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Thermoplastic Biodegradable Elastomers Based on ϵ -Caprolactone and L-Lactide Block Copolymers: A New Synthetic Approach

Vitali T. Lipik¹, Jen Fong Kong¹, Sujay Chattopadhyay¹, Leonardus K. Widjaja¹, Sing S. Liow¹, Subbu S. Venkatraman^{1*} and Marc J.M. Abadie^{1,2}

*Corresponding Author: Prof. Subramanian S. Venkatraman, assubbu@ntu.edu.sg

¹ School of Materials Science & Engineering, Block N4.1, College of Engineering, 50 Nanyang Avenue, Nanyang Technological University, Singapore 639798 Tel: +65 83792515; Fax: +65 67909081.

² Laboratory of Polymer Science & Advanced Organic Materials LEMP/MAO, CC 021, Université Montpellier II, Sciences et Techniques du Languedoc, Place Eugène Bataillon, 34095 Montpellier Cedex 05, France.

Abstract

Although biodegradable polymers have found extensive application in medical devices, there are very few commercially available elastomeric biodegradable polymers. In this work, starting with the well-known monomers L-lactide and ϵ -caprolactone, we developed elastomers using a multiblock copolymer approach. This ensures that the degradation products of such elastomers are also acceptable from a cytotoxicity standpoint.

A series of polymers with various structures has been synthesized utilizing a design of experiment approach. The basic structure is that of a diblock, with each block being modified by the addition of co-monomer. The synthesized polymers exhibit a range of mechanical properties from a typical thermoplastic polymer to that approaching a good thermoplastic elastomer. ^{13}C -NMR analysis, SEC and DSC measurements have been utilized to relate the observed range of mechanical properties to the structure. In addition, the elastomeric nature has been established with the use of creep and recovery measurements.

Such elastomers may find a variety of biomedical applications ranging from stent coatings to atrial septal defect occluders.

Keywords: Poly(L-lactide), Poly(ϵ -caprolactone), Elastomer, Biodegradation

1. Introduction

Although biodegradable polymers have been used in medical implant applications for over 3 decades, starting with sutures and progressing through coatings on stents, there are some applications where elastomeric character is desirable. Such applications include a fully-biodegradable stent [1] where the deployment of the stent necessitates the use of a polymer with shape memory; a scaffold for stem cell differentiation into smooth muscle cells [2] and potentially, a scaffold for a tissue-engineered artificial blood vessel [3]. In addition, our group is working on a fully-degradable occluder for Atrial Septal Defect (ASD) [4], which requires an elastomer with good recovery properties for deployment using a transcatheter. In general, there is a need for biodegradable elastomers in applications that currently utilize the superelastic Nitinol alloy. For such applications, the polymers should be elastomeric (elongations-to-break greater than about 700%; recovery ratios greater than about 75% under different stresses) at body temperatures, and degrade into tissue-compatible oligomers and monomers. An additional characteristic is that of thermoplasticity, that allows for ease of processing.

Very few monomers satisfy the tissue-compatibility criterion: a few that do include L-lactide; glycolide and ϵ -caprolactone. We asked the question: is it possible to synthesize a copolymer out of these monomeric building blocks that would satisfy the requirements for thermoplastic elastomeric character? We have attempted to synthesize what we call multi-block copolymers of L-lactide and ϵ -caprolactone such that they exhibit phase

separation with a hard segment and a soft segment, but not necessarily a triblock copolymer. As is conventionally accepted, the soft phase gives elasticity, whereas the rigid phase gives mechanical strength and acts as a physical crosslinker [5]. Other work on block copolymer synthesis from the same two monomers [6-8] became the basis of our current synthesis efforts.

Simple diblock made of these homopolymers do not show elastomeric behavior, because both blocks are semi-crystalline. Certainly the homopolymers by themselves are not elastomeric. To reduce the crystallinity, we have added a co-monomer to each block in varying amounts. Amorphous random PCL-PLA copolymers obtained by reacting varying ratios of monomers together, have been reported [9,10] and attached to semi-crystalline LA segments at the ends. Such polymers do not appear to be elastomeric, however. Simply reacting the two monomers together yields a completely amorphous polymer, with no elastomeric character, especially when the ratio ranges from 0.3 to 0.7.

Mechanical properties of copolymers based on ϵ -caprolactone and L-lactide depend not only from the ratio of monomers, but also on the details of the macromolecule structure. The structure can depend on the temperature of synthesis, type of the catalyst, monomer reactivity, order of monomer addition during the synthesis, presence of transesterification reactions and other factors [11,12]. In our case, working with ϵ -caprolactone and L-lactide, we start with diblock structures. One block (PCL) would play the role of the soft segment (with sufficiently reduced crystallinity) while the PLA block would act as a pseudo-hard segment with anchoring (immobilizing) ability. Although a

triblock using this principle is more logical, we wanted to pursue the feasibility of diblock attaining similar properties to the extent possible.

Our approach was to disrupt the crystallinity of the PCL block by addition of varying amounts of L-lactide to the ϵ -caprolactone during the first stage of synthesis. We tried to change the properties of the hard PLA block as well by adding of some ϵ -caprolactone during the synthesis of PLA at the second stage of diblock synthesis. In this manner, we obtain multiblock copolymers with a complex structure which is defined not only by monomer ratio, but also by monomer reactivity and the course of trans-esterification reactions [12].

