CHAPTER 4

CONCLUSIONS

Bulk polymerization is one of the well-known processes for the production of polyesters via ring-opening of cyclic ester monomers. This type of polymerization has the advantages that very high molecular weights can be obtained, provided that the temperatures of polymerization and reaction conditions are well chosen. Moreover, less degradation products are produced during polymerization and avoid using the solvent. There are some disadvantages such as difficult and expensive to polymerize in a large batches, heat evolved during the reaction is difficult to eliminate, difficult to control the reaction due to the exothermically reaction and the resulting polymer always takes the shape of the reactor in which it is produced because it crystallized / solidified during the reaction.

Scale-up of the synthesis and processing operations is a necessary precursor to potential commercial development. Most literature reports 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"*.

In this research project, the PLC 50:50 mole% was synthesized by ROP in bulk using $SnOct_2$ and 1-hexanol as the initiating system. The influence of synthesis scale up (25 g, 250 g and 500 g) on the reaction profile in the bulk copolymerization of L-lactide and ε-caprolactone was investigated. Furthermore, the choice of reaction

conditions such as reaction temperature, reaction time and initiator concentration has a profound effect on the reaction profile and the properties of the final product. The structure and properties of the resulting polymers were characterized by a combination of analytical technique: spectroscopic methods (^{1}H-NMR and ^{13}C-NMR), molecular weight methods (GPC and dilute-solution viscometry), thermal analysis (DSC and TG), mechanical properties analysis (tensile testing and DMA) and rheological measurements. Moreover, PLC copolymer film and tube were processed by solvent casting, dip-coating and melt extrusion techniques for use as absorbable nerve guide.

Most of the results presented in the preceding Chapter 3 have already been summarized and divided up under the following topics.

- Synthesis of PLC 50:50 mole% copolymers in small scale (25 g)

- Synthesis of PLC 50:50 mole% copolymers in medium scale (250 g)

- Synthesis of PLC 50:50 mole% copolymers in large scale (500 g)

4.1 Synthesis of PLC 50:50 mole% copolymers in small scale (25 g)

The PLC copolymers in small scale (25 g) were synthesized by the ROP in bulk using SnOct$_2$ as a catalyst and 1-hexanol as an initiator. The reactions were carried out in the 50 ml round-bottomed flask. The influence of the reaction conditions such as the reaction time, the reaction temperature and the monomer to initiator molar ratio ([M]:[I]) on the copolymer properties (% yield, copolymer composition and microstructure, molecular weight, morphology and thermal properties) were investigated.

From the results obtained, the suitable reaction conditions that gave a high % yield ($\approx 90\%$), high molecular weight ($\overline{M}_w \approx$ 50,000-100,000) and a copolymer composition close to that of the comonomer feed ratio were 0.1 mole% $SnOct_2$ catalyst and 0.01 mole% 1-hexanol initiator at 120°C for 48 hours. The ^{1}H-NMR and ^{13}C-NMR results also confirmed that in the copolymer chain microstructure consist of both L-lactide unit and ε-caprolactone unit. The ^{13}C-NMR, carbonyl carbon region between 168-175 ppm provides valuable information about the sequence distribution of the caproyl (*C*) and lactidyl (*L*) units in the copolymer chains. Since the spectra of the PLC copolymers show not only peaks due to the *LLL* and *CCC* sequences but also intermediate peaks due to *CCL, LCL, CLL, LLC* and *CLC* sequences, it confirms that copolymerization has indeed occurred. It is relevant to note that all of the synthesized copolymers here are random, as evidenced by their ^{13}C-NMR spectra, but with some blocky character as reflected in their low degrees of randomness (*R*) and transesterification coefficients ($T_{(II)}$). Hence, the PLC copolymers were taper microstructure. 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 that confirmed by peak at $\delta = 170.9$ ppm from ^{13}C-NMR technique. Thus, transesterification plays an important role in the redistribution of monomer sequences, thereby influencing the microstructure. The morphology of the PLC copolymer product at 48 hours was amorphous as deduced from absence of T_m in DSC measurement. The predicted T_g values of the PLC copolymer from Fox Equation is approximately -5.1°C. The PLC copolymer had a tensile strength of 15.9±2.5 MPa, a

strain at break of 810±54.7% and Young's modulus of 14.4±1.9 MPa that present soft and tough material.

