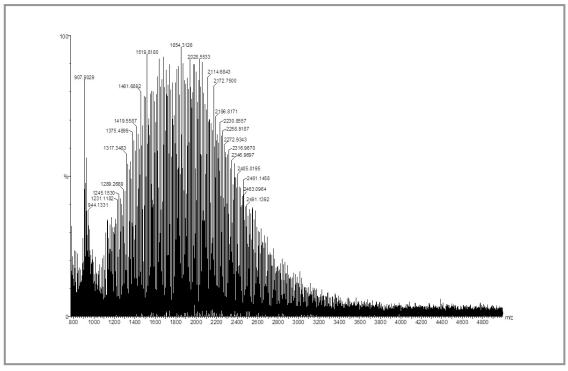

Figure 4. MALDI-MS spectrum from one of the GPC fraction spot on the MALDI target plate. The spectrum is a summation of 100 laser shots.

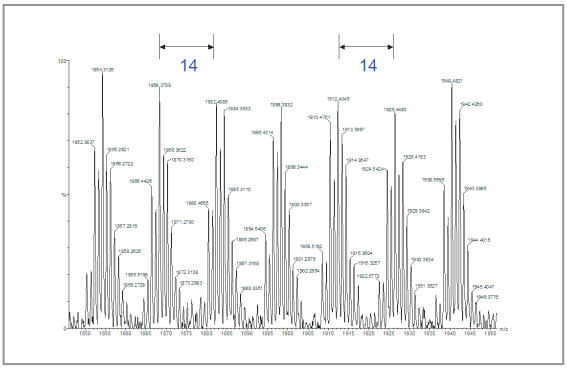

Figure 5. Partial spectrum from Figure 4. The 14 mass units different among the oligomers indicates that the sample is PLG co-polymer (see structure from the introduction section of the poster).

Figure 6 is a series MALDI-MS spectra taken from various fractions of the GPC separation.

The molecular distributions are observed between ~ 2,000 amu and ~ 5,000 amu, although the vendor's average molecular weight specification is between 5,000 amu and 15,000 amu.

Repeated test runs under the same conditions yielded similar results. Thus, additional studies are needed to determine the cause of the disparity between the two sets of values.

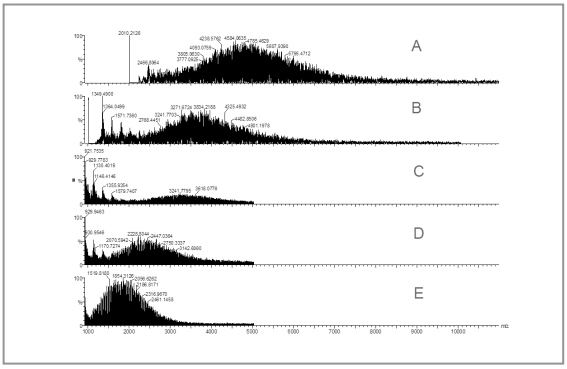

Figure 6. MALDI-MS spectra of PLG co-polymers from GPC fractionation. Elution order A to E. Each spectrum is a summation of 100 laser shots.

CONCLUSION

MALDI data confirms that the Poly-(DL-lactide-co-glycolide) (PLG) polymer has been separated into narrow fractions by GPC.

The data resolution is vastly improved when using the combination of GPC and MALDI-MS. This method overcomes the inherent problems associated with polydispersity of polylactide glycolide by fractionation into narrower distribution ranges.

The LC-Transform provides an efficient and convenient alternative to fraction collection when preparing GPC/MALDI-MS samples.

Additional studies conducted under different GPC and MALDI conditions may be performed to further confirm the molecular weight distribution of the sample in the study.

ACKNOWLEDGEMENT

Waters Corporation: Dr. James Willis
Dr. Anders Lund
Dr. Jeanne Li

Lab Connections: Dr. Marilyn Briley
James L. Dwyer
Morgan Hynes

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