By doing this 2-step synthesis, we are able to obtain polymers with elastomeric character. The range of variables (monomer ratio at each step, overall molar mass), for which elastomeric character is obtained, is defined using a Design of Experiment approach. Rationalization of the observed properties is based on structural characterization using ^{13}C NMR, DSC and SEC.

2. Materials and Methods

2.1. Substrates and solvents

ϵ -caprolactone (99%) was obtained from Fluka, dried over CaH_2 and distilled under nitrogen at reduced pressure. L-lactide was obtained from Sigma Aldrich and purified by

recrystallization from dry ethyl ether (Sigma-Aldrich, anhydrous, $\geq 99.7\%$ contains 1 ppm BHT as inhibitor). The monomer was dried for 24 h under reduced pressure at room temperature prior to polymerization. Stannous 2-ethylhexanoate (96%) ($\text{Sn}(\text{Oct})_2$) from Sigma, hydroxyl butyl vinyl ether (HBVE) stabilized by 0.01% of KOH from BASF, methanol anhydrous (99.8%) from Aldrich, tetrahydrofuran (99%) from Alfa Aesar were used as received. Toluene anhydrous (99.8%) was purchased from Aldrich, dried over CaH_2 and distilled under nitrogen.

2.2. Size exclusion chromatography

Number average molar mass of polymers were determined by size exclusion chromatography, SEC (Agilent 1100 Series HPLC, with RI detector). Twelve polystyrene standards (Fluka) with narrow molar mass distribution in the range of 580- 400,000 g/mol were used for calibration. Measurements were made at 45°C with three linear PLgel $5\mu\text{m}$ mixed C columns (of Polymer Laboratory) connected in series. Chloroform was used as solvent with a flow rate of 1 mL/min.

2.3. Nuclear Magnetic Resonance Spectrometry (NMR)

^{13}C -NMR spectra were obtained with a Bruker 400 spectrometer using the solvent (CDCl_3) as an internal standard. Samples were dissolved in deuterio-chloroform in sample tubes 5 mm in diameter. Solution concentration was 100 mg of polymer in 1 mL solvent.

Average lengths of poly(ϵ -caprolactone) (L_{CL}) and poly(L-lactide) blocks (L_{LA}) were calculated from the intensities of the peaks of the carbonyl signals [8,13] using the equations below:

$$L_{PCL} = \frac{I_{CCC}}{I_{LCC}} + 1, \quad (1a)$$

$$L_{PLA} = \frac{I_{LLL}}{I_{LLC}} + 1. \quad (1b)$$

where I_{CCC} and I_{LLL} are the intensities of ϵ -caprolactone - ϵ -caprolactone and L-lactide - L-lactide triads, respectively; I_{LCC} and I_{LLC} represent the intensities of ϵ -caprolactone - L-lactide and L-lactide - ϵ -caprolactone triads and tetrads peaks, respectively.

2.4. Tensile testing

Tensile tests were performed on an INSTRON 5567. Polymer films were prepared by casting from solution of polymer powder in tetrahydrofuran. Films were dried in vacuum oven at 40°C for a week. The films had a thickness of approximately 0.2 mm and were preconditioned before testing (48 h at 50±5% relative humidity and 23±1°C). The dog bone shape specimens, cut from the film by means of a Schmidt Press, were pulled in the vertical direction at a crosshead speed of 50 mm/min. A minimum of 5 specimens per sample were used for tensile testing. The strain at break was calculated using grip separation due to the large elongation of the sample.

A cyclic loading test was also done on an INSTRON 5848 microtester using the INSTRON Bluehill software. Dog bone shape specimens were pulled in vertical direction at a rate of 10 mm/min at 25°C.

Three samples of each film were used for shape recovery measurement. They were pulled to 100, 200 and 300% at 10 mm/min. After the desired elongations were achieved, the microtester was stopped and the sample was taken out. The resultant recovery allowed the sample to regain its original size to different extents. The final sizes of the sample were measured after 5 minutes of recovering.

2.5. Differential Scanning Calorimetry (DSC)

Melting temperatures, glass-transition temperatures and crystallization of the polymer samples were measured using TA Instruments Model Q10 DSC machine which was equipped with a DSC Refrigerated Cooling System so as to achieve low temperatures. The software used was called TA Instruments Control. Polymer samples were weighed (4 mg – 8 mg) and placed into standard aluminum pans individually. DSC analysis was done by first heating of the sample up to 200°C to eliminate internal stresses, then equilibrating the samples at -80°C and after that the temperature was ramped up to 200°C at a rate of 10°C per minute.

