

## RELEVANCE OF THE RESEARCH WORK TO THAILAND

In the Biomedical Polymers Technology Unit, Department of Chemistry, Faculty of Science, Chiang Mai University, the possibility is being studied of using novel polyesters based on L-lactide and  $\epsilon$ -caprolactone as absorbable nerve guides that are of sufficiently high quality and lower cost for nerve repair in Thailand. Artificial nerve guides, where a tube bridges the nerve gap, offer a promising alternative to peripheral nerve repair. As the work described here moves towards its logical and, hopefully, successful conclusion, a 20-fold scale-up from the 25 g scale to the 500 g scale would enable more detailed experiments to be carried out on the same batch of material, thereby reducing the uncertainty arising from batch-to-batch variations. Although the literature contains sufficient information on the choice of suitable reaction parameters for bulk polymerization in a small-scale reaction, the prior art contains no teaching as to how the reaction can be carried out on an industrial scale. Thus, the main aim of this research project has been to study the influence of synthesis scale-up (25 g, 250 g and 500 g) on the reaction profile in the bulk polymerization of L-lactide and  $\epsilon$ -caprolactone. At the same time, the choice of reaction conditions such as reaction temperature, reaction time and initiator concentration, which have a profound effect on the reaction profile and the properties of the final product, has also been studied.

## APPENDIX

### CONFERENCES

#### 1. POSTER PRESENTATION

**Booncharoen Wathuka**, Punyodom Winita, Molloy Robert and Nalampang Kanarat, “*Influence of Synthesis Scale on the Reaction Profile in the Bulk Copolymerization of L-lactide and  $\epsilon$ -Caprolactone*”, **The 5th PERCH Annual Scientific Congress (PERCH-CIC CONGRESS V)**, Pattaya, Chonburi, Thailand (2007).

#### 2. POSTER PRESENTATION

**Booncharoen Wathuka**, Punyodom Winita, Molloy Robert and Nalampang Kanarat, “*Influence of Synthesis Scale on the Reaction Profile in the Bulk Copolymerization of L-lactide and  $\epsilon$ -Caprolactone*”, **The 2<sup>nd</sup> International Conference on Advances in Petrochemicals and Polymers (ICAPP 2007)**, June 25<sup>th</sup>-28<sup>th</sup> 2007, Bangkok.

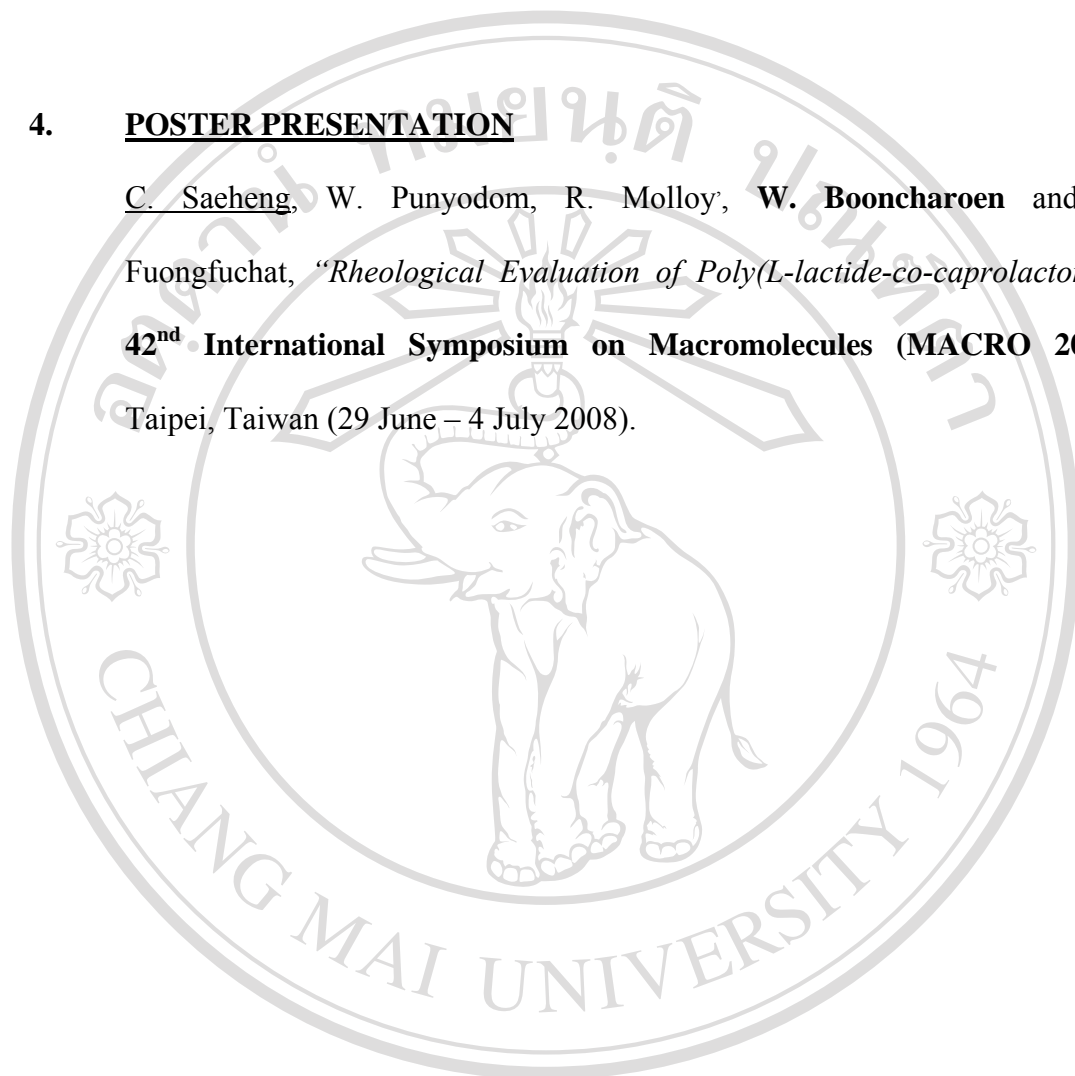
#### 3. POSTER PRESENTATION

**W. Punyodom**, R. Molloy, T. Wongchanapiboon, B. Thapsukhon, **W. Booncharoen**, C. Saeheng, P. Teerawonganan, K. Sanapanich, A. Pleunsamran, V. Chaisukasant, A. Fuogfuchar and P. Supaphol. “*Fabrication of Biodegradable Polyester Conduits for Use as Absorbable Nerve Guides*”,

**42<sup>nd</sup> International Symposium on Macromolecules (MACRO 2008)**,  
Taipei, Taiwan (29 June – 4 July 2008).

4. **POSTER PRESENTATION**

C. Saeheng, W. Punyodom, R. Molloy, **W. Booncharoen** and A.  
Fuongfuchat, “*Rheological Evaluation of Poly(L-lactide-co-caprolactone)*”,  
**42<sup>nd</sup> International Symposium on Macromolecules (MACRO 2008)**,  
Taipei, Taiwan (29 June – 4 July 2008).



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**(PERCH-CIC CONGRESS V)**

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## Influence of Synthesis Scale on the Reaction Profile in the Bulk Copolymerization of L-lactide and $\epsilon$ -Caprolactone

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### Objective

To study the effects of synthesis scale-up and reaction time on the % yield, copolymer composition, molecular weight, thermal property and morphology of poly(L-lactide-co- $\epsilon$ -caprolactone), PLC.

### Methods

PLC 50:50 mol% (25 g, 250 g and 500 g) was synthesized *via* ring-opening bulk polymerization using stannous octoate and 1-hexanol as the initiating system at 120 °C. The copolymer products were purified by dissolving in chloroform followed by re-precipitation in cold methanol. The structures and properties of the resulting copolymers were characterized by a combination of  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$ , GPC and DSC.

### Results

The effects of reaction time on the % yield, copolymer composition and molecular weight of the PLC from the small-scale synthesis (25 g) are shown in Figure 1. From the results obtained, the % yield and molecular weight of the copolymer both increase with reaction time. When comparing the copolymer composition (LL:CL) with time, it can be seen that the reactivity of L-lactide is higher than that of  $\epsilon$ -caprolactone. The most suitable reaction time that gave a high % yield (92%), high molecular weight ( $M_w=52,000$ ) and a copolymer composition (LL:CL = 49.6:50.4 mol%) close to that of the comonomer feed ratio was 48 hours. For the larger-scale syntheses (250 g and 500 g), the bulk polymerization presented practical problems arising from solidification during the polymerization leading to difficulties in removing the product from the reactor. Furthermore, problems associated with heat transfer as the mass-to-volume ratio increased resulted in increased temperature variations, transesterification reactions and thermal decomposition of the copolymer.