The reaction time required depends on the reactivity of the monomers. As we already known that the reactivity of L-lactide is higher than that of ε-caprolactone. At the initial period of the reaction times, the PLC copolymer is semi-crystalline with T_m = 139-147°C and this subsequently decreased as the ε-caprolactone content increased with increasing reaction time. The peak at δ = 2.6 and 4.2 ppm from ^{1}H-NMR spectrum that corresponding to ε-caprolactone monomers were confirmed that the ε-caprolactone was remaining in the reaction during the initial period of polymerization.

The %yield and molecular weight of the PLC copolymer both increase with the reaction time and the reaction temperature. However, at the longer reaction times (> 72 hours) and the higher reaction temperatures (> 120°C), the molecular weight of PLC copolymer began to decrease, as a result of transesterification reaction.

Furthermore, the PLC average molecular weight and %yield increased as the initiator (1-hexanol) concentration decreased. The weight-average molecular weight ($\overline{M}_w$) could be controlled in the range of $\overline{M}_w$ = 4.5x10^4 – 8.4x10^4 g mol^{-1} by varying [M]:[I] ratio. The result indicated that hydroxyl-containing compounds (e.g. alcohol) are real initiator, which can stoichiometrically control the molecular weight of the polymer. Excess alcohols act as a transesterification agent and caused a drop in the average molecular weight. These results are conformed to both of the mechanistic pathways proposed by Kricheldorf *et al.* [31, 33] and Penczek *et al.* [32, 34-35] as described in section 1.6.

4.2 Synthesis of PLC 50:50 mole% copolymers in medium scale (250 g)

The PLC copolymers in medium scale (250 g) were synthesized by ROP in bulk using 0.1 mole% $SnOct_2$ as a catalyst and 0.01 mole% 1-hexanol as an initiator at 120°C. The reactions were carried out in the 250 ml flat-flange flask. The effects of the reaction time between 2 and 121 hours on the %yield, copolymer composition and molecular weight of the PLC copolymer were studied. From the results obtained the % yield and molecular weight of the copolymer both increase with the reaction time. This is similar to the polymerizations of PLC copolymer in the small scale (25 g). However, both %yield and molecular weight of PLC copolymers in the medium scale is lower than that of the PLC copolymers in the small scale synthesis under the same conditions. It is possible that the problems associated with heat transfer as the mass-to-volume ratio increases resulting in increased temperature variations and transesterification reaction. The most suitable reaction time that gave a high %yield (94%), high molecular weight ($\overline{M}_w = 48,000$) 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.

The PLC 50:50 mole% copolymer was synthesized by ROP in bulk at 120°C for 96 hours using 0.1 mole% $SnOct_2$ as a catalyst and 0.01 mole% 1-hexanol as initiator for use as absorbable nerve guide. The tensile mechanical properties of PLC films had stress at break was 16.3±2.3 MPa, strain at break was 807±18.5 % and Young's modulus was 11.6±2.2 MPa. These results meant PLC films were elastic polymer. Furthermore, from DMA technique, the PLC copolymer has a glass

transition temperature (T_g) at -6.3°. The rheological properties of PLC at 150°C is a long linear viscoelastic region in range 0-46%. 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. From the master curve can be confirmed that the PLC copolymer was elastic polymer and PLC melted and flowed approximately homogeneously in the temperature range of 140-150°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 process. Moreover, from temperature sweep data, the PLC melt exhibited a transition from a solid-like to a liquid-like state at 83°C and the thermal degradation was above 160°C. Thus, the range of extrusion temperature was 83-150°C.