2.6. Synthesis of polymers

The synthesis was carried out in a three-necked round bottom flask (100 mL) equipped with a thermometer, a condenser and a magnetic stirrer. The flask was purged by argon, vacuumed twice and after that was kept under the argon atmosphere. Argon was dried using a water absorption system with silicagel. The temperature of synthesis was maintained by immersing of flask into silicone oil bath. A mixture of HBVE and $\text{Sn}(\text{Oct})_2$ was added to the toluene at 90°C and stirred for 30 minutes. The quantity of HBVE used was based on the desired degree of polymerization. In a typical synthesis, the ϵ -caprolactone “block” is first polymerized using the above conditions, with the addition of a (relatively) small amount of L-lactide monomer, and then the temperature is raised to 110°C and maintained for 24 hours. Following that, the L-lactide “block” is polymerized whereby L-lactide monomer together with a much smaller amount of ϵ -caprolactone is added to the mixture, and the polymerization is further maintained for another 24 hours at 110°C to complete the diblock synthesis. In this way, we end up with one segment that is rich in PLA (with some degree of blockiness, as explained later) and another that is richer in PCL (also with some degree of blockiness). Such polymers have varying degrees of blockiness that depend on the ratios of the monomers used in each of the two “block” syntheses.

In the case of completely random copolymer synthesis (typically monomer ratios are in the range 3:7 to 7:3 for complete randomness), the necessary quantity of L-lactide and ϵ -caprolactone monomers were added to the flask at 90°C (Toluene, catalyst and initiator

had been mixed already, as in the case of the diblock synthesis). Subsequently the temperature is raised to 110°C and polymerization carried out for 24 hours. Polymer was precipitated in cold methanol and dried in the vacuum oven at 40°C for 24 hours.

2.7. Creep and recovery

The TA Instruments' Dynamic Mechanical Analyzer (DMA Q800) was utilized to measure creep and recovery under different stress levels. The DMA Q800 was operated in film tension mode with sample thickness between 0.2 and 0.3 mm. For creep and recovery test (in film tension mode), two levels of stress were applied amounting to 30% and 80% of the maximum stress determined for each polymer during a tensile test done at a rate of 10% strain per minute up to 200% elongation. The films were subjected to displacement under the two stress levels for 30 min and then recovery was monitored for 30 minutes after the stress removal. A minimum of 3 polymer specimens were studied for each experiment.

2.8. Degradation procedure

The degradation of the polymers was studied by monitoring the change in number average molar mass and mass of sample over immersion time. Films (5mm x 5mm x 0.2mm) made from each polymer were used for the SEC measurement. Four representative samples were considered for each data point. Each piece of the film was then immersed in 1.5 mL PBS buffer [1M, pH7.4] solution and incubated at 37°C. The

PBS solutions were changed frequently to maintain the pH at around 7.4. After every time interval, samples were taken out washed with fresh water and dried in vacuum oven before measurement of molecular mass using SEC. % change in M_n (number average molar mass) or mass loss, ML was obtained by means of Equation 2 comparing the initial molar mass (M_n^0) /mass of sample and the molar mass/mass of sample measured at various intervals (M_t).

$$ML = \frac{M_n^0 - M_t}{M_n^0} \times 100\%, \quad (2)$$

3. Results and discussion

3.1. Optimization of polymer properties

PCL and PLA have been used in medical implant applications for several years as biodegradable matrices. As such these polymeric structures are acceptable in terms of the biocompatibility of the starting polymers as well as of the degradation products. As homopolymers, PCL and PLA are typical thermoplastic semicrystalline polymers that resemble commercial synthetic polymers such as poly(ethylene terephthalate) or PET in their behavior. Therefore these polymers are not elastomeric. In fact there are very few elastomeric degradable polymers reported, other than those obtained by chemical crosslinking, and used mainly as scaffolds in tissue engineering [14]. The first report of a thermoplastic biodegradable elastomer is probably the one featuring biodegradable polyurethanes in 2001 [15]. A year later, Lendlein and Langer reported a new

thermoplastic elastomer based on PCL and poly(dioxanone), with both homopolymers having been used as suture materials before [15]. The polymer described by Lendlein *et al* [16] is a block copolymer based on PCL and poly(dioxanone), with PCL acting as a ‘switching’ segment that allows for trigger temperatures of 40°C or below for shape memory effects, while the poly(dioxanone) segment acts as the hard block with a T_m of 80°C. The copolymers are coupled together with a 2,2,4-trimethylhexanediisocyanate, and are degradable by hydrolysis at a fairly slow rate. Although the elastomeric properties are not measured in detail, it is reported that the polymers have elongations to break of about 1000% and switchable shape memory properties at around 40°C (the melting point of poly(ϵ -caprolactone)). These polymers, however, are not elastomeric at ambient or even at 37°C, which is the objective of our present work.

Our approach was to use PCL and PLA as the basic building blocks, as these degrade into acceptable oligomers and monomeric units. For good elastomeric properties, a substantial part of the copolymer must be amorphous. Furthermore, to get a truly thermoplastic elastomer, the so-called soft segment must be completely or almost completely amorphous at ambient or at 37°C, with the hard segment having a transition temperature (either T_g or T_m) well above 37°C. Thus our approach was to base the soft segment on PCL with disrupted crystallinity, while the hard segment would be predominantly PLA also with disrupted (but not completely disrupted) crystallinity. In either segment, the crystallinity disruption would be accomplished by addition of the other co-monomer, i.e., by adding L-lactide to a predominantly PCL block and vice versa. A priori, it is not clear what the optimum extent of crystallinity is for the hard segment and how much of the

crystallinity should be permissible in the soft segment. There should be an optimum range for the amount of PCL or PLA added, as too little will result in semi-crystalline thermoplastics, and too much may result in a completely amorphous structure which may even be a viscous liquid depending on the overall molecular mass achieved.

