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Pyrolysis-Gas Chromatographic/Mass Spectrometry as an Alternative to H1-NMR and Gas Chromatography with Chiral Column for the Analysis of Lactide/ Caprolactone Mole Ratio of Biodegradable Copolymers

Dave Pinson[1*], Thu-Ngoc Tran[1], Ryo Kamberi[1], Marika Kamberi[1]

[1]Analytical Chemistry and Biocompatibility, Abbott Medical Devices 3200 Lakeside Drive, Santa Clara, CA 95054 USA

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***Corresponding author :** Dave Pinson, Analytical Chemistry and Biocompatibility, Abbott Medical Devices 3200 Lakeside Drive, Santa Clara, CA 95054 USA. E mail: David.Pinson@abbott.com*

Abstract

A novel pyrolysis-gas chromatographic mass spectrometry (PY-GC/MS) method was developed to determine the mole ratio of lactide/ caprolactone copolymers and physical mixtures of the two polymers. The method employs a simple sample preparation. The copolymer sample is dissolved in dichloromethane and ten microliters of the solution transferred to a sample cup for analysis. The analytical results for lactide/ caprolactone copolymers samples of 5 to 30 mole % caprolactone compositional ratios were in good agreement with those obtained by H1-NMR spectrometry and gas chromatography using flame ionization detection with a chiral column.

Keywords: Copolymer mole ratio; Polylactides; Polycaprolactone; Pyrolysis–GC/MS.

Introduction

Degradable polymeric biomaterials are preferred candidates for developing therapeutic devices such as temporary prostheses, bioresorbable drug-eluting stents, three-dimensional porous structures as scaffolds for tissue engineering and as controlled/ sustained release drug delivery vehicles. Each of these applications demands materials with specific physical, chemical, biological, biomechanical and degradation properties to provide efficient therapy [1]. Recently, copolymers have got tremendous impetus on the ongoing research in the area of drug delivery technology, due to their capability to provide a biomaterial having a broad range of amphiphilic characteristics, as well as targeting the drugs to specific site. Thus, copolymers based on polyethylene glycol (PEG) and polycaprolactone (PCL) or polylactide (PLA) are receiving increasing attention for biomedical applications. By varying the copolymer composition, monomer sequencing and molecular weight, the copolymer properties can be tailored to meet the specific requirements of each particular application. In view of the importance of copolymer composition to the tailoring of copolymer properties, the development of adequate analytical methods for the analyses of chemical composition of copolymers is as important as the design of new polymer architectures.

Historically, H1-NMR [1- 4] and chiral gas chromatography with flame ionization detection [5] have been employed to determine the composition of lactide/ caprolactone copolymers and polymer mixtures. While H1-NMR analysis is relatively easy and does not require extra steps for sample preparation, such as separation or derivatization, the low sensitivity remains a weak point for NMR compared with mass spectrometry. Conversely, the sample preparation for analysis by chiral gas chromatography with flame ionization detection is significantly more time-consuming and complex due to the necessity to first hydrolyze the copolymer to their respective monomers and then derivatize to facilitate chromatography, but the analysis and data interpretation are straight forward and simple.

Pyrolysis–Gas Chromatography/Mass Spectrometry (PY-GC/MS) is a method of chemical analysis which has extended the range of possible tools for characterization of synthetic polymers/ copolymers. In PY-GC/MS, the sample is thermally decomposed in an inert atmosphere to produce smaller volatile molecules that can be separated by gas chromatography and detected using mass spectrometry. At a given pyrolysis temperature, the input of thermal energy will cause chemical bonds to break in a reproducible manner that depends on the structure of the molecule. Mass spectrometry can then be used to identify and quantify the individual peaks in the chromatogram. Therefore, it can a be used for quantitative determination of polymer compositions by comparing peak area ratios of monomers and/ or primary pyrolysis products.

The aim of this work was the development of a simple, sensitive and efficient PY-GC/MS method for the determination of the mole fraction caprolactone and the mole fraction lactide in the lactide-caprolactone copolymer. Data generated by the developed method were compared with data from the H1-NMR and gas chromatography with chiral column methods to demonstrate that equivalent results can be achieved by replacing the H1-NMR method by a faster and more convenient method. The advantage of the PY-GC/MS method presented here is that

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both sample preparation and analysis and data interpretation are relatively simple and straight forward.

Methods

Materials

Methanolic 3N hydrochloric acid, Methanolic 1N potassium hydroxide and dichloromethane were purchased from Sigma Aldrich (St. Louis, Mo). Poly (L-lactide), RESOMER® L210S resin, inherent viscosity= 3.9 dl/g, was purchased from Evonik Industries (Essen, Germany). Poly (caprolactone), Purasorb PC12, inherent viscosity= 1.2 dl/g was purchased from Corbion (Amsterdam, Netherlands). PLC7015, 70/30 L-lactide/ caprolactone copolymer resin, inherent viscosity= 1.5 dl/g, PLC9517, 95/5 L-lactide/caprolactone copolymer resin, inherent viscosity= 1.7 dl/g, PLC9010, 90/10 L-lactide/caprolactone copolymer resin, inherent viscosity= 1.0 dl/g, PLC9015, 90/10 L-lactide/caprolactone copolymer resin, inherent viscosity= 1.5 dl/g, PLC8515, 85/15 L-lactide/caprolactone copolymer resin, inherent viscosity= 1.5 dl/g, and PLC8535, 85/15 L-lactide/ caprolactone copolymer resin, inherent viscosity= 3.5 dl/g, were purchased from Corbion (Amsterdam, Netherlands).

Polymer Nomenclature

All L-lactide/ Caprolactone copolymer ratios are expressed as mole %.

Poly (L-lactide), abbreviated PLLA, poly ((3S-cis)-3,6-dimethyl-1,4-dioxane-2,5-dione), CAS Registry No. 33135-50-1, is also known as poly (L-lactic acid), poly ((S)-2-hydroxypropionic acid) and poly (sarcolactic acid).

Poly (caprolactone), abbreviated PCL or PC, (1,7)-polyoxepan-2-one, CAS Registry No. 24980-41-4, is also known as 2-Oxepanone homopolymer and 6-Caprolactone polymer.

Poly (L lactide/ caprolactone) copolymer, (3S-cis)-3,6-dimethyl-1,4-dioxane-2,5-dione, polymer with 2-oxepanone, abbreviated PLC, CAS Registry No. 65408-67-5, is also known as PLCL, poly(l-lactide-co-ε-caprolactone).