The PLC copolymer has been fabricated into small tubes by using 2 techniques: dip-coating and melt-extrusion. Transparent rubber-like tubes with an internal diameter of 1.2 mm and a wall thickness of 0.3-0.4 mm have been produced by dip-coating which, although rather laborious and time-consuming, yielded tubes of uniform controllable dimensions but of limited length. Transparent elastic tubes with an internal diameter and wall thickness of 0.7 mm and 0.2 mm respectively were also produced using melt extrusion. 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.

4.3 Synthesis of PLC 50:50 mole% copolymers in large scale synthesis (500 g)

For the largest scale synthesis (500 g), the PLC copolymers were synthesized by the ROP in bulk using $SnOct_2$ as a catalyst and 1-hexanol as an initiator. The reactions were carried out in the 1000 ml Parr Reactor. The conditions of reaction were studied as shown below:

Batch 1 : 120°C and 96 hours

Batch 2 : 120°C and 48 hours

Batch 3 : 100°C and 72 hours

Batch 4 : 120°C and 6 hours followed by 100°C and 18 hours

Batch 5 : 120°C and 6 hours, 9 hours and 24 hours

The PLC copolymer products were decomposed when using longer reaction time in Batch 1 and 2 because of the leading to transesterification reaction. This is due to the problems associated with heat transfer as the mass-to-volume ratio increases resulting in increased temperature variations during 110°C to 160°C. The transesterification occurred at temperature higher than 130°C. However, when the reaction temperature decrease to 100°C (batch 3), the polymerization reaction cannot occur.

Batch 4, the copolymer product is opaque brittle solid after polymerization occurred for 6 hours at 120°C because of LL content in the copolymer composition is higher than CL content (LL:CL = 78.1 : 29.9 mol%). After decreasing the reaction temperature to 100°C for 18 hours, the copolymer product became transparent flexible solid and copolymer composition close to that of the comonomer feed ratio

(LL:CL = 51.8 : 48.2 mol%). When increasing the reaction time from 6 to 18 hours, both of a %yield (from 72% to 88%) and the intrinsic viscosity ([η] from 0.16 to 0.33 dl/g) were increased due to the higher molecular weight of PLC copolymer was produced.

Batch 5, when increasing the reaction time from 6 to 9 hours, both of a %yield (from 74% to 88%) and the intrinsic viscosity ([η] from 0.61 to 0.99 dl/g), were increased and copolymer composition close to that of the monomer feed ratio. However, with longer reaction time, both of a %yield (33%) and the intrinsic viscosity ([η] = 0.32 dl/g), were decreased and the copolymer product became pale yellow transparent solid due to transesterification reaction occurred. These results suggest that the reaction temperature and time are very important for the polymerization reactions.

It can be concluded that in the largest scale synthesis, synthesis and purification of the resulting copolymer is troublesome because of the increased mass of the solid product leading to difficulties in removing the product from the reactor. Moreover, the polymerization reaction is exothermic and heat transfer became a problem, especially as the melt viscosity increases and the PLC copolymer products also decompose at higher reaction temperatures (> 130°C) and longer reaction times (> 24 hours). From the results obtained in largest scale synthesis, the most suitable conditions that gave a transparent flexible solid, high %yield (88%), high molecular weight ($\overline{M}_w \approx 280000$) and a copolymer composition close to that of the comonomer feed ratio was 120°C for 9 hours.