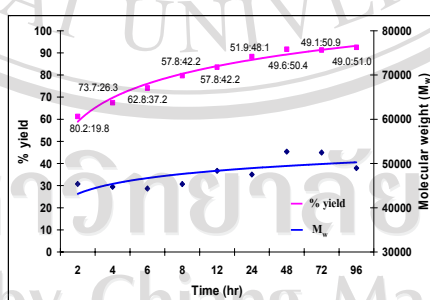


Figure 1: Effect of reaction time on the % yield, copolymer composition and molecular weight of PLC.

### Conclusions

The reaction time required depends on the reactivity of the monomers and the synthesis scale. Scale-up plays an important role in the final outcome of the process and special attention has to be paid to the reactor design and the choice of reaction parameters.

**Keywords:** poly(L-lactide-co- $\epsilon$ -caprolactone), ring-opening polymerization, bulk polymerization, synthesis scale-up

**Selected Reference:** B. Buchholz, M. Schellhorn and A. Weber, *US Patents*: 6,706,854 B2 2004.

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## INFLUENCE OF SYNTHESIS SCALE ON THE REACTION PROFILE IN THE BULK COPOLYMERISATION OF L-LACTIDE AND $\epsilon$ -CAPROLACTONE

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Biodegradable polyesters have attracted increasing interest through their use in biomedical applications. For large-scale synthesis ( $> 1$  kg) where high polymer molecular weight is required, ring-opening polymerization (ROP) in bulk is the preferred method. It is generally accepted that, due to the highly exothermic nature of bulk polymerization reactions, larger-scale synthesis invariably requires a purpose-designed reactor with possible modification of the reaction conditions. The choice of reaction conditions such as temperature, time, type and concentration of the initiating system, and monomer purity has profound effect on the reaction profile and the properties of the final product. In this research, poly(L-lactide-co- $\epsilon$ -caprolactone) was synthesized *via* ROP in bulk using stannous octoate and 1-hexanol as the initiating system at 120 °C. The effects of synthesis scale-up (25 g, 250 g and 500 g) and reaction time on the % yield, copolymer composition, microstructure, thermal properties and molecular weight have been studied. From the results obtained, the reaction time required depends on the reactivity of the monomers and the synthesis scale, while the copolymer microstructure is controlled by the thermodynamic monomer polymerisabilities and equilibrium monomer concentrations. Scale-up plays an important role in the final outcome of the process and special attention has to be paid to the reactor design. The choice of suitable reaction parameters for each of the different scale reactions was another prime consideration and, from the results obtained, the influence of synthesis scale-up is discussed.

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### ABSTRACT

Biodegradable polyesters have attracted increasing interest through their use in biomedical applications. For large-scale synthesis (> 1 kg) where a high polymer molecular weight is required, ring-opening polymerization (ROP) in bulk is the preferred method. It is generally accepted that, due to the highly exothermic nature of bulk polymerization reactions, larger-scale synthesis invariably requires a purpose-designed reactor with possible modification of the reaction conditions. The choice of reaction conditions such as temperature, time, type and concentration of the initiating system, and monomer purity has profound effects on the reaction profile and the properties of the final product. In this research, poly(L-lactide-co- $\epsilon$ -caprolactone) was synthesized *via* ROP in bulk using stannous octoate and 1-hexanol as the initiating system at 120°C. The effects of synthesis scale-up (25 g, 250 g and 500 g) and reaction time on the % yield, copolymer composition, microstructure, thermal properties and molecular weight have been studied. From the results obtained, the reaction time required depends on the reactivity of the monomers and the synthesis scale, while the copolymer microstructure is controlled by the thermodynamic monomer polymerisabilities and equilibrium monomer concentrations. Scale-up plays an important role in the final outcome of the process and special attention has to be paid to the reactor design. The choice of suitable reaction parameters for each of the different scale reactions was another prime consideration and, from the results obtained, the influence of synthesis scale-up is discussed.

### 1. INTRODUCTION

Biodegradable polymers, especially aliphatic polyesters, have been investigated worldwide as biomaterials for medical, pharmaceutical and industrial applications due to their biocompatibility and biodegradability. Cyclic ester monomers widely used include L-lactide, D-lactide, DL-lactide, meso-lactide, glycolide and  $\epsilon$ -caprolactone. Polymerization processes for preparing aliphatic polyesters have been known for a long time. Since polycondensation processes can only be used to produce relatively low molecular weight aliphatic polyesters, they are preferably prepared by ring-opening polymerization (ROP) of cyclic monomers. [1-5] The choice of reaction conditions such as temperature, time, type and concentration of the initiating system, and monomer purity has a profound effect on the reaction profile and the properties of the final product. [6-9] Most literature reports [2, 6-9] describe the choice of suitable reaction parameters in a small-scale reaction. However, it is generally accepted that, due to the highly exothermic nature of bulk polymerization



reactions, larger-scale synthesis invariably requires a purpose-designed reactor with possible modification of the reaction conditions.[3-5, 10] In this research, poly(L-lactide-*co*- $\epsilon$ -caprolactone), PLC 50:50 mol %, was synthesized via ROP in bulk using stannous octoate ( $\text{SnOct}_2$ ) and 1-hexanol as the initiating system. The effects of synthesis scale-up and reaction time on the % yield, copolymer composition, molecular weight, thermal properties and morphology of the PLC products are described.

## 2. EXPERIMENTAL

### 2.1. Materials

L-lactide (LL) was synthesized from L-lactic acid (purchased from Carbo Erba) via a 2-step reaction: firstly, the linear polycondensation of L-lactic acid to low molecular weight poly(L-lactic acid) (PLLA) followed, secondly, by thermal decomposition of the PLLA to yield L-lactide as the primary decomposition product. The crude L-lactide was recrystallized four times from ethyl acetate and dried for 48 hours at  $55^\circ\text{C}$  under reduced pressure before polymerization.  $\epsilon$ -Caprolactone (CL, purchased from Acros, USA) and  $\text{SnOct}_2$  (from Sigma, Aldrich) were distilled under reduced pressure. 1-Hexanol (from Fluka) was dried with sodium metal for 1 hour followed by fractional distillation.

### 2.2. Copolymerization

The monomers,  $\text{SnOct}_2$  and 1-hexanol were weighed and added to the reaction flask (Figures 1(a-c)) under dry nitrogen in a controlled atmosphere glove box at room temperature. The copolymerization was carried out at constant temperature. When the copolymerization was complete, the reaction product was purified by dissolving in chloroform followed by re-precipitation in cold methanol. The copolymer products were dried in a vacuum oven at  $55^\circ\text{C}$  to constant weight.

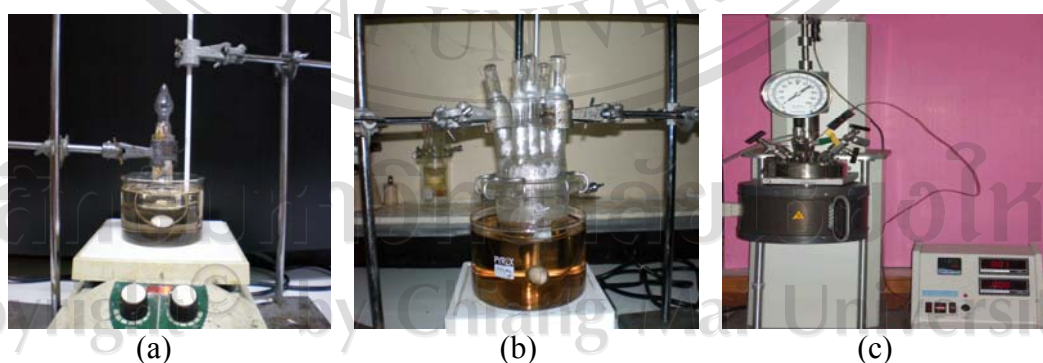


Figure 1: Apparatus for ROP of L-lactide and  $\epsilon$ -caprolactone (a) small scale, 25 g (b) large scale, 250 g (c) large scale (Parr Reactor Model 4843), 500 g.