In order to arrive at an optimized set of synthesis parameters that yield the best elastomer, we have used a Design of Experiments approach [17]. The targeted overall molar mass was 40,000 Da. The quantity of L-lactide, added to the ϵ -caprolactone at the first stage of synthesis, and quantity of ϵ -caprolactone, added to L-lactide on the second stage of synthesis, were varied at four levels and were equal 5, 10, 20, 30 % mol. Thus we have a two-factorial (% LA, % CL) experiment with four levels of factor variation.

3.2. Designing an Elastomer: Design of Experiments

Using controlled anionic ring opening polymerization, we synthesized block copolymers with molar mass of each block around 20,000 Da, and the total targeted molar mass of polymers around 40,000 Da. Based on preliminary experiments with lower molar masses (which do not produce elastomers regardless of composition), we believe these to be the minimum molar masses required for elastomeric character. The quantity of L-lactide, added to the ϵ -caprolactone at the first stage of synthesis, and quantity of ϵ -caprolactone, added to L-lactide on the second stage of synthesis, were varied at four levels and were equal 5, 10, 20, 30% mol. Thus we have two-factorial experiment with four levels of factor variation.

We limited the range in each case to 5 to 30% in order to retain the largely blocky nature of the PCL and the PLA. Beyond these limits, we simply obtain diblock or random copolymer in each sequence. Based on a design of experiment strategy [18], the composition chosen to synthesize polymers, the molar masses obtained using SEC and the measured mechanical properties are presented in Table 1.

Table 1. Physical characteristics of diblock polymers

N	% LA in PCL, (mol)	% CL in PLA, (mol)	Mn by SEC, (Da); [PDI]	Elongation at break, (%)	Young's Modulus, (MPa)
1	5	5	45,080 [1.66]	610±23	61.0±1.5
2	5	10	59,440 [1.42]	790±25	49.0±1.3
3	5	20	53,360 [1.51]	850±29	44.0±1.4
4	5	30	42,690 [1.45]	770±27	33.0±1.5
5	10	5	72,600 [1.58]	890±24	38.0±1.4
6	10	10	60,090 [1.63]	1010±39	34.0±1.5
7	10	20	36,960 [1.35]	850±34	28.5±1.1
8	10	30	49,170 [1.66]	850±30	25.0±0.7
9	20	5	39,605 [1.67]	1010±36	29.0±1.2
10	20	10	51,010 [1.57]	1000±41	26.0±1.0
11	20	20	48,900 [1.46]	800±24	17.0±0.7
12	20	30	51,440 [1.46]	1050±44	9.0±0.6

13	30	5	59,040 [1.61]	930±47	19.0±0.8
14	30	10	42,660 [1.45]	860±31	19.0±1.3
15	30	20	53,280 [1.64]	1170±62	16.0±0.5
16	30	30	47,090 [1.51]	1060±46	5.0±0.2

We note here that the molar masses obtained by SEC (using polystyrene standards) are different from the target M_n of 40000 Da. The reasons are two-fold:

The SEC molar masses, in general, are different from the more direct molar masses obtained by MALDI-TOF (we have made the comparison for molar masses less than 10,000 DA, where we find that SEC M_n 's are ~20-40% higher than MALDI-TOF measurements). Secondly, some fluctuation is expected due to the inherent synthesis variability.

Nevertheless, there are indications here that over certain composition ranges, an elastomer-type polymer may be obtained. For example, the elongations to break of polymers 12, 15 and 16 are high enough to be elastomeric, although this requires further confirmation with recovery experiments; high elongations are also possible with yielding behavior, and such elongations are not fully recoverable.

The next step was to further refine the composition range. In order to do so, approximate mathematical fits were made to the data with reasonable correlation coefficients. Using the fitting equations, we generated surfaces involving the 2 key variables, in order to locate minima in modulus, maxima in elongation-to-break and recovery. Since the data fit

is rather crude, we limit the validity range of fit to about 60% of each monomer (CL or LA) for the 2 variables (beyond this range, we obtain either brittle thermoplastics or liquid polymers).

3.3. Young's modulus minimization

Value of Young's modulus and quantities of L-lactide added to PCL and ϵ -caprolactone added to PLA at the first and second steps of synthesis (Table 1) can be described by the quadratic mathematical equation (3) obtained by a least squares fit ($R^2=0.985$ – correlation between calculated and measured values). Among the possible simple fits, we select the one with the bigger coefficient of correlation:

$$M=81.7-1.1\times\%CL-4.7\times\%LA+0.01\times\%CL\times\%LA+0.01\times\%CL^2+0.095\times\%LA^2 \quad (3)$$

where M – Young's modulus, in MPa; %LA is the quantity of L-lactide in PCL, in % mol; %CL – quantity of ϵ -caprolactone in PLA, in % mol.

The dependence of modulus values on the polymer composition calculated using the above presented equation is given in the Figure 1.