Instrumentation, Chromatography and Sample Preparation for the PY-GC/MS Method

Instrumentation and Chromatography

The PY-GC/MS system used in this work consisted of a Frontier Lab Model EGA/PY3030D pyrolyzer, a Frontier Lab Model AS1020E autosampler (Koriyama, Fukushima, Japan) and an Agilent Technologies 6890N series gas chromatograph interfaced to an Agilent Technologies 5973C series quadrupole mass spectrometer (Santa Clara, CA, USA). Pyrolysis was performed in deactivated stainless-steel cups from Frontier Lab. The pyrolyzer was operated at a constant temperature of 600°C. The separation of pyrolysis products was accomplished using a Frontier Lab Ultra Alloy 5 metal column, 30 m long, 0.25 mm i.d. with 5% diphenyldimethyl polysiloxane bonded stationary phase. The column was installed in the split/splitless injection port set to 300°C, with a split ratio of 100:1. The helium carrier gas with a purity of 99.99% (Air Liquide, Paris, France) was set to 1.0 mL/minute (min) in the constant flow mode. The gas chromatographic conditions were as follows: the column oven was initially held at 50°C for 2 min, then ramped to 120°C at 5°C/min and held for 1 min. Finally, the column was heated at 30°C/ min to 320°C and held one minute to insure all pyrolyzates were eluted from the column. The capillary direct transfer line temperature was maintained at 300°C. Pyrolytic degradation products were detected by the mass spectrometer operated in the positive electron ionization mode. The ion source temperature was set to 230°C. The ionization occurred with a kinetic energy of the impacting electrons at 70 eV. The column effluent was scanned from mass 33 to 450 m/z. The quadrupole temperature was 150°C. The GC/MS data were processed with Agilent Technologies ChemStation or MassHunter software and the National Institute of Standards and Technology NIST17 Mass Spectral Library (Agilent Technologies, Santa Clara, CA, USA).

Sample Preparation

Polymer samples were prepared for PY-GC/MS analysis as follows. Samples were prepared at a polymer concentration of about 2 mg/mL in dichloromethane. Spiked recovery samples were prepared gravimetrically by weighing PLLA and PCL resins into vials at amounts targeting 5, 15 and 30 mole % PCL. Each spiked recovery sample was dissolved in dichloromethane at a polymer concentration of about 2 mg/mL. Ten microliters of sample preparation were transferred to a clean pyrolysis cup. The solvent was allowed to evaporate at room temperature prior to PY-GC/MS analysis under the parameters provided in the Instrumentation and Chromatography section.

Calibration Standard Preparation

A 100% PLLA calibration standard stock solution at approximately 2 mg/mL in dichloromethane was prepared by adding about 30 mg of PLLA, accurately weighed, into a 20 mL scintillation vial. A volume of 15.0 mL of dichloromethane was added using a glass Class A volumetric pipette.

A 100% PCL calibration standard stock solution at approximately 2 mg/mL in dichloromethane was prepared by adding about 30 mg of PCL, accurately weighed, into a 20 mL scintillation vial. A volume of 15.0 mL of dichloromethane was added using a glass Class A volumetric pipette.

The Calibration Stock Standard preparations were shaken overnight at ambient room temperature on a table shaker set at 200 motions per minute to insure complete dissolution. Calibration standards from approximately 3 to 36 mole % PCL were then prepared by volumetric dilution of the PLLA and PCL stock calibration standard solutions in dichloromethane.

Instrumentation, Chromatography and Sample Preparation for the Gas Chromatography–Flame Ionization Detection (GC–FID) Method

Instrumentation and Chromatography

The chiral gas chromatographic system consisted of an Agilent 6890N series gas chromatograph with a flame ionization detector (GC/FID). A CycloSil-B fused silica capillary column; 30 meter

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x 0.25 mm ID, 0.25 µm coating thickness with 30% hepatkis (2,3-di-O-methyl-6-O-t-butyl dimethylsilyl)-ß-cyclodextrin in DB-1701 Agilent Catalog # 112-6632, was installed in the split/splitless injection port set to 250^{0}C, operated in the split mode with a 75:1 split ratio. Helium carrier gas with a purity of 99.99% (Air Liquide, Paris, France) was set to 1.8 mL/min in the constant flow mode. The gas chromatographic conditions were as follows: the column oven was initially held at 90°C for 5 min, then ramped to 200°C at 10°C/min and held for 0 min. Finally, the column was ballistically heated at 100°C/ min to 220°C and held for 2.8 minutes.

Sample Preparation

Polymer samples were prepared for chiral GC/FID analysis as follows. Accurately weigh about 25 mg of PLLA / PCL resin into a 20 mL scintillation vial. Add 2 mL of 1N methanolic potassium hydroxide. Heat at 65°C with agitation for 40 minutes in the capped vial to hydrolyze PLLA and PCL polymers into their respective monomers. Allow vial to cool to room temperature and add 2 mL of 3N Methanolic HCl to derivatize (methylate) the respective monomers. Heat at 65°C with agitation for 15 minutes in the capped vial. Add 2.5 mL of water to dissolve the potassium chloride precipitate and 8.0 mL of dichloromethane. Mix vial and allow the layers to separate. Transfer an aliquot of the bottom dichloromethane layer to an autosampler vial for analysis by GC/FID.

Results and Discussion

Rationale for the Analytical Parameters Selected

An Ultra Alloy 5 metal chromatographic column was selected due to its well-known inertness at high column temperatures and the ability to separate a wide range of analytes, based primarily on their boiling points. The column oven profile, from 50°C to 320°C, was employed to detect species over a wide boiling point range. The column effluent was swept into the mass spectrometer via a capillary direct connection to optimize sensitivity. The mass spectrometer was operated in the positive ion EI (electron ionization) mode at 70eV to facilitate NIST17 Library searches of peak mass spectra. In addition, at this level of energy, small changes in the electron beam do not significantly affect the fragmentation patterns of polymers. The scan range, from mass 33 to 450 m/z, captured as many pyrolyzates as possible while maintaining good sensitivity for a quadrupole mass filter.

Pyrolysis temperatures in the range of 550 to 650°C were evaluated using a 70/30 PLLA/PCL copolymer. A pyrolysis temperature of 600°C resulted in pyrograms with a greatest number of pyrolyzates at the highest abundances and therefore was selected for analysis of the samples. A comparison of PLC 7015 lactide caprolactone copolymer resin pyrograms at 550, 600 and 650°C are presented in Figure 1.

The impact of resin viscosity, a surrogate for molecular weight, was investigated. Total ion current pyrograms for a low, 1.5 dL/g,