### 2.3. Characterization

The  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra of the copolymers were recorded in deuterated chloroform,  $\text{CDCl}_3$ , with a Bruker Avance NMR spectrometer. Thermal characteristics were measured on a Perkin-Elmer DSC7 Differential Scanning Calorimeter. Copolymer molecular weights were determined by means of GPC using

a Water Autosampler 707 System operating using THF as solvent at 40°C and calibrated with polystyrene standards.

### 3. RESULTS AND DISCUSSION

#### 3.1 Influence of Reaction Temperature and Time on the Reaction Profile in Small Scale Synthesis (25 g)

The influence of reaction temperature on the % yield and molecular weight of the PLC in small-scale synthesis (25 g) are shown in Figure 2. The most suitable reaction temperature that gave both a high % yield (90%) and high molecular weight ( $\bar{M}_w = 60,000$ ) was 120°C. The data shows that a higher reaction temperature is not recommended, since it increases the probability of degradative side reactions such as transesterification.

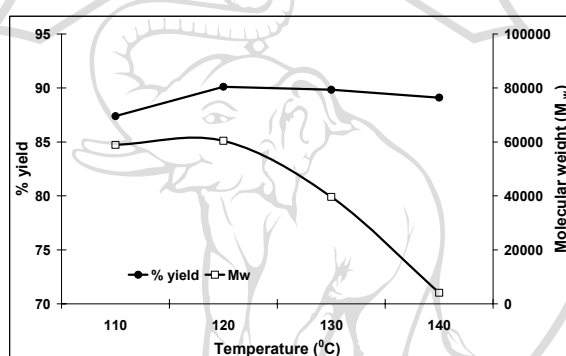


Figure 2: Influence of reaction temperature on the % yield and molecular weight of PLC in small scale synthesis (25 g).

The  $^1\text{H-NMR}$  spectrum of the PLC copolymer synthesized at 140°C is shown in Figure 3(a). The methine proton resonance of the lactidyl units is seen in the range 5.3-5.0 ppm (peak b) and the methylene proton resonances of the caproyl units in the ranges 4.2-4.0 ppm (peak c) and 2.5-2.2 ppm (peak g). From  $^{13}\text{C-NMR}$ , the carbonyl carbon region between 169-174 ppm provides valuable information about the sequence distribution of the caproyl (*Cap*) and lactidyl (*LL*) units in the copolymer chains (Figure 3(b)). Since the spectra of the PLC copolymer in this work show not only peaks due to the *LLL* and *CapCapCap* sequences but also intermediate peaks due to *CapCapL*, *LCapL*, *CapLL* and *CapLCap* sequences, it confirms that random copolymerisation has indeed occurred. In addition, two types of transesterification reaction were recognized in which a lactidyl unit (*LL*) undergoes bond cleavage leading to the formation of anomalous sequences of *-CapLCap-* and *-CapLLLCap-*, both with an odd number of half-lactidyl (*L*) units. Thus, transesterification plays an important role in the redistribution of monomer sequences, thereby influencing the microstructure.

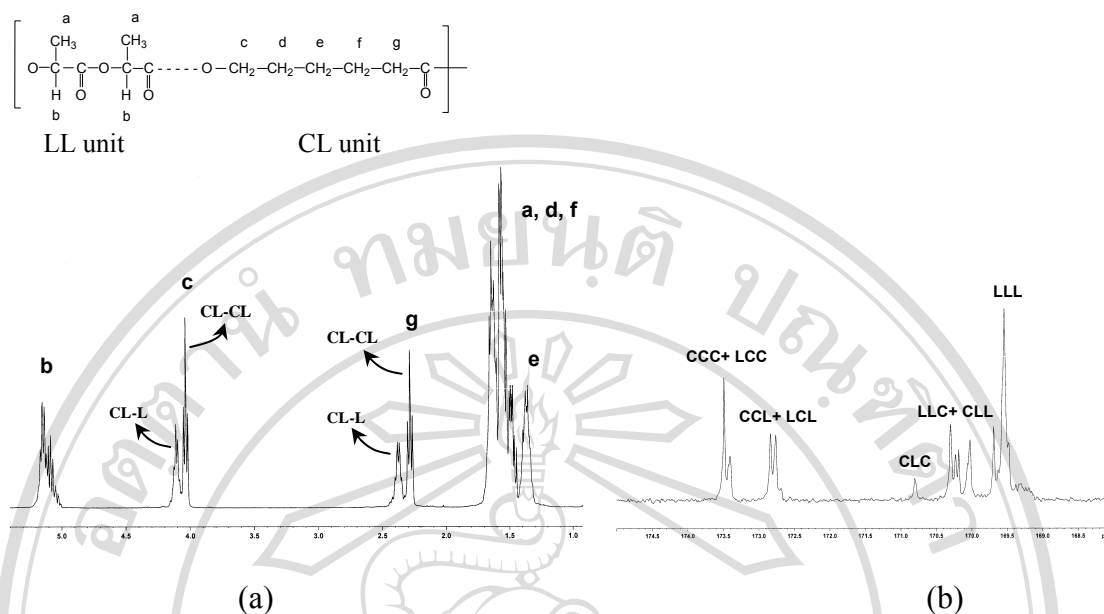


Figure 3: (a)  $^1\text{H-NMR}$  spectrum and peak assignments and (b)  $^{13}\text{C-NMR}$  carbonyl carbon region between 175.0-168.0 ppm, and peak assignments, as reported by Kasperczyk *et al.* [11]

The influence of reaction time on the % yield, copolymer composition, molecular weight, thermal properties and morphology of the PLC in the small scale (25 g) are shown in Figure 4. From the results obtained, the % yield and molecular weight of the copolymer both increase with reaction time (Figure 4(a)). However, at longer reaction times of up to 72 hours, the molecular weight of PLC began to decrease, as a result of transesterification. When comparing the copolymer composition (LL:CL) with time, it can be seen that the reactivity of L-lactide is higher than that of  $\epsilon$ -caprolactone. From the DSC results (Figure 4(b)), the copolymer initially showed a melting temperature ( $T_m$ ) because of the higher L-lactide content, but this subsequently decreased as the CL content increased with increasing reaction time. The morphology of the copolymer product was amorphous at 48 hours. The most suitable reaction time that gave a high % yield (92%), high molecular weight ( $\bar{M}_w = 52,000$ ) and a copolymer composition (LL:CL = 49.6:50.4 mol %) close to that of the comonomer feed ratio was 48 hours.

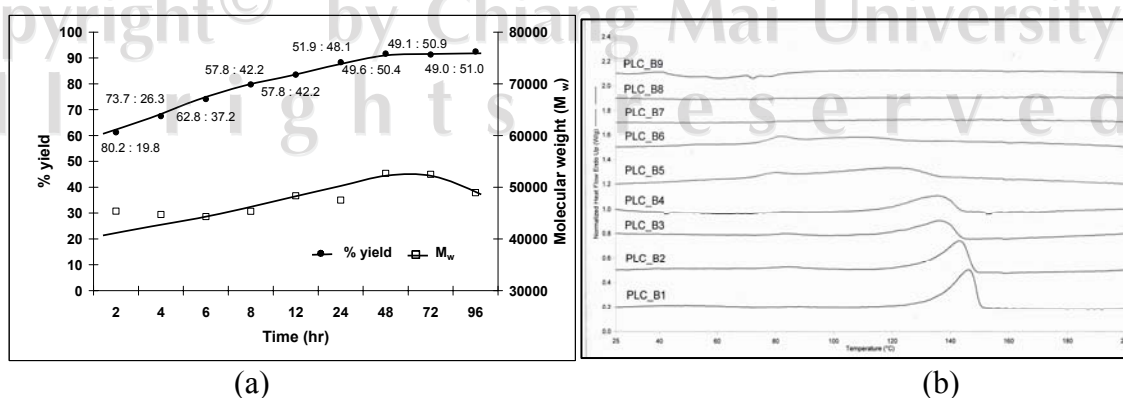


Figure 4: Influence of reaction time on the (a) % yield, copolymer composition and molecular weight and (b) thermal properties and morphology of PLC in small scale synthesis (25 g).