(Figure 1)

The minimum modulus (as per the equation) is located at the composition where quantity of L-lactide in PCL is 26.2%; quantity of ϵ -caprolactone in PLA is 48.7%. Such a polymer was then synthesized and cast into film for mechanical characterization. The modulus was equal 3.8 MPa, and elongation at break was 745%. This composition is not optimized with respect to elongation. The area of polymer composition giving small modulus values can be defined as 18-28% of L-lactide added to PCL and 40-70% of ϵ -caprolactone added to PLA.

3.4. Elongation at break

In a similar way, the elongation at break can be related to the reaction variables using a quadratic expression, with an R^2 value of 0.7 (correlation between calculated and actual experimental data).

The dependence of elongation at break values from polymer composition calculated by the expression is given in the Figure 2.

(Figure 2)

The maximum elongation, as per the equation, is found when the quantity of L-lactide in PCL (“block 1”) is 26%; and the quantity of ϵ -caprolactone in PLA (“block 2”) is 25%. Calculated elongation at break of polymer with such optimized composition is 1,030 %. This value has a good correlation with measured elongations at break of our real

polymers. We can see from the Table 1 that the biggest values of elongation at break belong to the two following polymers: N 12 - amount of L-lactide added to PCL is 20% and amount of ϵ -caprolactone added to PLA is 30%; and N15 - amount of L-lactide added to PCL is 30% and amount of ϵ -caprolactone added to PLA is 20%. Based on the top view of Figure 2, the area of polymer compositions which provide maximum elongation at break can be localized as 15-35% of L-lactide added to PCL and 10-40% of ϵ -caprolactone added to PLA.

3.5. Elastomeric nature: Creep & Recovery properties

In order to truly optimize the polymer structure to obtain an elastomer, we need to use a third mechanical characteristic: recovery from imposed stress or strain. One way to estimate this is by rapidly elongating the sample in an Instron-type mechanical tester, then removing the load and measuring the change in sample dimensions. In this case, we estimate recovery using the equation 4:

$$R = \frac{L_M - L_R}{L_M - L_0} \times 100 \% , \quad (4)$$

where L_M is maximum sample length at elongation, mm; L_R - sample length after recovery, mm; L_0 - initial length of sample, mm.

Such values were obtained after rapidly elongating the film samples by 100%, 200% and 300%, then allowing it to recover: the values are given in Table 2. As a crude measure of

crosslink density, we also calculated an apparent M_c (or molar mass between “crosslink” points) by using [19] :

$$M_c = \frac{3 \times \rho \times R \times T}{M}, \quad (5)$$

where ρ – polymer density g/cm^3 ; R – ideal gas constant equals 8.3145 J/(mol.K) ; T – temperature, K; M – Young’s modulus, MPa. The density of polymer was calculated as $\rho = m/V$, where the mass was measured using a Sartorius BP 221S balance (deviation = $\pm 0.1 \text{ mg}$), and the volume calculated from sample dimensions at $T=298 \text{ K}$.

Here crosslink points are physical crosslinks, either due to entanglements or due to hard segments, or both.

Table 2 – Recovery after simple elongation

N	% LA in PCL (mol)	% CL in PLA (mol)	M_c (Da)	Recovery of the sample after elongation on, (%)		
				100%	200%	300%
1	5	5	147.5	39	37	33
2	5	10	182.9	49	48	36
3	5	20	199.8	57	56	43
4	5	30	268.2	72	70	53
5	10	5	238.4	75	44	42

6	10	10	264.4	79	65	52
7	10	20	313.2	81	62	51
8	10	30	362.3	79	71	62
9	20	5	310.9	70	53	45
10	20	10	344.4	73	55	53
11	20	20	517.7	87	73	63
12	20	30	945.8	88	88	73
13	30	5	465.9	83	63	55
14	30	10	482.0	83	69	55
15	30	20	570.2	89	86	76
16	30	30	1657.7	89	88	81

When recovery % is independent of elongation, we are approaching true elastomeric behavior. Such compositions are found for the higher ratios of each variable, i.e., amount of L-lactide added to the PCL and amount of ϵ -caprolactone added to PLA.

In order to reinforce our findings obtained by simple elongation, creep and recovery was performed on polymers 6, 11 and 16 from Table 2. Their yield strength, applied stress and recovery % are presented in Table 3.

Table 3 – Recovery after creep

	% LA in PCL (mol)	% CL in PLA (mol)	Max stress (MPa)	Recovery at 30% of max	Recovery at 80% of max
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				stress, (%)	stress, (%)
6	10	10	8.7	74±1	52±3
11	20	20	3.5	76±1	56±4
16	30	30	3.2	78±2	77±1

From the results obtained, it is clear that the polymers do not have significant differences in recovery under a low stress level. With higher stress applied, only polymer 16 is able to retain its initial recovery while the other polymers have significantly lower values. This coincides with the simple elongation results (Table 2) with polymer 16 maintaining its recovery behavior while polymer 6 and 11 cannot achieve the same level of recovery at all elongation levels.

Again, fitting the data for recovery (Table 2) is also possible, by means of a quadratic expression as above, with coefficient of correlation $R^2=0.877$ (using only the recovery values after 100% elongation):

Plotting the recovery equation gives (Figure 3).