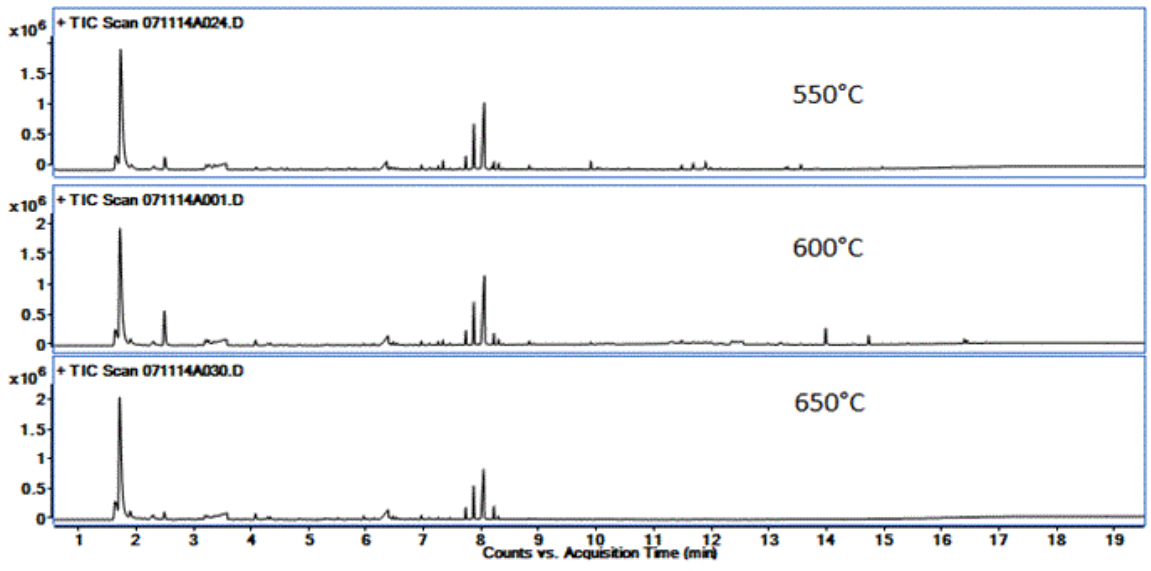

Figure 1: Effect of Temperature on the Pyrolyzate Profile

and a higher viscosity, 3.5dL/g, 85/15 PCL/PLLA copolymer resin preparations are presented in Figure 2. The comparison of the low and higher viscosity pyrograms showed identical fragmentation fingerprints of polymers, indicating that method was not affected by the viscosity of the resin.

Selection of the Peaks and Masses for Quantification

PCL Resin

Figure 3 shows the total ion current (TIC) pyrogram of pure PCL resin. The NIST17 GC/MS library was used to

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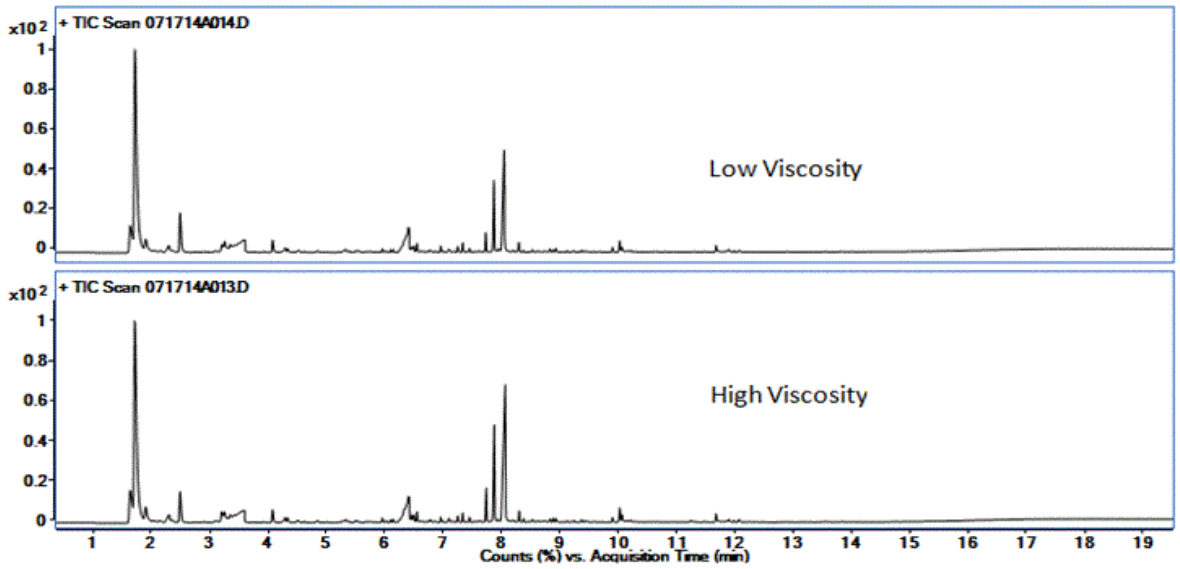

Figure 2: Pyrolyzate Profile Comparison of Low and High Viscosity 85/15 Lactide/ Caprolactone Copolymer Resin

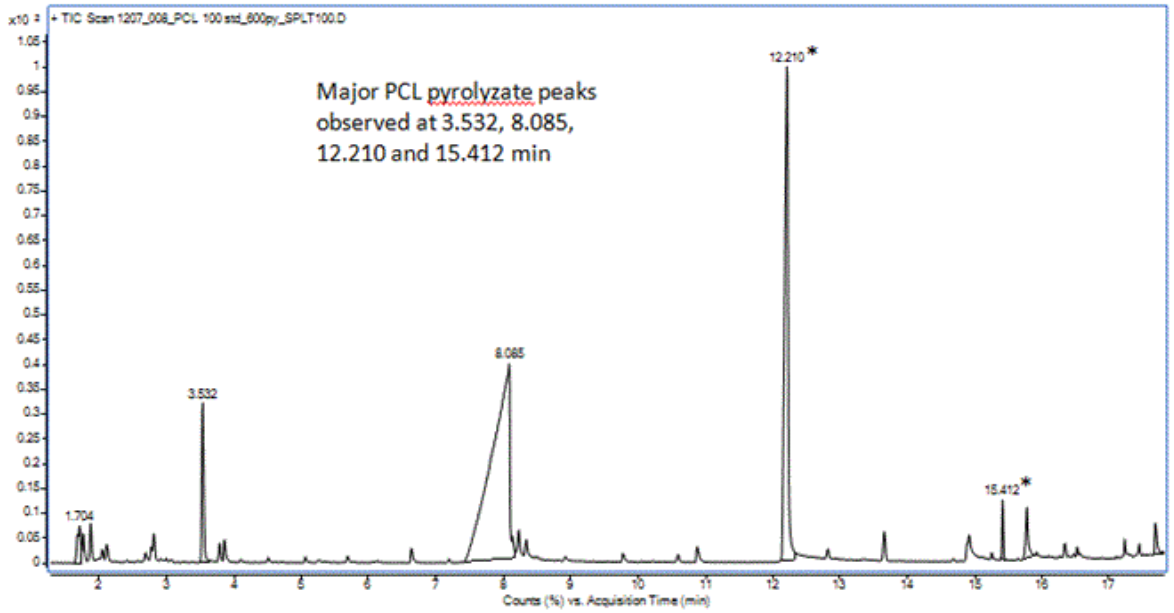

Figure 3: Total Ion Current GC/MS Pyrogram of 100% Polycaprolactone Resin *Peaks Selected for Caprolactone Quantification

identify the major components formed upon pyrolysis of PCL. The best matching compounds of the four major pyrolyzates were cyclopentanone (CAS #120-92-3), 5- hexanoic acid (CAS #142-62-1), ε-caprolactone (CAS #502-44-3) and acetic acid, 4-oxocyclohexyl ester (CAS #66405-41-2) for peaks at retention times of 3.532, 8.085, 12.210 and 15.412 minutes, respectively. The largest peak at an approximate retention time of (RT) 12.210 minutes and an additional peak at 15.412 minutes were selected for quantitation. Mass spectra of these two peaks are presented in Figure 4. The unique ion m/z 84 and the most abundant ion m/z 114 were selected as quantitation ions for peaks at RT 12.210 and 15.412 minutes, respectively. The summed peak areas of the extracted quantitation ions from the TIC pyrogram were used to determine the caprolactone response ratio.

