Synthesis of Diblocks Copolymers PCL-b-PLLA and Optimization of its Mechanical Characteristics

Vitali T. Lipik[1a], Leonardus K. Widjaja[1b], Sing S. Liow1c, Subramanian S. Venkatraman1d & Marc J.M. Abadie1, [2e]

[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

Biodegradable polymeric materials have a wide application in medicine, ecology and a number of other branches of industry. Overwhelming majority of such polymers is well exposed to the biodegradation, but they have mechanical properties which don't correspond to the requirements of application areas. As a rule, these materials possess low elasticity.

In this work, optimization of mechanical properties of biodegradable polymers and the search of structure of block polymer on the basis of ε-caprolactone and L-lactide with the maximal elasticity are considered. The purpose of the work is to receive the diblock polymer with mechanical properties as close as possible to elastomer for medical devices. The task is reached due to application of design of experiment with the subsequent optimization of the received results. Maximization of elongation at maximum load of received polymer is solved by the greatest possible reduction of crystallinity with a variation of molar weight of both part of diblock: polycaprolactone and polylactide.

The absolute maximum of elongation at maximum load of synthesized diblock polymers is found. It is established that diblock with the following structure possesses the best mechanical properties in this class of polymers. Molar weight of the polycaprolactone block is 5000 Da while polylactide block is 7000 Da. Elongation at maximum load of this polymer was about 30%.

In the second stage of our research, we try to improve the mechanical properties by making one block partly random (PCL-co-PLLA). Second block was made from homopolymer (PLLA). Maximum received elongation at break is 200%. First block of this polymer contains 25% of lactide, has molar weight of 10000 Da. Second block is the pure polylactide, with molar weight 10000 Da. All the experimental results and mathematical modeling pointing direction to maximum elongation could be achieved by multi-block structures.

Introduction

In recent years, biodegradable polymers have attracted great attention in the biomedical field because scientists are looking for more ways to exploit their capabilities and then used them in the human body. Biodegradable polymers are mainly poly (glycolic acid), polycaprolactone, poly (ethylene glycol) and poly (lactic acid). Their commercial applications in the biomedical field include heart stents, surgical sutures and long-term drug delivery [1]. Also, biodegradable polymers can be used as temporary scaffolds which can facilitate the regeneration of tissues on the cell growth in the field of tissue engineering. The main advantages of using biodegradable polymers as implants are firstly, a second surgical procedure to remove the implants after they have served their purpose is not required, secondly, they are useful for short-term applications and thirdly, they overcome problems caused by permanent implanted devices.

Thermoplastic elastomers or TPE are a type of polymeric materials that do rely on cross-linking, *i.e.* vulcanization, to achieve large amount of elastic deformation. They exhibit elastomeric (or rubbery) behaviour at ambient conditions but yet are thermoplastics in nature. One of the best known

*corresponding author. E-mail: vitali@ntu.edu.sg

and widely used is a block copolymer consisting of block segments of a hard and rigid thermoplastic, that alternate with block segments of a soft and flexible elastic material. Normally, the hard segments are located at the chain ends while the soft segments are located in the middle, between the two hard segments. One common example would be styrene-butadiene-styrene (SBS) copolymer [2]. At ambient temperatures, the soft, amorphous, central segments grant the material elastomeric behaviour and the hard segments prevent sliding of the chains. Furthermore, below the melting temperature of the hard component, hard chain-end segments from numerous adjacent chains aggregate together to form rigid crystalline domain regions. These domains are pseudo crosslinks or physical crosslinks that act as anchor points so as to restrict soft-chain segment motions; they function in much the same way as chemical crosslinks for thermoset elastomers. But when the thermoplastic elastomers are heated to elevated temperatures above the melting temperature of the hard component, the physical crosslinks are destroyed, and the polymer melts just like any other thermoplastic, which makes fabrication easy, unlike thermoset elastomers as they do not experience melting. Since the melting-solidfication process is reversible and repeatable for thermoplastic elastomers, they can be recycled to be made into other shapes or parts, hence production costs and time are much reduced compared to thermoset elastomers as they are generally not recyclable [2].

Two biodegradable polymers, polylactide and polycaprolactone, can be copolymerized together using coordinated anionic ring opening polymerization (CAROP) into diblocks and then characterized according to their morphology, i.e. the amount of hard and soft blocks, the block lengths, block arrangement, molecular weight, mechanical properties etc [3]. From this characterization, we would like to find the optimum concentration of polylactide and polycaprolactone to be added that can achieve the maximum elongation value.