### 3.2 Influence of Reaction Time on the Reaction Profile in the Large-Scale Syntheses (250 g and 500 g)

The influences of reaction time on the % yield, copolymer composition and molecular weight of the PLC in the large scale (250 g) are shown in Figure 5. From the results obtained, the % yield and molecular weight of the copolymer both increase with time. The copolymer composition (LL:CL) was close to that of the comonomer feed ratio after 48 hours. The most suitable reaction time that gave a high % yield (94%), high molecular weight ( $\bar{M}_w = 48,000$ ) and a copolymer composition close to that of the comonomer feed ratio was 96 hours. It can be concluded that, for large scale syntheses, longer reaction times are required.

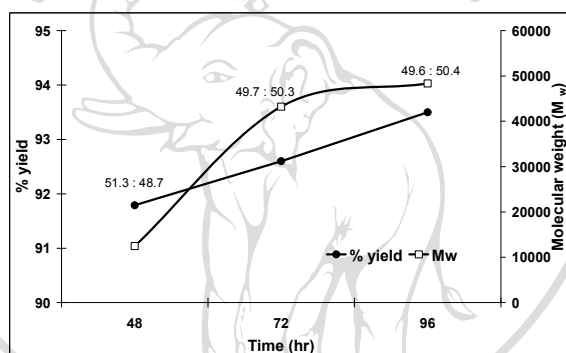


Figure 5: Influence of reaction time on the % yield, copolymer composition and molecular weight of PLC in large scale synthesis (250 g).

When we consider the effects of synthesis scale-up, as the amount of polymer increases from 25 g (small scale) to 250 g (large scale), both the % yield and molecular weight of the PLC decrease. This is due to problems associated with heat transfer as the mass-to-volume ratio increases resulting in increased temperature variations and transesterification. Furthermore, the largest scale (500 g) synthesis presented practical problems arising from solidification during the polymerization leading to difficulties in removing the product from the reactor. The copolymer products also decompose at higher temperatures and longer times.

## 4. CONCLUSIONS

This research has shown that, for small scale synthesis (25 g), the most suitable conditions were 48 hours and 120°C. For the large scale syntheses (250 g and 500 g), processing and purification of the resulting copolymer is troublesome because of the increased mass of the solid product. Also, because the polymerization reaction is exothermic, heat transfer becomes more of a problem, especially as the melt viscosity increases. Thus, synthesis scale-up requires careful consideration of reactor design and choice of reaction conditions.

**ACKNOWLEDGEMENTS**

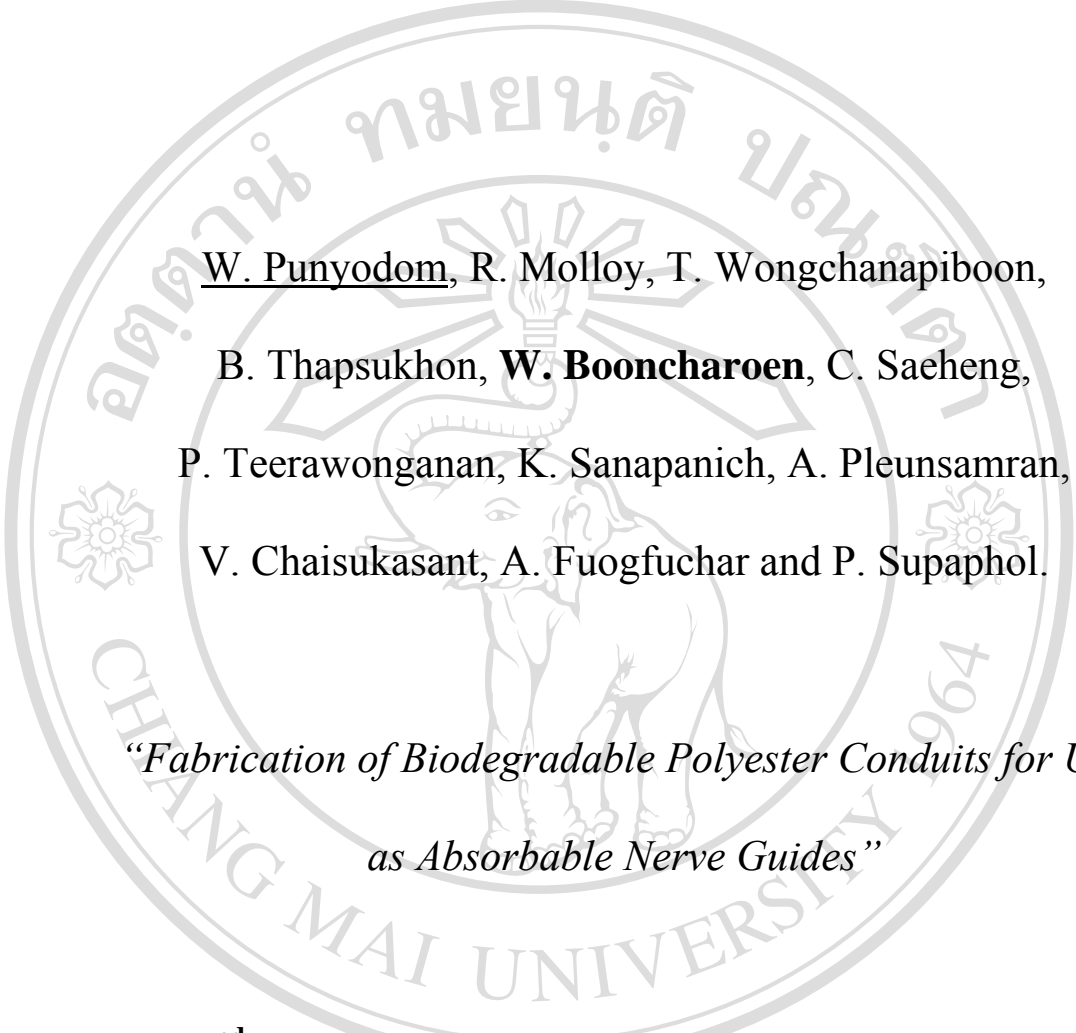
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**REFERENCES**

1. Nieuwenhuis, J. (1992). *Clinical Materials*. **10 (1-2)**, 59-67.
2. Grijpma, D.W., Zondervan, G.J. and Pennings, A.J. (1991). *Polym. Bull.* **25 (3)**, 327-333.
3. Buchholz, B., Schellhorn, M. and Weber, A. (2004). US Patent No. 6,706,854 B2.
4. Yamane, K., Kawakami, Y., Sato, H. and Hoshi, T. (2003). WO Patent No. 03/006526 A1.
5. Wal, A. V. D. and Mol, A.C. (2006). US Patent No. 0258834 A1.
6. Finne, A. and Albertsson, A.-C. (2002). *Biomacromolecules*. **3 (4)**, 684-690.
7. Deng, X., Yuan, M., Li, X. and Xiong, C. (2000). *Eur. Polym. J.* **36 (6)**, 1151-1156.
8. Kowalski, A., Libiszowski, J., Duda, A. and Penczek, S. (2000). *Macromolecules*. **33 (6)**, 1964-1971.
9. Kowalski, A., Duda, A. and Penczek, S. (2000). *Macromolecules*. **33 (20)**, 7359-7370.
10. Meyer, T. (2003). *Org. Process. Res. Des.* **7 (3)**, 297-302.
11. Kasperczyk, J. and Bero, M. (1993). *Makromol. Chem.* **194 (3)**, 913-925.



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## Fabrication of Biodegradable Polyester Conduits for Use as Absorbable Nerve Guides

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**Introduction.** Peripheral nerve regeneration remains a clinical challenge especially when there is a large gap between the nerve stumps. Transplantation of autologous nerve grafts is now a standard method when direct anastomosis is difficult. Due to the disadvantages of this standard method (neuroma formation and sensory deficits at the donor-site, limited availability of donor-material, additional operation time and impaired regenerative results), various tubulisation techniques have been considered as an alternative method [1-3]. Biodegradable synthetic polymers are advantageous as nerve conduits because their properties can be tailored through their molecular design, synthesis and processing [4]. Neurotube® (Neurogen LLC, USA) and Neurolac® (Polyganics BV, The Netherlands) have already been approved by the FDA as commercial absorbable nerve conduits made from polyglycolic acid and poly(lactide-*co*- $\epsilon$ -caprolactone) respectively. Although several studies have been published, the results are still inconclusive. Current research is still striving to achieve the goal of developing nerve conduits with structural components that accurately match the nerve

anatomy and that deliver the correct physiologic sequence of growth factors over the entire period of regeneration.