The bulk polymerization presented major problems when performed on a large scale as the reaction mass solidify during the polymerization. It was not possible to carry out the reaction in stirred reactors. The copolymer product difficult to removing from the reactor because of the reaction products takes on the shape of the inner wall of the reactor and has to be removed from the reactor as a compact block. Thus, as the reaction mixtures are scaled up, ever larger blocks of material are produced. A further difficulty is the removal of the heat of the reaction. As the polymerization reactions are strongly exothermic, and moreover the polymer mass formed has very poor heat conductivity, in larger reactors temperature gradients may be formed which give rise to serious and unacceptable inhomogeneities in the product. These inhomogeneities may take the form of different molecular weights and in the case of PLC copolymers, in different molar compositions. The effect of the generation of heat during polymerization is schematically given in Figure 4.1.
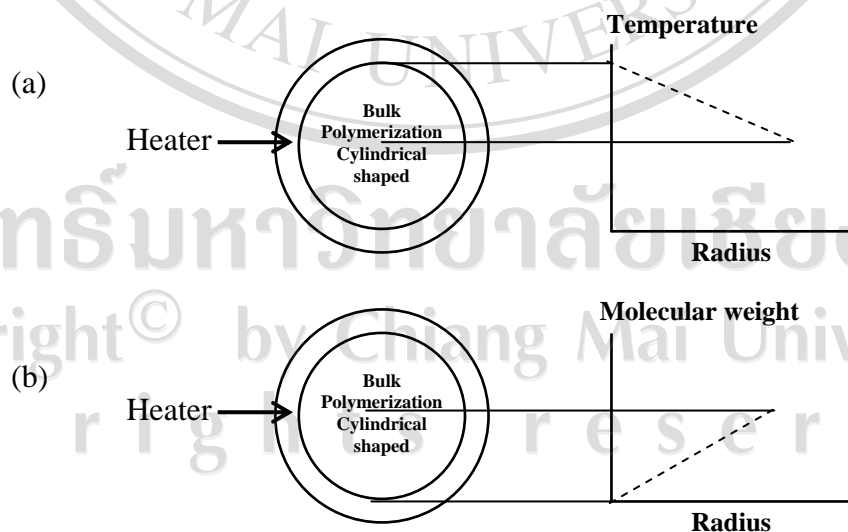

Figure 4.1 Schematic representation of (a) the effect of radius on temperature and

(b) the effect of radius on molecular weight.

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Figure 4.1 represented a bulk polymerization in a cylindrical reactor. At center of the reactor the temperature will be nearly the same temperature as the thermocouple, for instance the heat maintained at 120°C. Going from the outside wall to the inside of the reacting mixture, the temperature will decline due to the poor heat transfer. Under normal conditions, the increasing of the temperature is approximately 20 - 40°C. The molecular weight decrease from the inside to the outside is presented in the same Figure. This problem is self-evident. The PLC copolymers can exhibit brown color exteriors and fully white color interiors at 120°C for 48 and 96 hours. The brown color of the exteriors is due to the longer reaction time leading to the degradation of polymer and side reactions such as trasesterification reaction. Thus, the 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 conditions.

The reactions are preferably carried out isothermically. In some case, however, it is advantageous to start at lower temperature in order to avoid strongly exothermic reactions, and to raise the temperature as the reaction proceeds in order to increase the speed of reaction of the monomers. Moreover, the reaction temperatures should be lower than the ceiling temperature, the temperature above which no polymerization will occur or, in other words, no polymer will be formed. In this research project, the suitable reaction temperature was 120°C. However, it can be seen that either the decreasing the reaction temperature (100°C) or increasing the activation energy will result in a decrease in rate of reaction, in addition polymerization cannot occur.

The copolymer product difficult to removing from the reactor because of the reaction products takes on the shape of the inner wall of the reactor and has to be

removed from the reactor as a compact block. Thus, as the reaction mixtures are scaled up, ever larger blocks of material are produced. A further difficulty is the amorphous polymers tend to be stickier than crystalline and thus remove from the reactor proves more difficult. The handling and also subsequent grinding up into workable granules therefore becomes impossible upwards of a certain order of magnitude.

In the literature [53, 59] related to a process for preparing resorbable polyesters by bulk polymerization, while the reaction components are melted and homogenized in a stirred reactor, then the reaction mixture is converted into a plurality of smaller-capacity containers, *e.g.* plastic bottles, the reaction mixture is polymerized in these containers and the polyester obtained is isolated by removing it from the containers.