(Figure 3)

Maximum recovery occurs at 25 % L-lactide added to PCL and 42% of ϵ -caprolactone added to PLA. This ratio is very similar to the one found for modulus minimum (26% L-lactide and 48% ϵ -caprolactone), but somewhat different for the maximum in elongation

(25% of CL in LA and 27% of LA in CL). In view of this, we synthesized and tested several new polymers with monomer ratios located around the maximum/minimum points. Polymer composition, recovery % and modulus values for these polymers are presented in the Table 4. Molar mass of each block was targeted as 20,000 Da.

Table 4 – Shape recovery properties of optimized polymers

N _{rev}	% LA in PCL (mol)	% CL in PLA (mol)	Modulus (MPa)	% of recovery after elongation on		
				100%	200%	300%
1	10	70	12.19	79	70	59
2	20	50	4.48	87	85	78
3	20	55	8.56	87	84	77
4	26	48	3.82	88	85	77
5	30	30	5.42	89	88	81
6	30	40	5.16	92	87	73
7	40	30	11.11	87	86	73
8	50	15	24.05	73	62	45

These data show that as far as recovery is concerned, the actual maximum occurs around 30% of LA in PCL and 40% of CL in PLA, if we use only the 100% elongation values (close to the predicted maximum, which is 25% of L-lactide and 42% of CL). However, another important recovery parameter is also invariance of the recovery values with elongation percent, as ideal elastomers exhibit high levels of recovery at all values of the

elongation prior to recovery. **From this standpoint, the 30-30 polymer (polymer 5 in Table 4) exhibits the best performance and more ideal elastomeric characteristics** (This is the same polymer as N16 in Table 2). It is also noted that the “maximum” is a fairly broad maximum, covering the range of about 25-30% of L-lactide added to PCL, and about 30-50% of CL added to PLA.

It appears that optimizing with respect to just elongation does not yield a truly elastomeric polymer. This is because at the rates of elongation employed, we have plastic and elastic deformation, and the maximum value is a combination of both types of deformation. Clearly, optimizing with respect to recovery is the ideal approach to obtaining elastomers, and the invariance of recovery with elongation % is also a critical feature. In the above exercise, it appears that, for this molecular weight range of each block, a nearly ideal elastomer is obtained for 30% of each co-monomer added to the respective monomer. Coincidentally, this also reflects the minimum in modulus (and hence the maximum in M_c). At this composition, the elongation to break is still high, at about 1,100%.

3.6. Biodegradability test

Bio-degradation of five different copolymers (5%-5%, 5%-40%, 20%-20%, 40%-5%, and 40%-40%), spanning the complete range of CL-LA % variation, was carried out in the manner stated above. During the initial four weeks (Figure 4a), all polymers show

rapid degradation and the % loss in M_n (as per Equation 2) are found to be 12.1%, 14%, 20.9%, 22.5%, and 31.5% respectively for the above copolymers.

(Figure 4a)

In a semi-quantitative manner, the rates of degradation appear to be related to the amorphous content, as seen below in Table 5.

Table 5 - Crystallinity of PCL-b-PLA used for the degradation study

Polymer PCL-b-PLA: Composition (mol)	PCL crystallinity (%)	PLA crystallinity (%)
5-5%	24.8	40.6
20-20%	0	25.4
40-40%	0	6.2
5-40%	0	25.4
40-5%	0	21.4

The copolymer with 5% of LA and CL added to each end-block shows high crystallinity in both blocks, and also appears to be the slowest-degrading. Conversely, the copolymer with 40% of CL and LA added to each end-block shows the fastest rate of hydrolysis, at least up to 4 weeks of degradation, and exhibits minimum crystallinity levels.

The mass loss (%) of the various copolymers films were obtained as shown in Figure 4b.

(Figure 4b)

For up to one week the weight loss % is very low (<1%) but increases during week 2 (2-4%) and by the fourth week the loss is about 4-7% for nearly all the composition. The loss is maximum for 40-40%, which is also reflected in molar mass loss of the same polymer.

3.7. Relationship of the measured polymer properties to polymer structure

In order to rationalize the results obtained above using a Design of Experiments approach, we characterized the polymers for the following attributes: length of block segments, crystallinity, and molar mass of polymer. We used ^{13}C NMR analysis to estimate the average lengths of the PCL and PLA segments (Figure 5). Segments lengths have been calculated according to the well-accepted formulae [8,13] given in Sec 2.3.

(Figure 5)

The calculated block lengths as well the degree of crystallinity for all the copolymers are given in Table 6. The % crystallinity has been calculated using the heat of fusion (ΔH_f^0) of the totally crystalline PCL (139.5 J/g) [20], and totally crystalline PLA (93 J/g) [21].

Table 6 – Characteristics of PCL-b-PLA polymer structure

N	% LA in PCL, (mol)	% CL in PLA, (mol)	T _g , °C	Crystallinity* of PCL, %; (Melting point, °C)	Crystallinity* of PLA, %; (Melting point, °C)	PCL length, monomer units	PLA length, monomer units
1	5	5	-	24.8 (50)	40.6 (162)	18.1	21.5
2	5	10	-	13.3 (51)	42.0 (137)	16.3	14.5
3	5	20	-	0	34.3 (133)	12.8	11.8
4	5	30	4	0	30.3 (128)	12.2	8.7
5	10	5	-3	0	24.7(122)	4.6	8.3
6	10	10	3	0	34.45 (133)	4.2	7.4
7	10	20	18	0	27.9 (127)	4.1	7.5
8	10	30	18	0	37.0 (127)	5.5	9.1
9	20	5	10	0	20.7 (104)	3.2	9.4
10	20	10	19	0	29.3 (136)	4.8	11.8
11	20	20	20	0	25.4 (125)	3.6	7.7
12	20	30	20	0	24.6 (123)	3.45	7.5
13	30	5	19	0	21.0 (138)	3.2	10.5
14	30	10	27	0	35.2 (138)	3.0	10.5
15	30	20	28	0	39.15 (135)	3.6	7.4
16	30	30	-7	0	10.2 (130)	4.4	7.2

* Crystallinity measurements were made on as-prepared/dried polymers, and the reported values are for heat 1.