PLLA Resin

Figure 5 shows the TIC pyrogram of pure PLLA resin. The NIST17 GC/MS library was used to identify the major components formed upon pyrolysis of PLLA. The best matching compounds for the four major pyrolyzates were acetaldehyde (CAS #75-07-0), pentane-2,3-dione (CAS #600-14-6), prop-2-enoic acid (CAS #79-10-7) and 3,6-Dimethyl-1,4-dioxane-2,5-dione (CAS #95-96-

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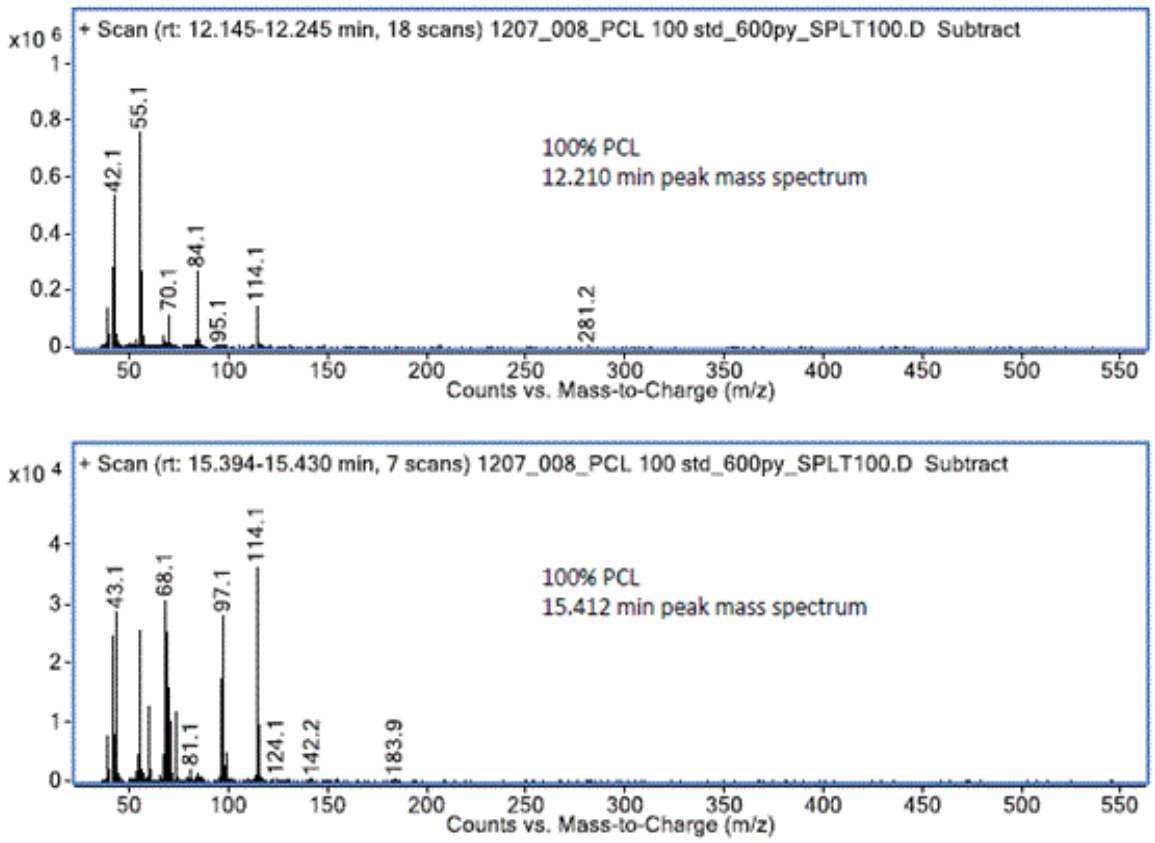

Figure 4: Mass Spectra of 12.210 and 15.412 Minute Retention Time Peaks Selected For PCL Quantification

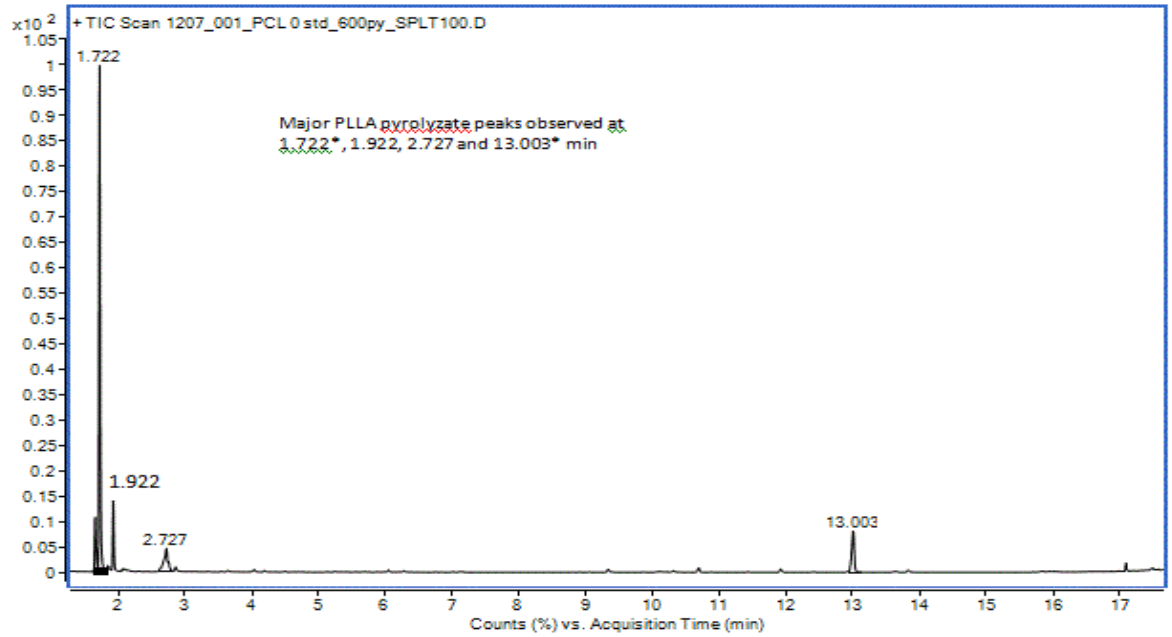

Figure 5: Total Ion Current GC/MS Pyrogram of 100% Poly (Lactide) Resin *Peaks Selected for Quantification of Lactide Amount