Experimental section

Substrates and solvents

ε-caprolactone (99%) was obtained from Fluka, dried over CaH2 and distilled under nitrogen at reduced pressure. L-lactide was obtained from Sigma Aldrich and purified by recristallization in dry ethyl ester. The monomer was dried for 24 h

under reduced pressure at room temperature prior to polymerization. Stannous 2-ethylhexanoate (96%) ($Sn(Oct)_2$) from Sigma, hydroxy butyl vinyl ether (HBVE) stabilized by 0.01% of KOH from BASF, methanol anhydrous (99.8%) from Aldrich were used as received. Toluene anhydrous (99.8%) was purchased from Aldrich, dried over CaH_2 and distilled under nitrogen.

Size exclusion chromatography

The molar weights of polymers were determined by size exclusion chromatography, SEC (Agilent 1100 Series HPLC) as well. Polystyrene standards with a narrow molar weight distribution in the range of 580-400000 g/mol were used for calibration. Measurements were made at room temperature with linear PL gel 5μm mixed C columns. Chloroform was used as solvent with a flow rate of 1 mL/min.

Mechanical test

Using the INSTRON 5848 microtester and its software INSTRON Bluehill, the bone shape specimens were pulled in the vertical direction at a rate of 20 mm/min. Tests were performed at the temperature 25°C. A minimum of 5 specimens per sample were tested.

DSC analysis

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 – 6 mg) and placed into standard aluminum pans individually. DSC analysis was done by first exposing the sample at 100°C for 5 minutes to eliminate internal stresses, then equilibrating the samples at -65 °C and after that the temperature was ramped up to 200°C at a rate of 5°C per minute.

Synthesis of polymers

The syntheses were realized in a three necks round bottom flask (100 mL) equipped by thermometer, condenser and magnetic stirrer. The flask was purged by nitrogen, vacuumed twice and after that was kept under the nitrogen atmosphere.

Nitrogen was blown through the water absorption system with silicogel. The temperature of synthesis was maintained by immersing of flask into silicone oil bath. A mixture of HBVE and $Sn(O_{ct})_2$ was added to the toluene at 90°C and stirred for 30 minutes. Quantity of HBVE was taken according to the desired degree of polymerization. Subsequently ε-capolactone monomer was added to the mixture and the temperature has been increased up to 110°C.

In case of random copolymer synthesis necessary quantity of L-lactide monomer was added first to the flask following by the ε-capolactone adding.

After that the mixture was maintained for 24 hours. In the case of diblock synthesis defined quantity of L-lactide was added to the flask and the mixture was kept at toluene boiling point temperature another 24 hours. Polymer was precipitated in cold methanol and dried in the vacuum oven at 45°C during 24 hours.

Results and Discussion

The properties of diblock depend from two factors: molar weight of PCL and molar weight of PLLA. It is difficult to predict what will be the elongation and crystallinity of diblock at different combinations of these two factors. Therefore we made 16 syntheses according to the design of experiment [4] for creating the mathematical model allowing to describe the behavior of the system and to find the optimal combination of two above stated factors. 16 different diblock copolymers of PCL-b-PLLA with a large variety of molecular weights were first synthesized to relate how the different molecular weights affected mechanical properties. Molar weight of polycaprolactone block was varied at the levels: 2000, 5000, 7000, 10000 Da. Molar weight of polylactide block was changed at the same levels (table 1).

Variation of theoretical molar weight from actual molar weight could be due to impurities during polymerization. Still, a conclusion from the table can still be made. From Table 1, it is generally observed that when the total molecular weight of the polymers increases, the percentage of elongation value also increases. But when the molar weight of PLLA increases beyond a certain limit, there is a decrease in the percentage of elongation value. This limit is dependent on the molar weight of PCL. This is because as the amount of PLLA increases, the degree of crystallinity would increase, causing

Table 1.

Different molar weights of diblock copolymer PCL-b-PLLA affecting elongation and modulus