In this work, comparisons are made between the processing methods (dip-coating, melt extrusion and electrospinning) used to fabricate nerve guide conduits from poly(L-lactide-*co*- $\epsilon$ -caprolactone), PLC, that have been developed for the reconstruction of peripheral nerve defects. An experimental study for repairing segmental nerve defects using nerve conduits in the rat model is also discussed. Multiple measurements were used to evaluate nerve regeneration and functional results.

**Methods.** A PLC random copolymer 50:50 mole % was synthesized by ring-opening bulk polymerization (ROP) at 120°C for 48 hours using SnOct<sub>2</sub> and 1-hexanol as the initiating system [5]. The structures and properties of the polymer were characterized by various techniques: spectroscopic methods (<sup>1</sup>H-NMR and <sup>13</sup>C-NMR), thermal analysis (DSC), molecular weight (GPC) and tensile testing. A high yield (97%) of the random copolymer was obtained with  $\bar{M}_n$  and polydispersity from GPC of 90,000 and 1.9 respectively. The copolymer

composition from the  $^1\text{H-NMR}$  spectrum (LL:CL = 50.5:49.5 mole %) was found to be similar to the 50:50 comonomer feed ratio. The copolymer was completely amorphous, as deduced from the absence of any melting peak in its DSC thermogram. Mechanical (tensile) testing of solvent cast copolymer films of  $0.11\pm 0.02$  mm thickness gave a tensile strength of  $16.3\pm 2.3$  MPa, an elongation at break of  $806.9\pm 18.5$  % and a Young's modulus of  $11.6\pm 2.2$  MPa.

#### **Fabrication of Nerve Guide Tubes.**

**Dip-coating.** The copolymer was dissolved in distilled ethyl acetate (30-40% w/v) and Kirchner (K) wires with diameters of 1.2 mm used as moulds. After drying in air, the tube was stored in a desiccator under vacuum for complete drying before being manually removed from the K-wire. A photograph and SEM images of the tube obtained are shown in Figs. 1(a-c). Transparent rubber-like tubes with an internal diameter and wall thickness of 1.2 mm and 0.3-0.4 mm respectively have been produced by the dip-coating method which, although rather laborious and time-consuming, yields tubes of uniform and controllable dimensions.

Microporosity was introduced into the copolymer tubes by a solvent-casting-leaching method [6] using water-soluble polyethylene glycol (PEG<sub>8000</sub> and PEG<sub>3000</sub>) as porogens. The copolymer and fraction of PEG<sub>8000</sub> and PEG<sub>3000</sub> (5, 10, 15% w/w) were dissolved in chloroform, cast onto glass moulds, and dried at room temperature for 12 hours. Each tube was then immersed in distilled water for 7 days with the water being replaced every day to assure complete leaching out of the PEG. An SEM

image of the cross-sectional pore structure prepared using 15% PEG<sub>3000</sub> as the porogen is shown in Fig. 1(d). From the results obtained, it was found that the pores formed were spherical with sizes of approximately 7-20  $\mu\text{m}$  depending on the molecular weight ( $\bar{M}_w$ ) of the PEG. The pore size created by PEG<sub>3000</sub> was larger than that by PEG<sub>8000</sub> while the number of pores increased as the amount of PEG increased.

**Melt extrusion.** An alternative technique, melt extrusion, was also used to prepare nerve guide tubes of similar dimensions. A small-scale melt spinning apparatus was modified by using a tubular-shaped die instead of a spinnerette. A copolymer rod was first made by heating at  $140^\circ\text{C}$  under compression with maximum load of 400 kg. The temperature was then held constant for 15 min before cooling to room temperature and removing from the cylinder. For melt extrusion, the copolymer rod was carefully inserted into the extrusion cylinder, heated up to  $135^\circ\text{C}$  and melt extruded as a tube at a ram speed of 2 mm/min through a tubular-shaped die. The tube was drawn down manually to a designated diameter and cooled in the water bath ( $10\text{-}15^\circ\text{C}$ ).

Melt extrusion can produce longer tubes, is quicker and more convenient than dip-coating, and also avoids the use of an organic solvent. Photographs and SEM images of the tube obtained are shown in Figs. 2(a-d). Transparent elastic tubes with an internal diameter and wall thickness of 0.7 mm and 0.2 mm respectively were obtained. However, the tube from melt extrusion was less uniform in its dimensions than that from dip-coating due to the multivariate nature of melt extrusion process and the viscoelastic properties

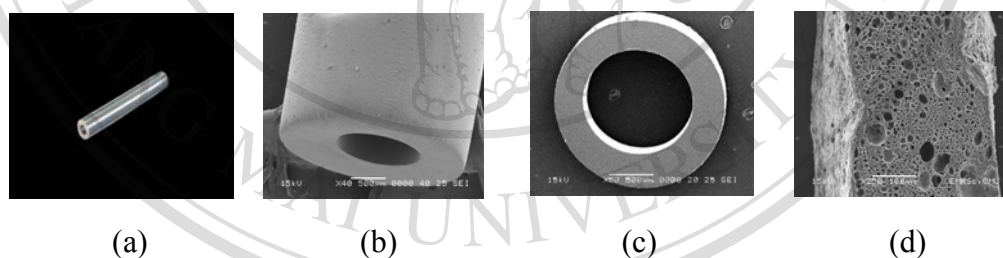


of the polymer melt. The rheological properties of the copolymer using a rotational rheometer (Bohlin Gemini HR<sup>nano</sup>) and a Rosand capillary rheometer have been studied to improve process control. Tests were performed in both dynamic and steady modes.

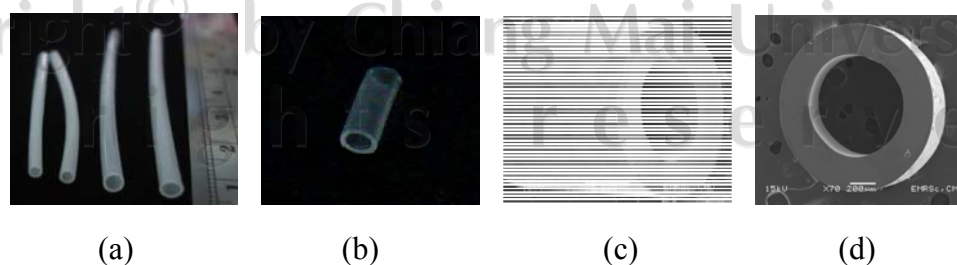
**Electrospinning.** For electrospinning, the copolymer was dissolved in a mixed-solvent of dichloromethane (DCM) : dimethylformamide (DMF) 7:3 v/v at a concentration of 10% w/v. The solution was placed in a 5 ml glass syringe equipped with a 20-gauge blunt-end stainless-steel needle (outer diameter 0.91 mm) as a nozzle. For fabricating the tubular-shaped conduits, a horizontal K-wire rod (1.2 mm in diameter) rotating at approximately 1000 rpm was used as the mandrel. In order to be able to remove the tube from the mandrel

easily, PEG<sub>8000</sub> (4% w/v) was dissolved in chloroform and pre-electrospun onto the mandrel for 3 min. The PLC solution was then electrospun using a Gamma High Voltage Research DC power supply at 12.5 kV potential between the needle tip and the mandrel for 6 h. Fibers were collected on the mandrel at a distance of 13 cm from the needle tip.