As can be seen in Table 6, the average segment lengths of the copolymers vary from about 3 to 18 for the CL segment, and from 7.2 to 21.5 for the LA segment. As we show below (Table 8), a completely random copolymer (produced by reacting the two monomers together) has segment lengths of 3.5 (LA) and 2.3 (CL). Thus these polymers show varying degrees of non-randomness, which correlates well to the measured degrees of crystallinity. For instance, as all the measured LA segment lengths are above the random value of 3.5, the LA segment shows crystallinity in all the copolymers. On the other hand, for CL segments close to the random value (3.5) there is no measurable crystallinity for the CL segment. As we discuss below, the segment lengths (and the crystallinity) have an important effect on the elastomeric character of the copolymers.

To clarify this further, we did a correlation analysis of the measured properties against selected structural features. Table 7 shows the linear correlation (expressed as R^2) between the three mechanical properties and structural parameters.

We attempted to identify the key structure-property relationships in these polymers by correlation analysis. Correlation is considered (Chedoke scale) as weak if $0.1 < R^2 < 0.3$; as medium if $0.3 < R^2 < 0.5$; as significant if $0.5 < R^2 < 0.7$; as high if $0.7 < R^2 < 0.9$; as very high if $0.9 < R^2 < 0.99$.

Table 7 – Correlation between polymer structure parameters and polymer properties

Polymer properties / Linear Correlation	Young's	Elongation	Degree of
Coefficients	modulus,	at break,	recovery *,

	(MPa)	(%)	(%)
Molar mass of polymer, Da	0.157	0.156	-0.126
Amount of PCL in polymer, % mass	0.317	-0.409	-0.119
Amount of PLA in polymer, % mass	-0.325	0.410	0.127
PCL segment length, monomer unit	<u>0.823</u>	<u>-0.695</u>	<u>-0.688</u>
PLA segment length, monomer unit	<u>0.760</u>	<u>-0.651</u>	<u>-0.750</u>
PLA crystallinity, %	<u>0.600</u>	-0.389	-0.452

* Coefficients of correlation for degree of recovery were calculated as average value for degrees of recovery for specimens after 100, 200 and 300% of elongation (Table 2).

The only significant correlations are those of Young's modulus and recovery with PLA and PCL segment lengths. To evaluate the nature of the correlation, we can examine the R^2 values as well (Table 7). We see that as the PLA and PCL segment lengths increase, the recovery decreases. Conversely, the modulus increases with the segment lengths, clearly indicating that randomness of either block enhances the elastomeric character of the polymers. Of course, Table 6 shows this clearly, in that Polymers 15 and 16, which show excellent recovery also show minimum segment lengths for the PLA and the PCL. It does appear that as the PLA segment length increases, the elastomeric character is adversely affected, in all likelihood due to increasing crystallinity of the PLA segment. Thus, it does not pay to have too high a crystallinity for the "hard segment" which is the PLA.

The elongation at break depends more weakly on the segment lengths, also in a negative sense. This probably reflects the same dependence via crystallinity.

Although the correlation is not strong, it does appear that crystallinity of both polymers PCL and PLA affects mechanical properties of the copolymer. There is also an optimum of polymer composition which connects crystallinity, modulus and degree of recovery. It is clearly seen in Table 6. A low amount of L-lactide added to PCL retains some PCL crystallinity. Hence the polymer has high modulus and low shape recovery. When we add more L-lactide to PCL we destroy PCL crystallinity, the modulus becomes lower and the recovery property improves. But above 40% of L-lactide added to PCL, the PLA segment becomes longer, PLA crystallinity increases, the modulus grows and shape recovery worsens.

3.8. “Blockiness” of each block

The question may be asked: “how do we know that all the polymers are not completely random”? The answer comes for the structural characterization data.