Theoretical molar weight of PCL-b-PLLA [Da – Da]	Actual molar weight of PCL-b-PLLA measured by GPC [Da]; PDI ( )	Elongation at maximum load [%]	Elastic Modulus [MPa]
2000 - 2000	7437 (1.40)	6.5±0.95	66.64±3.54
5000 - 2000	11178 (1.26)	0.88±0.14	73.23±4.58
7000 – 2000	19677 (1.52)	4.03±1.05	150.26±7.05
10000 – 2000	16997 (1.33)	0.54±0.11	87.59±3.95
2000 – 5000	10974 (1.55)	5.39±0.98	115.01±6.81
5000 – 5000	12718 (1.32)	18.04±1.56	45.03±3.11
7000 – 5000	23849 (1.35)	3.45±0.84	104.94±8.49
10000 – 5000	17735 (1.34)	1.62±0.48	164.71±10.97
2000 – 7000	20290 (1.55)	0.65±0.29	245.65±16.18
5000 – 7000	25061 (1.54)	28.05±2.37	54.05±2.68
7000 – 7000	16574 (1.42)	8.72±1.45	105.17±7.39
10000 – 7000	18802 (1.45)	1.92±0.28	285.86±18.22
2000 – 10000	16903 (1.82)	1.70±0.22	96.15±4.58
5000 – 10000	26334 (1.37)	14.34±1.24	207.54±16.57
7000 – 10000	18868 (1.44)	18.67±2.11	75.00±3.95
10000 – 10000	26253 (1.58)	10.08±1.13	115.16±8.08

the polymer to lose its elasticity. Hence, a certain amount of PCL is actually needed to counter the effects of crystallization on the polymer's elasticity. Some block polymers were synthesized to study dependence between crystallinity and molar weight of polymer. It is obvious that crystallinity and melting enthalpy increase with grow of polymer molar weight (Figure 1, melting peak of PCL is located around 50-55°C and of PLLA one is in the range 140-160°C)
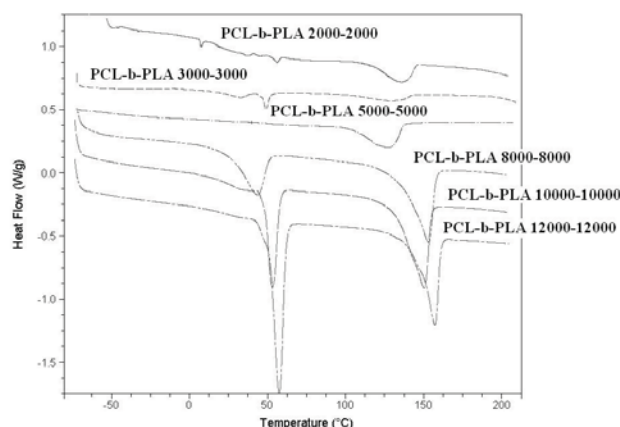

Fig. 1. Influence of polymer molar weight on crystallinity

From the diblock copolymers of PCL-b-PLLA synthesized, there was a need to think of alternative ways to optimize the elongation value which had only a value close to 30% (PCL-b-PLLA / 5000-7000).

We used a method of the least squares to receive a mathematical equation for describing the behavior of the system PCL-b-PLLA [5]. Mathematical behavior of mechanical properties (elongation at maximum load) from molar weight of each part of diblock can be expressed by the following equation (1):

$$\text{Elongation}=8.20202+0.00508809\times M_{PCL}+$$
$$+0.00172086\times M_{PLLA}+4.52539*10^{-7}\times$$
$$\times M_{PCL}\times M_{PLLA}-7.08721\times10^{-7}\times$$
$$\times M_{PCL}^2 -2.40444\times10^{-7}\times M_{PLLA}^2 \qquad (1)$$

where M_{PCL} – molar weight of polycaprolactone block, Da; M_{PLLA} – molar weight of polylactide block, Da.

We are interested to find a maximum of elongation of our polymers. We found a derivation of our function and making it to zero we found a maximum. According to the calculation maximum elongation should be at molar weight of PCL – 7000 Da and molecular weight of PLLA is 10000 Da and it equals 17.5%. It corresponds to the practical received results. Elongation at maximum load of diblock with molar weight of PCL 7000 and PLLA 10000 is 18.67%. We can suggest that the maximum of elongation is located into the limit M_{PCL} 5000-7000 Da and M_{PLLA} 7000-10000 Da and the maximal meaning should be very close to practical found. It confirms that there is no big value of elongation for block copolymer with such kind architecture.

Table 2.
Characteristics of diblock copolymer (PCL-co-PLLA)-b-PLLA

Targeted molar weight of partially random PCL [Da]	Amount of L-LA in PCL [%]	Targeted molar weight of PLLA [Da]	Actual molar weight of (PCL-co-PLA) -b-PLLA [Da]; PDI ( )	Elongation at maximum load [%]
10000	25	2000	14484 (1.68)	Impossible to cast film
10000	25	5000	14162 (1.88)	13.39± 7.81
10000	25	10000	21907 (1.87)	135.51± 5.76
10000	50	2000	13884 (1.41)	31.11±4.74
10000	50	5000	15093 (1.78)	14.69±7.39
10000	50	10000	18985 (2.16)	11.77±6.63
10000	75	2000	11151 (2.28)	48.58±7.92
10000	75	5000	16832 (2.31)	0.60±4.79
10000	75	10000	18712 (2.39)	0.35±5.06

Different approaches to increase the mechanical properties can be considered. We suppose that the main problem of low elongation is the crystallinity of PCL part. Therefore our next step was to copolymerize PCL, which will be randomized by some quantity of L-lactide to reduce the crystallinity.