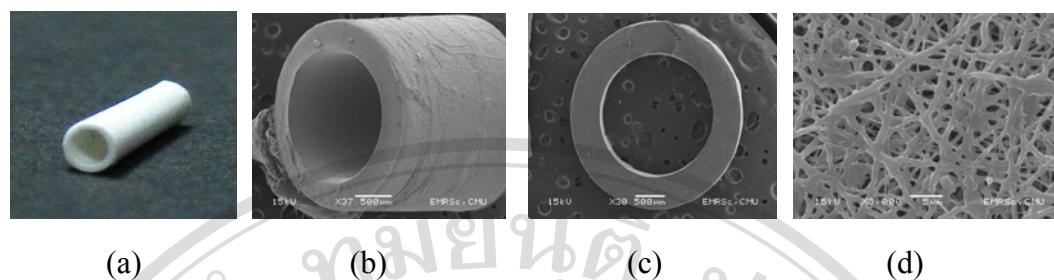
A photograph and SEM images of the electrospun copolymer tube are shown in Figs. 3(a-c). SEM images of the electrospun fibers showed nanoscale diameters and random orientation as shown in Fig. 3(d). The electrospun tube had a 1.2 mm inner diameter and was approximately 15-20 mm in length depending on the mandrel. Fibers with an average diameter of 760 nm over the range of 520 nm to 1320 nm were obtained.



**Figure 1.** (a) Photograph, (b) and (c) SEM images of the copolymer nerve guide tube prepared by dip-coating and (d) SEM image of cross-sectional pore structure prepared by the solvent-casting-leaching method using 15% PEG<sub>3000</sub> as porogen.



**Figure 2.** (a) and (b) Photographs, (c) and (d) SEM images of the copolymer nerve guide tube prepared by melt extrusion.



**Figure 3.** (a) Photograph of the copolymer nerve guide tube prepared by electrospinning from DCM : DMF 7:3 v/v (b), (c) and (d) SEM images of electrospun nanofibers.

Following their characterization, PLC copolymer tubes prepared by dip-coating was tested with respect to their *in vitro* hydrolytic degradation, *in vitro* cytotoxicity and *in vivo* animal (rat) biocompatibility as described below.

***In vitro* Hydrolytic Degradation Study.** The copolymer tubes prepared by dip-coating were immersed for up to 28 weeks in a phosphate buffer saline solution of pH 7.40 at  $37.0 \pm 1.0^\circ\text{C}$ . The tubes were seen to be readily hydrolysable in the aqueous environment (44% weight loss during 28 weeks), such as would exist in the human body. It was also found that the pH decreased with immersion time, indicating that the simple hydrolysis reaction is acid-catalysed by the new COOH end-groups formed, causing the pH of the immersion medium to decrease below 7. From SEM micrographs, hydrolytic degradation was considered to proceed via surface rather than bulk erosion, leading to surface microcrack formation and ultimately fragmentation. It is believed that hydrolytic degradation takes place preferentially in the amorphous regions of the copolymer due to their easier accessibility by diffusing water molecules.

***In vitro* Cytotoxicity Study.** Indirect assessment of cytotoxicity using both the test on extracts method

and direct contact method with human fibroblasts was carried out according to the ISO 10993-5: 1999(E) test procedure. Cytotoxicity testing of the extracts in a culture medium (Dulbecco's Modified Eagles Medium (DMEM) at  $25 \pm 5^\circ\text{C}$  for  $72 \pm 2$  hours) with human fibroblast cells (h-FBs) showed no significant difference in cell death when compared with the negative controls (Thermanox). Quantitative results showed that cell populations of all h-FB monolayers increased on both the reagent and the negative controls. Biological *in vitro* testing using a direct contact method with h-FBs suggested that no toxic substances were released from the test specimens into the culture media during the incubation period of 6 days. The cell response on the tested surfaces could not be examined as a result of surface properties, e.g. water absorption by the conduits. According to the ISO 10993-5: 1999(E) standards, the nerve guide materials showed no significant cytotoxic effect.

**Surgical Procedures and Evaluation Tests.** An evaluation of nerve regeneration after reconstruction using the tibial nerve in the rat model was conducted. A total of 24 Wistar rats were divided into 3 groups of 8 and each group subjected to a different nerve repair procedure. The 3

procedures involved the use of: (1) conventional nerve grafting, (2) a biodegradable nerve conduit made from a PLC copolymer and (3) a PLC copolymer filled with concentrated plasma. Evaluation of nerve regeneration was compared in terms of the tibial functional index (TFI), nerve conduction velocity (NCV), gastrocnemius muscle weight (GMW) and a histomorphometric study.

There was evidence of nerve regeneration across the gap from the histomorphologic study in every group. The TFI showed sequential improvements with implantation time ( $p < 0.05$ ). However, after 12 weeks post-operation, the TFI and GMW measurements revealed that the standard nerve graft group showed superior results to the 2 nerve guide groups with a statistical significance of  $p < 0.05$ . The NCV data supported the TFI data in general terms of nerve growth in all groups but the actual differences in the NCV values themselves were not considered to be large enough to be significant for ranking purposes ( $p > 0.05$ ). The effect of using plasma inside the copolymer conduit as a potential nerve growth factor was inconclusive. Based on these results, it was concluded that biodegradable copolymer nerve conduits, such as the PLC tubes described here, can lead to nerve regeneration across a 7 mm gap in the tibial nerve rat model.

**Conclusions.** It is clear from the results that, although the copolymer nerve guide conduits have potential for clinical usage, their overall performance needs to be improved further before they can be considered as a viable alternative to nerve grafting. The process for introducing

microporosity needs to be improved to give a uniform pore size. Microporosity is considered to be beneficial because it allows for cell infiltration as well as fluid and nutrient diffusion from the surrounding tissue to the lumen of the tube. In addition, the softness and flexibility also need to be improved, as well as dimensional control in melt extrusion, if these promising research products are to reach the commercialization stage.

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#### References:

- [1] Valentini R.F., Aebischer P. in Lanza R., Langer R.P. and Click W., ed., *Principles of Tissue Engineering*, Academic Press Inc., (1997).
- [2] Meek M.F. and Coert J.H., *J. Reconstr. Microsurg.* **2002**, *18*: 97.
- [3] Weber R.A., Breidenbach W.C., Brown R.E., Jabaley M.E. and Mass D.P., *Plast. Reconstr. Surg.* **2000**, *106* :1036.
- [4] Ciardelli G. and Chiono V., *Macromol. Biosci.* **2006**, *6*: 13
- [5] Punyodom W., Molloy R., Nalampang K., Kamcharoen C., Waraegsiri B., Sananpanich K. and Pleumsamran A., *Chiang Mai J. Sci* **2005**, *32*: 479.
- [6] Lin W.-J., Lu C.-H., *J. Membrane Sci.* **2002**, *198*:109.

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## Rheological Evaluation of Poly(L-lactide-co-caprolactone)

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**Introduction.** Many new applications are being developed for the use of biodegradable polymers in tissue regeneration. Nerves are one of the first tissues for which the method of guided tissue regeneration (GTR) has been tried. Direct reconnection by suturing of the proximal and distal nerve stumps is the first choice in the repair of nerve gaps caused by trauma. Transplantation of autologous nerve grafts is now a standard method when direct anastomosis is difficult. However, the results of nerve grafts are not entirely satisfactory because of the limited availability of donor nerves, morbidity at the donor site, mismatch between nerve and grafts and additional operation time. An alternative repair method is tubulization, which involves enclosure of the ends of a severed nerve by a tube which hold the stumps in place and offers a guide to regenerating axons to the distal stump [1-2].

Poly(L-lactide-co-caprolactone), PLC, is now a promising material for use as an absorbable nerve guide [3-5]. Regarding the preparation of the prosthesis, the copolymer tubes can be prepared by dip-coating and melt extrusion. The dip-coating method, although rather laborious and time-consuming, yields tubes of uniform and controllable dimensions. Melt extrusion is quicker and can produce longer tubes and is therefore more convenient than dip-coating. It also avoids the use of an organic solvent. However, tubes from melt extrusion

are less uniform in their dimensions than those from dip-coating due to the multivariate nature of the melt extrusion process and the viscoelastic properties of the polymer melt. The technologies for converting the biodegradable copolymer into useful items require knowledge about the rheological properties of the material. The rheological properties are essential for the design and optimization of process technologies [6]. Although the rheological properties of polylactide and poly( $\epsilon$ -caprolactone) have been studied in detail, there is limited information on the rheological behavior of their copolymer [7-9]. Knowledge about the flow instabilities of the copolymer is essential for the design of processing equipment and for proper process control.

In this work, the rheological properties of the PLC copolymer using rotational and capillary rheometers were studied as a means of improving the melt extrusion process.