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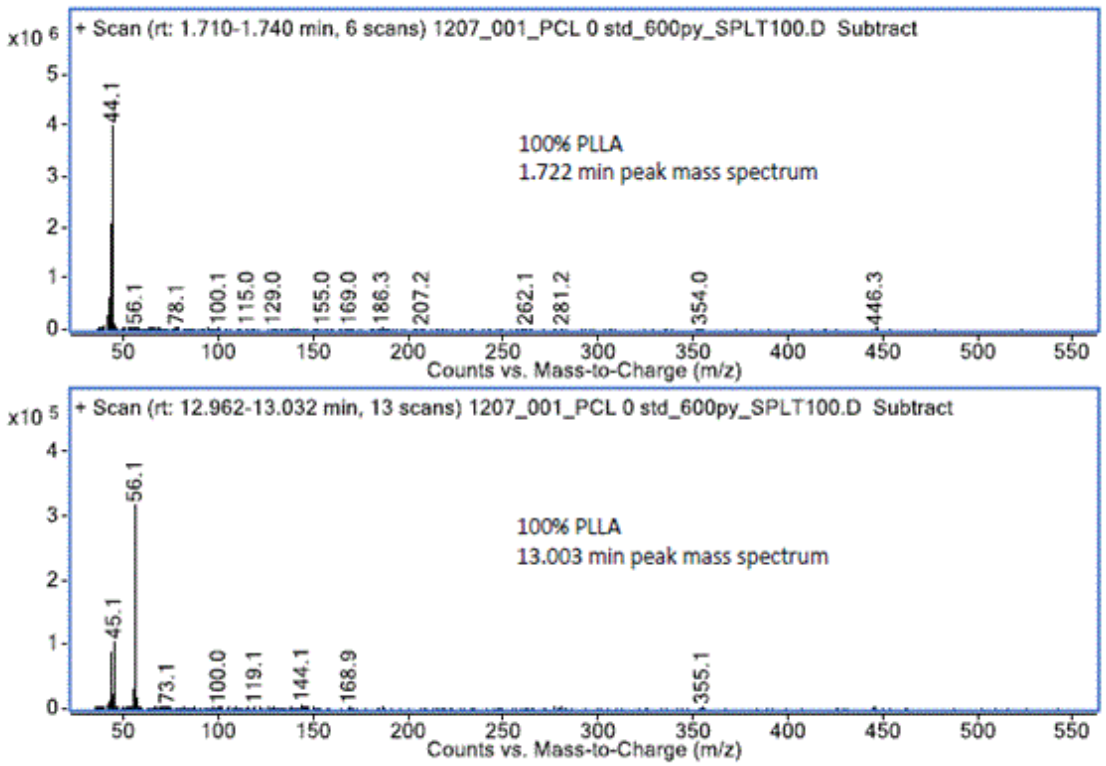

Figure 6: Spectra of Peaks at Retention Times of 1.7 and 13.0 Minutes Selected for PLLA Quantification

5), for peaks at RT 1.722, 1.922, 2.727 and 13.003 minutes, respectively. The largest peak at an RT of 1.722 minutes and an additional peak at 13.003 minutes were selected for the quantitation. Mass spectra of these two peaks are presented in Figure 6. The most abundant ion m/z 44 and m/z 56 were selected as quantitation ions for peak at RT 1.722 and 13.003 minutes, respectively. The summed peak areas of the extracted quantitation ions from the TIC pyrogram were used to determine the caprolactone response ratio.

Quantitation of PCL in PCL/PLLA Copolymer

Quantification was accomplished by linear regression analysis using a calibration curve created with calibration standards prepared per Calibration Standard Preparation in the Instrumentation, Chromatography and Sample Preparation for the PY-GC/MS Method section. The caprolactone response ratios were determine by dividing the sum of the caprolactone peak areas of the extracted ions by the total sum of caprolactone and lactide peak areas of the extracted ions. The caprolactone response ratios were plotted against the mole % caprolactone. The caprolactone response ratio was calculated according to the equations below:

Caprolactone response ratio = (AC12.2 + AC15.4) / (AC12.2 + AC15.4 +AL1.7 + AL13.0)

Where:

AC12.2 is the area for the 84 m/z extracted ion caprolactone peak at 12.210 minutes

AC15.4 is the area for the 114 m/z extracted ion caprolactone peak at 15.412 minutes

AL1.7 is the area for the 44 m/z extracted ion lactide peak at 1.722 minutes

AL13.0 is the area for the 56 m/z extracted ion lactide peak at 13.003 minutes

Selectivity Assessment

The method selectivity was evaluated by the absence of significantly interfering peaks at retention times of caprolactone and lactide peaks selected for the quantification analysis. The extracted ion pyrograms of 100% poly (caprolactone) and poly (lactide) were compared for each quantification peak to assess the presence of peaks which may pose an interference for caprolactone or lactide quantification ions, which represented the worst-case scenario for selectivity.

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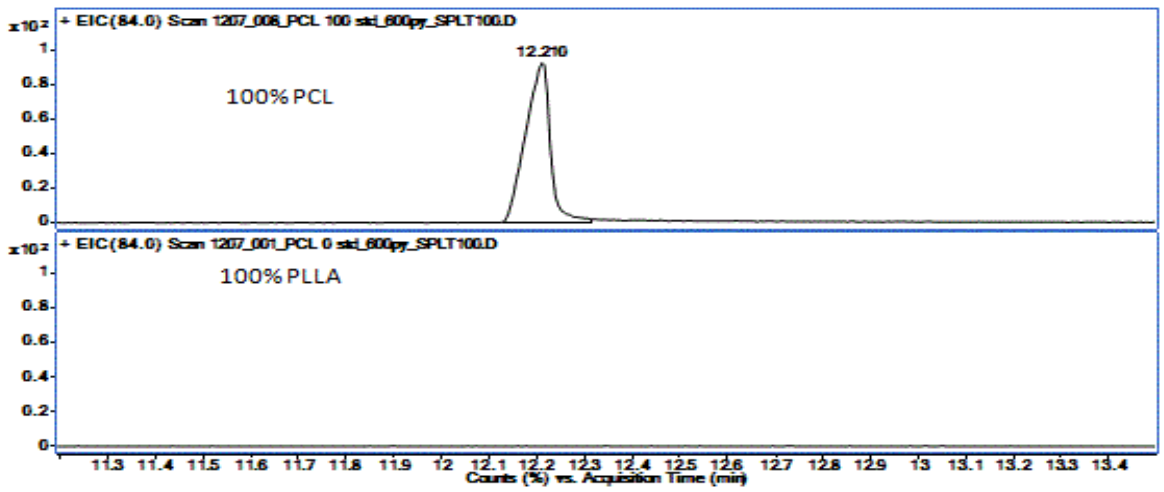

Figure 7: Selectivity Assessment for the Caprolactone Quantification Peaks at 12.210 Minutes 84 m/z Extracted Ion Pyrograms for the 100% poly (lactide) and 100% poly (caprolactone) resins

The 84 m/z extracted ion pyrograms of 100% poly (caprolactone) and 100% poly (lactide) resins are presented in Figure 7. No peaks were observed in the 100% poly (lactide) pyrogram at 12.210 minutes, the retention time of the poly (caprolactone) peak utilized for caprolactone quantification, demonstrating good method selectivity.

The 114 m/z extracted ion pyrograms of 100% poly (caprolactone) and 100% poly (lactide) resins are presented in Figure 8. No peaks were observed in the 100% poly (lactide) pyrogram at 15.412 minutes, the retention time of the poly (caprolactone) peak utilized for caprolactone quantification, demonstrating good method selectivity.