In overall conclusions, a small scale the method is simple; the processing and purification of the resulting polymer could be done by common methods. On a large scale the processing and purification of the resulting polymer is troublesome as follow:

- the reaction mass solidify during the polymerization.
- the polymer mass formed has very poor heat conductivity.
- the polymer product difficult to removing from the reactor.
- inhomogeneities in the product due to temperature gradient.
- different molecular weights and different molar compositions for copolymer.

In conclusion, the scale-up plays an important role in the final outcome of the process.

SUGGESTIONS FOR FURTHER WORK

Continuing on the work described in this research project, the following suggestions for further work are made as following:

1. Monomer Synthesis

The purity of the monomers and initiator is very important for the end result of the polymerization. The deliberate contamination with impurity, for example water and free acid, caused the molecular weight of the resulting polymer to decrease. Thus, the monomers and initiator should not contain any impurities that initiate additional chains or hinder the build up of chains by forming non-reactive end-groups.

2. Polymer Synthesis

In this work, the PLC copolymers were synthesized via ROP in bulk, mainly in order to scale-up of synthesis which is a necessary precursor to potential commercial development. For small scale the method is simple; the synthesis and purification of the resulting polymer could be done by common methods. On a large scale (500 g) using the 1000 ml Parr Reactor is troublesome; the main problem is the reaction mass solidify during the polymerization. A further difficulty is the removal of the heat of reaction. As these polymerization reactions are strongly exothermic, and moreover the polymer mass formed has very poor heat conductivity, in larger reactors temperature gradients may be formed which give rise to serious and unacceptable inhomogeneities product. These products may take the form of different

molecular weights and, in case of copolymers, in different molar compositions. Consequently, further work should therefore focus in attention as following:

- Study the polymerization of homopolymer in order to avoid the effect of the monomer reactivity. ε-Caprolactone monomer should be used in the further work because of low costs and easy to bring poly(ε-caprolactone) products out of the reactor.

- The reaction components should be melted and homogenized in a stirred reactor and the reaction mixture is then transferred into a number of smaller plastic bottles and continued polymerization in the plastic bottles. After polymerization and cooling in the air, the bottle necks are cut of and the polymer is easily removed. [53, 59]

- The polymer may be obtained by polymerizing the reaction mixture in a tubular reactor. The shape of the reactor is tapered so that upon shrinkage of the resulting polymer, the polymer is released and can be removed from the reactor. Furthermore, the diameter of the tubular reactor should be 3 cm or smaller in order to prevent discoloration of the polymer. [85]

- During polymerization, the resulting polymer should be taken from different positions of the reactor and characterized. Moreover, the consistency of each sample should be determined to detect variations in the polymer delivered.

- Adjustments in the paddle stirrer should be targeted to solving the inhomogeneities of the polymer products problem, for example, a flat-paddle stirrer.

- Study the kinetic of the solution polymerization that may be easily to sampling the polymer from the Parr Reactor Instrument by using the liquid sampling valve.

3. Thermal Properties

The polymers should be treated in the same conditions before DSC characterization in order to get rid of the effect of their thermal history. The most useful methods for determining the thermal analysis background of the various transitions in polymers and relaxation process is DMA technique. Moreover, the greater sensitivity of the DMA to measure T_g's undetectable by the DSC technique.

3. Melt-extrusion technique

The PLC small tubes obtained from melt-extrusion technique were of reasonable quality, they still exhibited certain defects such as (1) non-uniformity in diameter and (2) internal voids. These defects may result from (a) non-uniform melt flow (rheology) through the tubular shaped-die, and/or (b) residue traces of solvent/non-solvent from the purification procedure. Design the tubular shaped-die and adjust the extrusion/take-up speeds may improve the uniform in diameter.