### Synthesis and Characterization.

A PLC random tapered copolymer 50:50 mole % was synthesized by ring-opening bulk polymerization (ROP) at 120°C for 72 hours using 0.1 mole % SnOct<sub>2</sub> and 0.01 mole % 1-hexanol as the initiating system. The copolymer product was a soft, transparent solid obtained in high yield (97%) with values of  $M_n$  and polydispersity from GPC of 90,000 and 1.9 respectively. The copolymer composition from its

$^1\text{H-NMR}$  spectrum (LL:CL = 50.5:49.5 mole %) was very close to the initial 50:50 comonomer feed ratio. The chain microstructure and monomer sequence distribution of the copolymer were studied by means of  $^{13}\text{C-NMR}$ . The copolymer was completely amorphous, as deduced from the absence of any melting peak in its DSC thermogram. Mechanical (tensile) testing of solvent-cast copolymer films of  $0.11 \pm 0.02$  mm thickness gave a tensile strength of  $16.3 \pm 2.3$  MPa, an elongation at break of  $806.9 \pm 18.5$  % and a Young's modulus of  $11.6 \pm 2.2$  MPa. The glass transition ( $T_g$ ) from DMA was  $-6.3^\circ\text{C}$ , making the copolymer soft, elastic and rubber-like at body temperature ( $37^\circ\text{C}$ ), as would be suitable for use as a nerve guide tube.

**Rheological Characterization Techniques.** The rheological properties of the PLC were determined using a Bohlin Gemini HR<sup>nano</sup> Rotational Rheometer and a Rosand Capillary Rheometer. PCL is a hygroscopic material and, in order to remove any absorbed moisture and avoid hydrolytic degradation, the copolymer chips were dried under vacuum at  $100^\circ\text{C}$  for 24 hours before measurements.

#### Dynamic (Oscillatory) Mode.

Dynamic measurements of the PLC copolymer under strain-controlled conditions were performed on a parallel plate Bohlin Gemini HR<sup>nano</sup> rotational rheometer. The diameter of the plates was 25 mm and the gap between the plates was set to 0.5 mm. The copolymer was placed between the plates and heated to the test temperature ( $150^\circ\text{C}$ ) in order to eliminate previous deformation and thermal history. After adjusting the gap

to 0.5 mm, the molten copolymer was trimmed off to give smooth-edged surfaces and the appropriate cylindrical sample form.

The first experiment involved determining the strain in the linear viscoelastic region at a frequency of 1 Hz (6.28 rad/s) by a strain sweep (range 0.1-100%). Fig. 1 shows the strain dependence of the storage ( $G'$ ) and loss moduli ( $G''$ ) of the PLC at  $150^\circ\text{C}$  with a frequency of 1 Hz by a strain sweep experiment. PLC has a long linear viscoelastic region with a critical strain ( $\gamma_c$ ) of about 46% due to a lack of interaction and a delicate microstructure which is susceptible to large strain. The range of linear viscoelasticity independent of strain extends up to a critical strain level of 46% strain, beyond which the behavior became nonlinear and the moduli decreased due to the polymer chains being broken at high deformation.

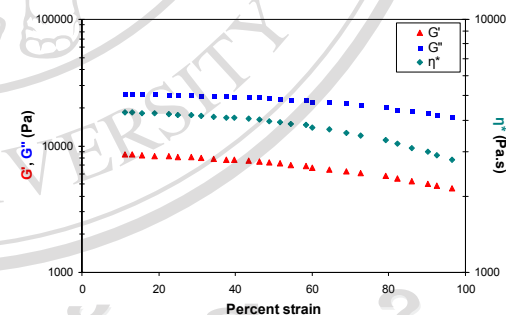


Figure 1. Strain dependence of  $G'$  and  $G''$  and complex viscosity ( $\eta^*$ ) of PLC at  $150^\circ\text{C}$  and a frequency of 1 Hz.

The frequency dependences of  $G'$  and  $G''$  measured within the frequency range of 0.628 to 628 rad/s with a 5% strain at various temperatures (30 to  $170^\circ\text{C}$ ) were used to construct a master curve representing a broad-range frequency dependence of these quantities.

The master curve showing the frequency dependence of  $G'$  and  $G''$  for PLC at a reference temperature ( $T_0$ ) of  $150^\circ\text{C}$  is shown in Fig. 2.  $G'$  and  $G''$  are frequency dependent and, by increasing the frequency, both moduli increase. At low frequency, the PLC shows predominantly viscous properties ( $G'' > G'$ ). By increasing the frequency,  $G'$  increases faster than  $G''$  so that the  $G'$  curve crosses the  $G''$  curve at a frequency called the “crossover frequency” ( $\omega_c$ ). At frequencies higher than  $\omega_c$ , the  $G'$  prevails over  $G''$  and the sample is predominantly elastic. The polymer melt displays a high degree of elasticity with  $G'$  only weakly dependent on frequency and greater than  $G''$  over the rubbery plateau region. The curve for  $G'$  indicates that the copolymer melt has a high rigidity and elasticity at high frequency. If the width of the rubbery plateau region increases, so does the elasticity of the copolymer. In the terminal region where flow is dominant,  $G'$  drops rather rapidly and  $G'$  and  $G''$  are proportional to  $\omega^2$  and  $\omega$  respectively.

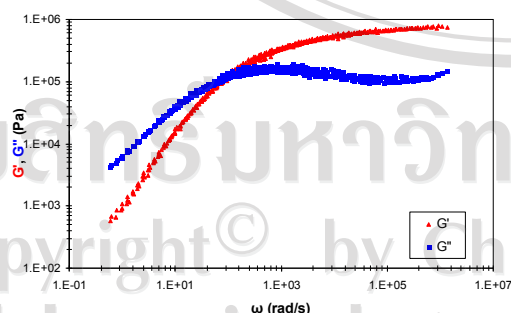


Figure 2. Master curve showing  $G'$  and  $G''$  of PLC at a reference temperature of  $150^\circ\text{C}$ .

Due to the amorphous nature of the PLC 50:50 copolymer, it is difficult to determine the melt flow temperature for use in melt extrusion. A frequency

sweep was therefore performed to determine the temperature at which the PLC melted and flowed homogeneously.

A comparison of the master curves at reference temperatures of  $130$  and  $140^\circ\text{C}$  is shown in Fig. 3(a). Both  $G'$  and  $G''$  at these reference temperatures in the rubbery plateau region are quite similar as the moduli in this region are not a function of temperature but depended on molecular weight and polymer chain length. In the terminal region, the effect of temperature on the moduli increases. The moduli at  $T_0 = 130^\circ\text{C}$  are higher than at  $T_0 = 140^\circ\text{C}$ . At reference temperatures of  $140$  and  $150^\circ\text{C}$ , as shown in Fig. 3(b), the curves of  $G'$  and  $G''$  are quite similar, especially in the terminal zone. PLC melts and flows approximately homogeneously in the temperature range of  $140$ - $150^\circ\text{C}$ . This data is applied to determine the most appropriate temperature for preparing a polymer rod in order to avoid air bubbles and void formation during melt extrusion.

To observe the rheological changes in the PLC copolymer during a temperature ramp of  $10^\circ\text{C}/\text{min}$ , a strain of  $5\%$  at a frequency of  $1$  Hz were used.

The temperature dependences of  $G'$ ,  $G''$ , loss factor ( $\tan \delta$ ) and complex viscosity ( $\eta^*$ ) are shown in Fig. 4. The PLC melt exhibited a transition from a solid-like to a liquid-like state at the crossover of  $G'$  and  $G''$  at  $83^\circ\text{C}$ . At the temperatures below  $83^\circ\text{C}$ , the value of  $G'$  is greater than  $G''$  so that PLC behaves like a solid. In contrast, when  $G''$  is higher than  $G'$  and  $G'$  drops dramatically, the PLC exhibits liquid-like properties at higher temperature above  $83^\circ\text{C}$ . In the terminal region,  $G'$  and  $G''$  generally decrease linearly ( $G'$

$\alpha \omega^2$  and  $G'' \propto \omega$ ). However, in this work, at temperature above 160°C, the variation in both moduli deviated from linearity due to thermal degradation. Thus, the experimental data was applied over the range of extrusion temperature of 83-150°C.