The 44 m/z extracted ion pyrograms of 100% poly (lactide) and 100% poly (caprolactone) resins are presented in Figure 9. A small peak is observed eluting at 1.669 minutes in 100% poly (caprolactone) resin pyrogram, just prior to the 1.722 minute lactide quantification peak. The peak at 1.669 minute was observed in the extracted ion pyrograms of the calibration standards, but was well-resolved, resolution of 1.9 as calculated per <USP 621>, from the 1.722 minute peak used for quantification. The relative intensity of the 1.669 minute peak was small, compared to the intensity of the 1.722 minute peak for both standards and the resolution was sufficient, that method quantification was not impacted by its presence.

The 56 m/z extracted ion pyrograms of 100% poly (caprolactone) and 100% poly (lactide) resins are presented in Figure 10. No peaks were observed in the 100% poly (caprolactone) resin pyrogram at about 13.003 minutes, the peak selected for caprolactone quantification, demonstrating good

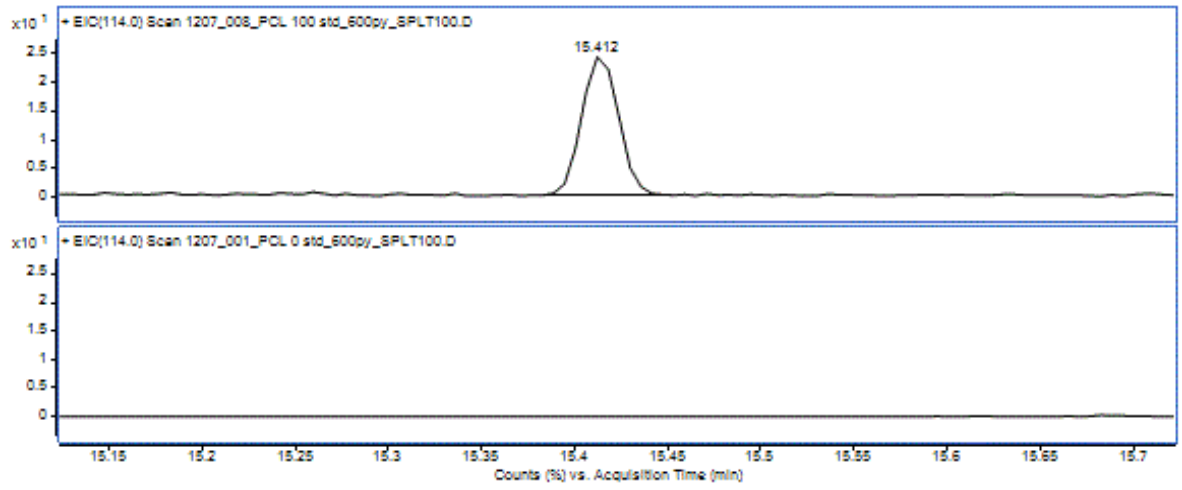

Figure 8: Selectivity Assessment for the Caprolactone Quantification Peak at 15.412 Minutes 114 m/z Extracted Ion Pyrograms for the 100% poly (lactide) and 100% poly (caprolactone) resins

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method selectivity.

PY-GC/MS Method

PY-GC/MS Linearity

Good method linearity was demonstrated over a range from 3.74 to 36.3 % PCL. The caprolactone response ratios were plotted against the caprolactone mole % with a coefficient of determination of 0.9937. A representative calibration curve is presented in Figure 11.

PY-GC/MS Accuracy

Method accuracy was assessed by six replicate determinations at three levels, low, medium and high with nominal targets of 6.5, 18 and 35% PCL, respectively. The results are presented in Table 1. The % recoveries of the fortified PCL amounts at each level ranged from 101.25 to 117.26%, 92.92 to 108.09% and 88.60 to 108.79% at the low, medium and high levels, respectively. The average % recoveries for the six replicate preparations at the low level, medium and high levels were 109.11, 98.03 and 101.32%, respectively. The method demonstrated good accuracy over the evaluated spiked recovery range from approximately 6.5 to 35 mole % PCL.

PY-GC/MS Precision

The PY-GC/MS method precision was assessed by evaluating the % RSD of the spiked recovery of Accuracy samples and the %RSD of %PLC determination of lactide/caprolactone copolymer resins.

The % RSD's of the six replicate preparations of Accuracy samples at the low, medium and high levels were 5.75, 5.68 and 7.48%, respectively (Table 1). Overall, the method demonstrated good precision over the evaluated range from approximately 6.5 to 35% PCL.

The %RSD's of six replicate caprolactone determinations at the nominal 5, 10 and 30 mole % PCL resins were 1.30, 3.71 and 4.73%, respectively (Table 2). The method demonstrated excellent precision for the determination of caprolactone in the

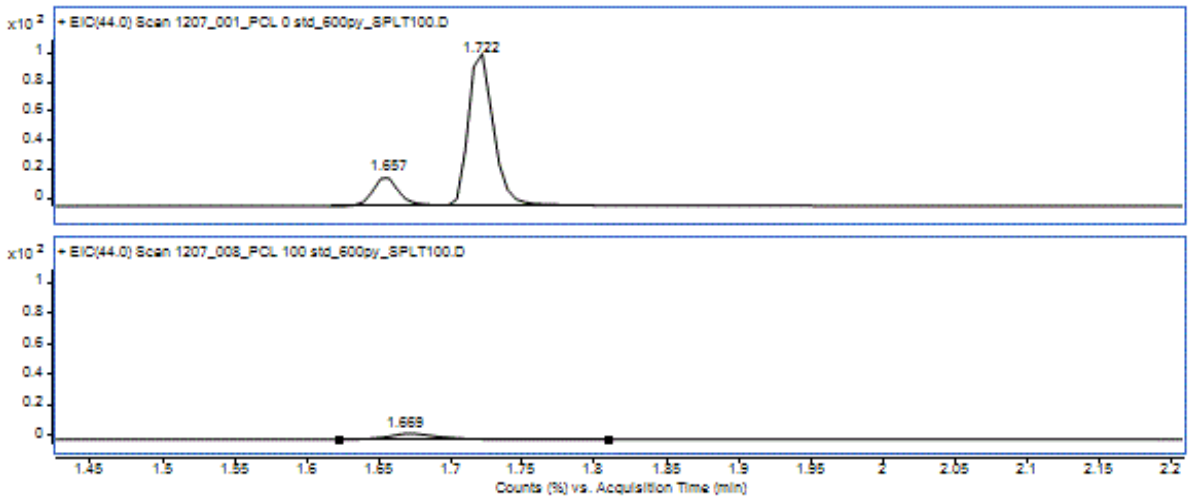

Figure 9: Selectivity Assessment for the Lactide Quantification Peak at 1.722 Minutes 44 m/z Extracted Ion Pyrograms for the 100% poly (lactide) and 100% poly (caprolactone) resins

Table 1: Accuracy and Precision Results of PCL from Fortified Mixtures of PCL and PLLA by PY-GC/MS Method