In principle, our synthesis scheme should yield polymers of a substantial blocky nature, but in fact we do not obtain very blocky copolymers because of trans-esterification reactions, whenever a co-monomer is added after reaction of the first block, as illustrated by the following example. First, a 75:25 copolymer (random) is synthesized by reacting the CL and L-lactide monomers together. This is expected to yield a random copolymer. In a second synthesis, a PCL block is synthesized, and L-lactide is added at 1/3rd the molar ratio of CL. In a third reaction, the process is reversed, by reacting L-lactide first

and adding CL at thrice the molar ratio: in both cases, the CL:LA ratio should be 75:25. We did ^{13}C NMR on the resulting polymers, and determined the average sequence lengths of each block (Table 8) as described above:

Table 8 – ^{13}C NMR analysis of sequence lengths for random and diblock copolymers

Order of monomer addition	Ratio CL:LA. % mole (by ^1H NMR)	PLA segment length, monomer unit	PCL segment length, monomer unit
Together	75:25	3.5 (random)	2.3 (random)
1 st CL 2 nd LA	76:24	49 (pure block)	30 (pure block)
1 st LA 2 nd CL	60:40	15	6

There are two observations to be highlighted here: first, when CL is reacted first, followed by LA addition, the blockiness is substantially preserved. When the reverse procedure is followed, blockiness decreases dramatically, signifying the influence of trans-esterification reactions when a more reactive monomer (i.e, CL) is added at the second step. This is also reflected in differences in the molar ratio as measured by ^1H NMR. Secondly, compared to the random polymer, the average CL and LA sequence lengths are higher for the diblock copolymers, even when the reactive monomer is added at the second step. This is reflected also in Table 6, where the sequence lengths of the synthesized polymers are above the values for random copolymer, particularly for the LA segment. And it is the blockiness of the LA block that leads to crystallinity of the PLA which in turn contributes to the elastomeric behavior by acting as an anchoring point (physical crosslink) for the polymer. In all the syntheses of diblock reported here, we have used the order of addition: LA first, followed by CL, for each block. This leads to

the relatively lower blockiness reported in Table 6, but still “non-random”. The ^{13}C NMR (Figure 6) confirms this, as the segment lengths calculated using formulae 1a, 1b lead to low values (Table 8).

(Figure 6)

The DSC thermograms also reflect this deviation from randomness. If we examine a copolymer (for example, the 20% LA added to PCL and 20% CL added to PLA (Polymer 11 in Table 6), we see that the LA segment retains some crystallinity, as shown below. There might even be two types of crystallites (due to either block) as shown in the first heat, which merges (co-crystallization) in the second heating cycle (not shown). As the relative amount of each co-monomer is decreased (5% LA in PCL and 5% CL in LA, Polymer 1 in Table 6), we even see crystallinity of the PCL in addition to the PLA crystallinity, as shown in the bottom DSC trace in Figure 7, below.

(Figure 7)

3.9 How does the degree of non-randomness help to create an elastomer?

Summarizing our data and inferences from the above, we find that over a small range of monomer ratios in each “block”, we obtain elastomers (as defined by high recovery ratios that are invariant with % elongation). We attribute the attainment of elastomeric character

to retention of a certain degree of non-randomness in PLA, based on the following observations:

- (a) When the copolymer is completely random, the block segment lengths are about 3.5 for PCL and 2.3 for PLA, and such a polymer is not elastomeric (as seen for the 25:75 copolymer example above).
- (b) When the 2-step synthesis procedure is used, copolymers with an overall composition of roughly 30% co-monomer in each step, yields elastomers.
- (c) Such a polymer has a PLA segment length of ~ 7.4 and PCL segment length of ~ 3.4 (Polymer N16 in tables 2 and 6). Thus PCL segment length is close to the random value, indicating that PCL will not crystallize in this copolymer; the PLA segment is about 3 times the random value, and does lead to some crystallinity of the PLA segment, which is the so-called “anchoring segment”. Values of PLC and PLA segment lengths too much below and above these values do not yield elastomers.
- (d) With such a polymer, we now have a mixture of ‘soft’ (PCL-PLA random segments) and “hard” (PLA non-random segments) blocks, that allow for elastomeric character, that probably approximates segmented PU elastomers in structural terms.

4. Conclusions

We have shown, using a Design of Experiments approach, how elastomers can be produced from 2 monomers, ϵ -caprolactone and L-lactide. To the best of our knowledge,

this is the first demonstration of such an approach to produce elastomers from two such monomers. We emphasize that to quantify truly elastomeric behavior, recovery at different stress levels (or after high elongation levels) should be measured. Completely random copolymers of L-lactide and ϵ -caprolactone do not yield elastomeric character, but randomizing (to a certain extent) the blockiness of each segment appears to result in an elastomer. The elastomeric nature of the polymer reaches a maximum at about 30% of each monomer added to the respective co-monomer; this is confirmed by recovery measurements following uniaxial elongation. The origin of this elastomeric behavior is in the control of the segment lengths of each monomer. In particular, the appropriate segment length of the hard segment (PLA) appears to be around 7, whereas for the soft segment (PCL), the ideal segment length is lower, about 3-4. The reason for the higher segment length of the PLA is that PLA needs to retain some crystallinity (approximately 10-15% appears to be sufficient) to act as the anchoring or hard segment; the softer segment (PCL) needs to minimize its crystallinity, hence the lower optimum segment length.

List of Abbreviations:

CL - ϵ -caprolactone,

LA - L-lactide

PCL- Poly(ϵ -caprolactone)

PLA- Poly(L-lactide)

L_M is maximum sample length at elongation, mm

L_R - sample length after recovery, mm

L_0 - initial length of sample, mm.

ρ – polymer density g/cm³

R – ideal gas constant, 8.3145 – J/(mol.K)

T – temperature, K

M – Young's modulus, MPa.

ML – Mass Loss %

PL – Polymer Laboratory

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PCI-PIA 20 kDa 25 LA 75 CL