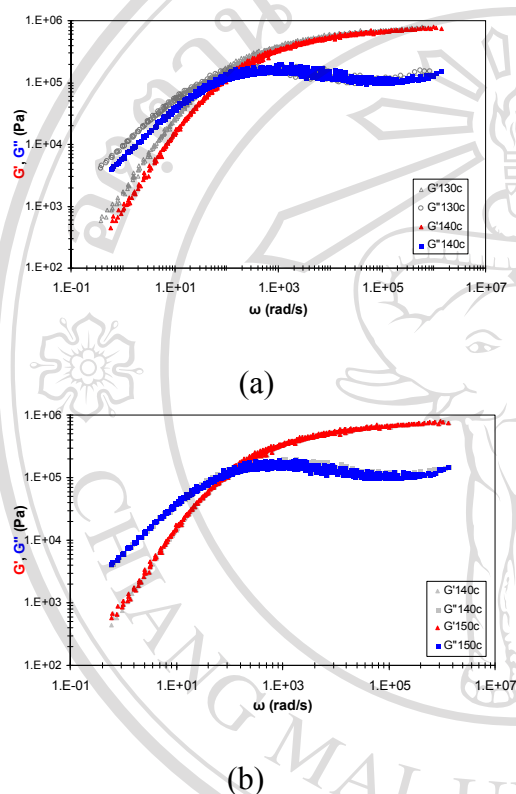


Figure 3. Comparison of the master curves at reference temperatures of (a) 130 and 140°C and (b) 140 and 150°C.

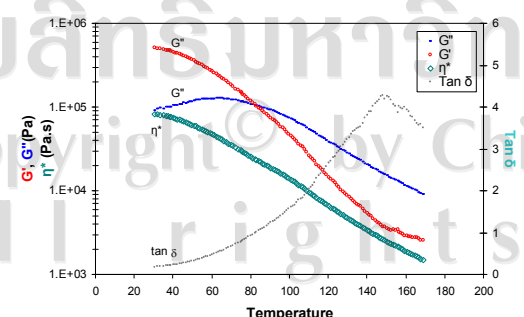


Figure 4. Temperature dependence of  $G'$ ,  $G''$ ,  $\tan \delta$  and  $\eta^*$  of PLC.

### Steady Shear Mode.

Measurements of shear viscosity ( $\eta$ ) as a function of shear rate were made by operating the parallel plate Bohlin Gemini HR<sup>nano</sup> Rotational Rheometer (plate diameter: 25 mm, gap: 0.3 mm) in steady shear mode during which the shear rate was varied between 0.01 and 10 s<sup>-1</sup>. The shear viscosity at shear rate ranging from 10 to 10,000 s<sup>-1</sup> was measured on a two-bore Rosand Capillary Rheometer. The flow behavior of PLC at 150°C, as shown in Fig. 5, is typically pseudoplastic with a well-developed Newtonian plateau region that extends up to a critical shear rate from which the viscosity is observed to decrease. The shear viscosity at low shear rate is essentially independent of the shear rate which indicates a lack of chain entanglement; thus the viscous fluid behaves as a Newtonian fluid. However, in the range of shear rate of 10-10,000 s<sup>-1</sup>, the polymer melt exhibits a straight line relationship between viscosity and shear rate in accordance with the Power Law. From the Newtonian region, a Newtonian viscosity ( $\eta_0$ ) was calculated by fitting with the Cross and Power Law Equations and extrapolating to zero shear rate. PLC at 150°C had a Newtonian viscosity ( $\eta_0$ ) of 4,085 Pa.s, a consistency index ( $k$ ) of 0.11 and a Power Law index of 0.30. At high shear rate (over 10 s<sup>-1</sup>), it can be seen that the shear viscosity decreases with increasing shear rate.



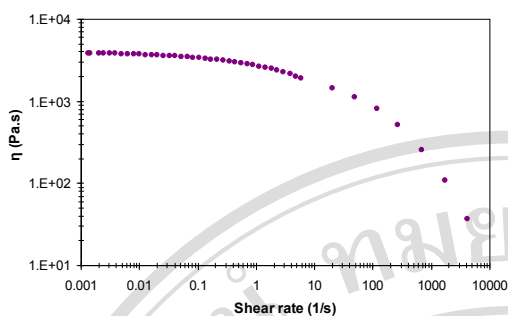


Figure 5. Shear viscosity of PLC at 150°C as a function of shear rate.

**Conclusions.** The rheology test results have shown that PLC exhibits pseudoplastic behavior but that the Cox-Merz Rule is not obeyed. PLC melts are likely to have certain microstructures that respond differently upon the application of steady and dynamic shears. Dynamic shear may be able to reveal the shear-thinning potential of materials but it does not alter the structure of the materials if applied within the linear viscoelastic region. In contrast, steady shear can effectively rearrange the molecular packing of materials along the shear direction.

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### References:

- [1] Valentini R.F., Aebischer P. in Lanza R., Langer R.P. and Click W., ed., *Principles of Tissue Engineering*, Academic Press Inc., **1997**.
- [2] Meek M.F. and Coert J.H., *J. Reconstr. Microsurg.* **2002**, *18*: 97.
- [3] Luis A.L., Rodrigues J.M., Lobato J.V., Lopes M.A., Amado S., Veloso A.P., Armada-da-Silva P.A.S., Raimondo S., Geuna S., Ferreira A.J., Varejao A.S.P., Santos J.D., Mauricio A.C. *Bio-Med Mater Eng* **2007**, *17*(1), 39.
- [4] Jansen K., Meek, M.F., van der Werff, J.F. A., van Wachem, P.B., van L., Marja J.A. *J. Biomed Mater Res A* **2006**, *77A*(2), 436.
- [5] Punyodom W., Molloy R., Nalampang K., Kamcharoen C., Waraegsiri B., Sananpanich K. and Pleumsamran A., *Chiang Mai J. Sci* **2005**, *32*: 479.
- [6] Kanev D., Takach E., Vlachopoulos J., *Polymer Processing XXII*, **2007**, *5*, 395
- [7] Dorgan J.R., Janzen J., Clayton M.P., Hait S.B., Kanuss D.M., *J. Rheo.*, **2005**, *49*(3), 607.
- [8] Jiang L., Wolcott M.P. and Zhang J., *Biomacromolecules*, **2006**, *7*, 199
- [9] Yamamoto M., et al., "Chapter 11 Biodegradable Aliphatic-Aromatic Polyester: Ecoflex®", in *Biopolymers*, Vol. 4, Doi Y and Steinbuechel, A. (Eds.), Wiley-VCH, Weinheim, Germany, p. 299-314, **2002**.

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**Conferences** :

1. **Booncharoen Wathuka**, Punyodom Winita, Molloy Robert and Nalampang Kanarat, *"Influence of Synthesis Scale on the Reaction Profile in the Bulk Copolymerization of L-lactide and  $\epsilon$ -Caprolactone"*, **The 5th PERCH Annual Scientific Congress (PERCH-CIC CONGRESS V)**, Pattaya, Chonburi, Thailand (2007).
2. **Booncharoen Wathuka**, Punyodom Winita, Molloy Robert and Nalampang Kanarat, *"Influence of Synthesis Scale on the Reaction Profile in the Bulk*

*Copolymerization of L-lactide and  $\epsilon$ -Caprolactone*”, **The 2<sup>nd</sup> International Conference on Advances in Petrochemicals and Polymers (ICAPP 2007)**, June 25<sup>th</sup>-28<sup>th</sup> 2007, Bangkok.

3. W. Punyodom, R. Molloy, T. Wongchanapiboon, B. Thapsukhon, **W. Booncharoen**, C. Saeheng, P. Teerawonganan, K. Sanapanich, A. Pleunsamran, V. Chaisukasant, A. Fuogfuchar and P. Supaphol. “*Fabrication of Biodegradable Polyester Conduits for Use as Absorbable Nerve Guides*”, **42<sup>nd</sup> International Symposium on Macromolecules (MACRO 2008)**, Taipei, Taiwan (29 June – 4 July 2008).
4. C. Saeheng, W. Punyodom, R. Molloy, **W. Booncharoen** and A. Fuongfuchat, “*Rheological Evaluation of Poly(L-lactide-co-caprolactone)*”, **42<sup>nd</sup> International Symposium on Macromolecules (MACRO 2008)**, Taipei, Taiwan (29 June – 4 July 2008).

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