Accuracy Level	Mole % PCL Fortified	Mole % PCL Found	% Recovery of Spiked	Average % Recovery	% Relative Standard Deviation
Low	6.38	7.11	111.44	109.11	5.75
	6.88	7.72	112.13		
	6.48	7.6	117.26		
	6.8	7.53	110.63		
	6.85	6.94	101.25		
	7.03	7.16	101.93		
Medium	18.49	17.55	94.87	98.03	5.68
	18.63	20.13	108.09		
	18.13	17.12	94.42		
	17.7	16.44	92.92		
	17.91	17.94	100.16		
	18.14	17.73	97.72		

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High	34.92	37.99	108.79	101.32	7.48
	34.72	36.15	104.14		
	35	31.01	88.6		
	35.3	33.91	96.09		
	35.44	36.73	103.63		
	35.24	37.6	106.7		

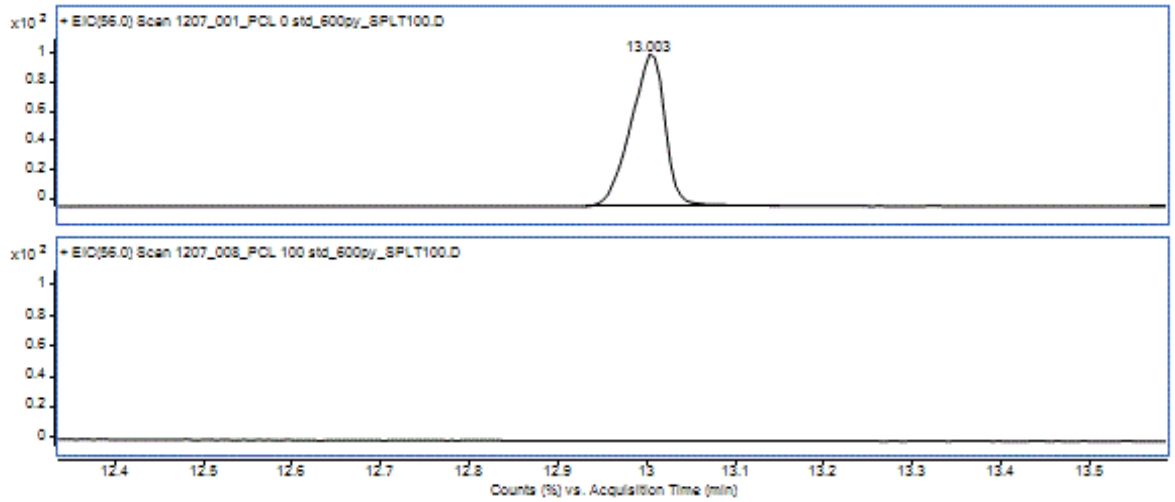

Figure 10: Selectivity Assessment for the Lactide Quantification Peak at 13.003 Minutes 56 m/z Extracted Ion Pyrograms for the 100% poly (lactide) and 100% poly (caprolactone) resins

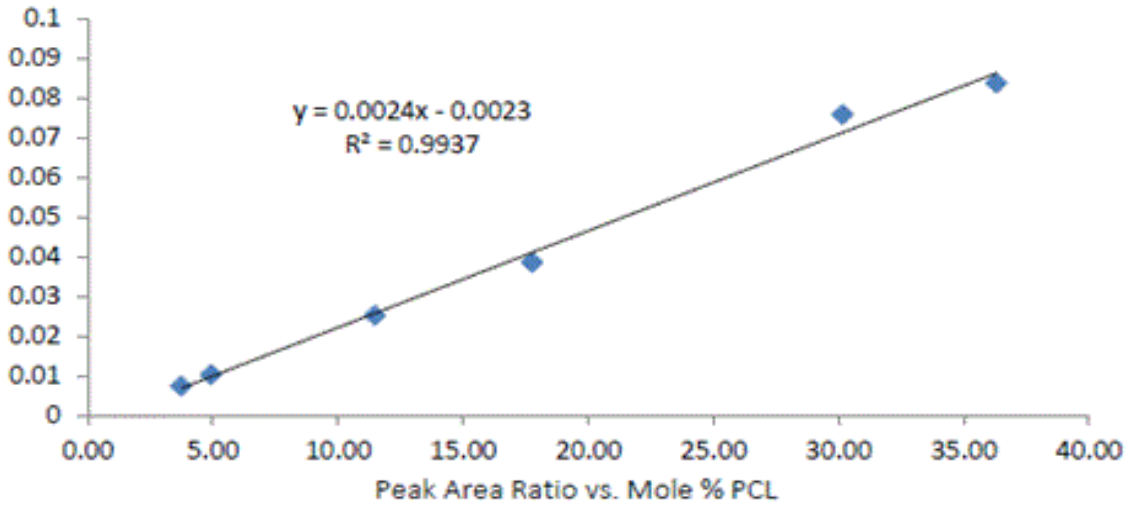

Figure 11: PY-GC/MS Mole % Caprolactone Calibration Curve

lactide/ caprolactone copolymer resins from 5 to 30% PCL.

Chiral GC/FID Method

Chiral GC/FID Accuracy

Method accuracy was assessed by three replicate determinations at three levels, low, medium and high with nominal targets of 3.5, 28 and 40 mole % PCL. The results are presented in Table 3. The % recoveries of the fortified PCL amounts at each level ranged from 99 to 101%, 98 to 99% and 99 to 100% at the low, medium and high levels, respectively. The average % recoveries for the six replicate preparations at the low level, medium and high levels were 100, 99 and 100%, respectively. The method demonstrated good accuracy over the evaluated spiked recovery range from approximately 3.5 to 40 mole percent PCL.

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Table 2: Precision Results of PCL from Lactide/Caprolactone Copolymer Resin by PY-GC/MS Method

Resin	Nominal Mole % PCL*	Mole % PCL by PY-GC/MS	Average % PCL by PY-GC/MS	% Relative Standard Deviation	% Agreement with Vendor C of A
PLC9517	5	4.82	4.86	1.3	96
		4.93			99
		4.89			98
		4.91			98
		4.76			95
		4.88			98
PLC9010	10	10.58	10.44	3.71	106
		9.81			98
		10.24			102
		10.4			104
		10.93			109
		10.66			107
PLC7015	30	28.84	29.37	4.73	96
		29.07			97
		28.6			95
		29.07			97
		32.16			107
		28.48			95

* The nominal mole %PCL values presented in this table were extracted from their respective vendor Certificates of Analysis, determined by H^1-NMR

Table 3: Accuracy and Precision Results of PCL from Fortified Mixtures of PCL and PLLA for GC/FID Method

Accuracy Level	Mole % PCL Fortified	Mole % PCL Found	% Recovery of Spiked	Average % Recovery	% Relative Standard Deviation
Low	3.5	3.54	101	100	1.2
	3.41	3.37	99		
	3.67	3.66	100		
Medium	27.9	27.67	99	99	0.5
	27	26.54	98		
	28.46	28.21	99		
High	38.9	38.6	99	100	0.4
	41.34	41.36	100		
	39.75	39.57	100		

Table 4: Precision Results of PCL from Lactide/Caprolactone Copolymer Resin by Chiral GC/FID Method

Resin	Nominal Mole % PCL*	Mole % PCL by GC/FID	Average % PCL by GC/FID	% Relative Standard Deviation	% Agreement with Vendor C of A
PLC9517	5	4.45	4.58	3.1	89
		4.4			88
		4.73			95
		4.58			92
		4.75			95
		4.55			91
PLC9010	9	9.6	8.93	7.2	107
		9.2			102
		9.1			101
		8.9			99
		9.1			101
		7.7			86

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PLC7015	30	28.66	29.57	6.4	96
		28.51			95
		28.78			96
		28.94			96
		32.94			110
		N/A			N/A

Chiral GC/FID Precision

The GC/FID method precision was assessed by evaluating the % RSD of the spiked recovery of Accuracy samples and the % RSD of % PLC determination of lactide/caprolactone copolymer resins.