We decided to synthesize the diblock copolymers with the structure (PCL-co-PLLA)-b-PLLA where the molar weight of first block was fixed at 10000 Da. The PCL soft block was randomized with L-lactide with the concentration of 25%, 50% and 75%. This block was then copolymerized with the homopolymer PLLA with different molecular weights varied at the levels 2000, 5000, 10000 Da. The results are shown at the table 2.

A surprising discovery was the elongation value of (PCL-co-PLLA)-b-PLLA 10000-10000 Da with 25% of LA in PCL which had a value close to 136% at maximum load and a value of elongation at break about 200%. The stress-strain curve of this polymer is shown on the Fig. 2.
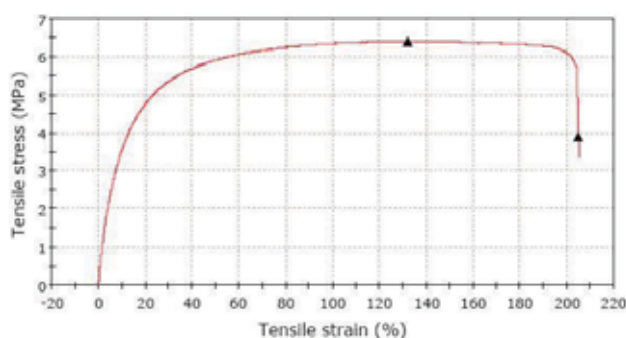

Fig. 2. Stress-strain curve of diblock copolymer (PCL-co-PLLA)-b-PLLA.

A mathematical model was drawn up equation of simulation (2) and calculations were made.

$$Elongation = -108.439 + 0.0352047 \times M_{PLLA} + 2.26019 \times \%LA - 5.93415 \times 10^{-4} \times \%LA \times M_{PLLA} \qquad (2)$$

where M_{PLLA} – molar weight of polylactide, Da; %LA – quantity of L-lactide in PCL block, % mol.

Maximal value of elongation according to the calculation by derivation of received function has shown that maximum elongation could be at Mn of PLLA – 3800 Da and quantity of L-lactide in PCL block about 60%. We made this film but elongation at maximum load was only 70% and elongation

at break – 210%. Making some simulation and mathematical calculation we then came up with some assumptions:

Optimum amount of lactic acid to be added to PCL should be between 20% and 30%.

- 20% of LA if molar weight of PCL is 6000 Da to 8000 Da

- 25% of LA if molar weight of PCL is 8000 Da to 12000 Da

- 30% of LA if molar weight of PCL is above 12000 Da

This diblock (PCL-co-PLLA)-b-PLLA combination could have several other possible maxima of L-lactide that can be added to PCL, besides the calculated amount of 20% to 30%. It is possible that we reached maximum elongation for such range of polymer molar weight.

Conclusion

From the studies conducted so far, we can conclude that there is no fixed percentage of lactic acid or caprolactone that can be added to PCL and PLLA respectively as the percentage value is dependent on the molecular weight of the individual blocks and how the polymers are copolymerized (*e.g.* diblock copolymer (PCL-co-PLLA)-b-PLLA 10000-10000 with 25% LA in PCL gives an elongation at maximum load value of 136%. Also, if we increase the molecular weight of PCL or the percentage of LA in PCL, the crystallinity of the polymer would increase, leading to a decrease in the elasticity of the polymer, but a certain amount of PLLA is still needed to act as the hard block of the elastomer. Therefore, we must strike a balance so that sufficient amount of PLLA can act as the hard block but yet would not decrease the elasticity of the polymer drastically. The most promising type of polymer to give high elongation value would be the diblock copolymer (PCL-co-PLLA)-b-(PLLA-co-PCL). Thus, more research could be done on this type of polymer. Simulation has shown that the value of elongation should be much better for this architecture of block polymer. And the next syntheses could be done according to the calculated rule. Based on the simulation results we can assume that the percentage ratio of L-lactide and caprolactone to be added to PCL and PLLA respectively is equal to the ratio of the molecular weight of the first block (PCL) and the second block (PLLA) used.

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