The % RSD's of the six replicate preparations of Accuracy samples at the low, medium and high levels were 1.2, 0.5 and 0.4%, respectively (Table 3). Overall, the method demonstrated good precision over the evaluated range from approximately 3.5 to 40 mole % PCL.

The %RSD's of six replicate caprolactone determinations at the nominal 5, 9 and 30 mole % PCL resins were 3.1, 7.2 and 6.4%, respectively (Table 4). The method demonstrated excellent precision for the determination of caprolactone in the lactide/ caprolactone copolymer resins from 5 to 30% PCL.

Comparison of PY-GC/MS and Chiral GC/FID Results with H1-NMR Data

PY-GC/MS Results Compared with H1-NMR

The PY-GC/MS resin composition results for commercially available resins were compared to their respective H1-NMR results extracted from vendor Certificate of Analysis (C of A). The average % agreement with H1-NMR value for lactide/ caprolactone copolymer resins at nominal 5, 10 and 30 mole % PCL, analyzed by PY-GC/MS, are presented in Table 5.

The average % agreement with the H1-NMR value for the nominal 5% resin, PLC9517, determined by PY-GC/MS was 97%. The composition by PY-GC/MS ranged from 4.76 to 4.93 mole % PCL, representing a range of 95 to 99% agreement with the H1-NMR value of 5 mole % PCL. The average % agreement with the H1-NMR value for the nominal 10% resin, PLC9010, determined by PY-GC/MS was 104%. The composition by PY-GC/MS ranged from 9.81 to 10.93 mole % PCL, representing a range of 98 to 109% agreement with the H1-NMR value of 10 mole % PCL. The average % agreement with the H1-NMR value for the nominal 30% resin, PLC7015, determined by PY-GC/MS was 98%. The composition by PY-GC/MS ranged from 28.48 to 32.16 mole % PCL, representing a range of 95 to 107% agreement with the H1-NMR value of 30 mole % PCL. The averaged PY-GC/MS results

Table 5: % Agreement for the PCL Composition of Commercially Available Resins by PY-GC/MS to the H^1-NMR

Resin	Mole % PCL by H1-NMR*	Average Mole % PCL by PY-GC/MS	% Agreement
PLC9517	5	4.86	97
PLC9010	10	10.44	104
PLC7015	30	29.37	98

* The nominal mole %PCL values presented in this table were extracted from their respective vendor Certificates of Analysis, determined by H^1-NMR results from.

Table 6: % Agreement for the PCL Composition of Commercially Available Resins by GC/FID to the H^1-NMR

Resin	Mole % PCL by H1-NMR*	Average Mole % PCL by GC/FID	% Agreement
PLC9517	5	4.58	92
PLC9010	9	8.93	99
PLC7015	30	29.57	99

* The nominal mole %PCL values presented in this table were extracted from their respective vendor Certificates of Analysis, determined by H^1-NMR. Note that different lots of PLC9010 were used for GC/FID and PY-GC/MS analysis, respectively.

Table 7: Comparison of the PY-GC/MS, Chiral GC/FID and the H^1-NMR Methods

% PCL by H^1-NMR*	% Agreement with H^1-NMR by PY-GC/MS	% Agreement with H^1-NMR by GC/FID
5	97	92
9	N/A	99
10	104	N/A
30	98	99

* The nominal mole %PCL values presented in this table were extracted from their respective vendor Certificates of Analysis, determined by H^1-NMR.

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for all three resins were well-correlated with their respective H1-NMR values from vendor C of A.

Chiral GC/FID Results Compared to H1-NMR

The chiral GC/FID resin composition results for commercially available resins were compared to their respective H1-NMR results extracted from vendor C of A. The average % agreement with H1-NMR value for lactide/ caprolactone copolymer resins at nominal 5, 9 and 30 mole % PCL, analyzed by chiral GC/FID, are presented in Table 6 The average % agreement with the H1-NMR value for the nominal 5% resin, PLC9517, determined by chiral GC/FID was 92%. The chiral GC/FID results ranged from 4.40 to 4.75 mole % PCL, representing a range of 88 to 95% agreement with the H1-NMR value of 5 mole % PCL. The average % agreement with the H1-NMR value for the nominal 10% resin, PLC9015, determined by chiral GC/FID was 99%. The chiral GC/FID results ranged from 7.70 to 9.60 mole % PCL, representing a range of 86 to 107 % agreement with the H1-NMR value of 9 mole % PCL. The average % agreement with the H1-NMR value for the nominal 30% resin, PLC7015, determined by chiral GC/FID was 99%. The chiral GC/FID results ranged from 28.51 to 32.94 mole % PCL, representing a range of 95 to 110% agreement with the H1-NMR value of 30 mole % PCL. The averaged chiral GC/FID results for all three resins were well-correlated with their respective H1-NMR values from vendor C of A.

Comparison of the PY-GC/MS, Chiral GC/FID and H1-NMR Methods

Lactide/ caprolactone copolymer resins ranging from 5 to 30% moles PCL were analyzed by H1-NMR, PY-GC/MS and chiral GC/FID methods. The % agreement of the PY-GC/MS and chiral GC/FID to the H1-NMR are presented in Table 7.

Conclusions

The pyrolysis GC/MS method described here employs a very simple sample preparation procedure. Compared to H1-NMR, the PY-GC/MS method described here offers comparable ease of sample preparation, far less technical data interpretation and quantification because the PY-GC/MS method does not require the highly specially and technical skills, as needed for H1-NMR. Compared to chiral GC/FID, the PY-GC/MS method described here is significantly easier to execute, while the data interpretation/ quantification is also comparably straight forward.

The PY-GC/MS method demonstrated good accuracy, precision and linearity and as a result was shown to be suitable to determine the caprolactone/ lactide mole ratio in copolymers and physical mixtures of the respective polymers of polylactide and polylactides from 5 to 30 mole percent caprolactone. Furthermore, the PY-GC/MS method produced comparable results to composition determination by H1-NMR or chiral GC/FID with chiral chromatography.

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Declarations

The authors certify that there is no conflict of interest with any financial/research/academic organization, with regards to the content/research work discussed in the manuscript.

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