Synthesis and characterization of poly (D,L-lactide-co-ε-caprolactone) for application in Tendon/Ligament Tissue Engineering

* *Wahida Abdul Rahman[1], Jean-Luc Six[2] and Cécile Nouvel[2]*

[1] Faculty of Applied Sciences, UiTM Perlis, 02600 Arau, Perlis, [2]Ecole Nationale Supérieure Industries Chimiques (ENSIC), 54000 Nancy, France.

wahida811@perlis.uitm.edu.my

Abstract:

In this research, copolymers of poly (D,L-lactide-co-ε-caprolactone) (PLCL) with 50:50 feed ratio were synthesized by the coordination-insertion ring opening polymerization (ROP) of cyclic esters at different temperature (130 ^{0}C, 150 ^{0}C and 200 ^{0}C). Both Sn(II)octoate ($SnOct_2$) and isopropanol (iPrOH) were used as catalyst and initiator respectively and polymerization reaction were took part from 24 hours until 1 week. The conversion of monomer D,L-lactide and ε-caprolactone, polydispersity index (PDI) and total average molecular weight of copolymer PLCL can be determined by proton nuclear magnetic resonance (^{1}H-NMR) and size exclusion chromatography coupled multi-angle laser light scattering (SEC-MALLS). Both analyses showed the increasing trend as the reaction temperature increased. The average sequence lengths of the lactidyl units (l^e_{LL}) and caproyl (l^e_{cap}) units, the degree of randomness (R) and the transesterification coefficients (T_I and T_{II}) were calculated from the ^{13}C-NMR spectra. The average sequence lengths showed the decreasing trends, meanwhile there were small significant value increased for degree of randomness and transesterification coefficients when reaction temperature increased from 130 ^{0}C to 200 ^{0}C. The fabricated PLCL copolymers have a potential to be transformed into three dimensional scaffold for application in tendon/ligament tissue engineering.

Keywords: coordination-insertion ring opening polymerization, transesterification, average sequence length, degree of randomness

Introduction

Accident and diseases lead to devastating tissue loses and organ failures, which resulted in more than 8 million surgical operations each year (Vacanti & Langer, 1999). Organ transplantation became successful in the early 1960s, however this approach is severely limited by the death of donor organs. Nowadays, tissue engineering is a new approach to resolve all the problems that discussed above. Tissue engineering approach for ligaments and tendons repair requires the knowledge combination in biology, materials science, engineering, manufacturing and medicine (Burdick & Mauck, 2011). With tissue engineering approach, the ligaments and tendons can be generated by seeding adequate living cells onto a biodegradable polymer template (scaffold). This seeded scaffold will be put into a bioreactor, then the cells will proliferate through *in vitro* environment, differentiate, secrete their own extra cellular matrices and finally form a neo-tissue meanwhile the scaffold degrades (Figure 1) (Meyer et al., 2009). Among the other biodegradable polyesters such as polyglycolide (PGA), polyhydroxybutyrate (PHB) and polyhydroxyalkanoate (PHA), polylactide (PLA) and poly(ε-caprolactone) has been chosen as a starting material for fabrication biodegradable tissue due to their few advantages. PLA are semicrystalline polymer with 37 % crystalline value, and it is also classified as hard materials (modulus = 2.7 GPa) with a melting point around 180

^{0}C and glass transition temperature (T_g) of 60-65 ^{0}C. The T_g of PLA is above body temperature; hence, these materials are stiff with little elasticity in the body. The elongation at break of PLA is under 25%. PLA is completely resorbable material because it degrades and produces lactide acid, which is also a natural metabolite for our body (Albertsson & Varma, 2003). Other study by Albertsson & Varma (2003), also proofed that there was no significant amount of accumulation degradation products is observed in vital organs. Poly (ε-caprolactone) PCL is chosen to copolymerizes with PLA because it exhibits high toughness, very flexible and melt at 61 ^{0}C. It has low T_g which is below room temperature (-60 ^{0}C). PCL in the rubbery state has modulus of 0.4 GPa and an elongation at break around 300-400 %. This rubbery property makes it suitable for scaffold tissue fabrication by electrospinning method as this process requires material with high flexibility and less stiffness (Albertsson & Varma, 2003). Based on study by Jeong et al. (2004) showed that PLCL scaffolds exhibited an elongation of more than 200 % because of the softness and flexibility of its structure. Apart from that, the fabricated scaffold also showed a recovery of 98 % after 200 % elongation at break which is good for ligaments and tendons replacement tissue. The objective of this project is to synthesize the poly(D,L-lactide-co-ε-caprolactone) by ring opening polymerization reaction. Apart from that, an attempt has been made to study the effect of reaction temperature on monomer conversion and microstructure of fabricated PLCL copolymer using ^{1}H-NMR and ^{13}C-NMR as there are less focused in this area of research.

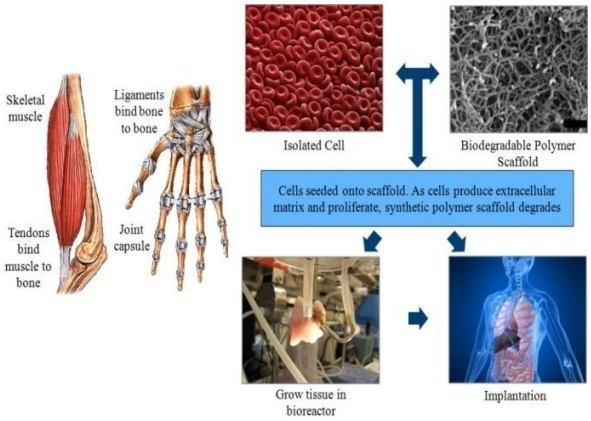

Figure 1: Principle of tissue engineering

Experimental

Preparation of materials

All glassware used in this experiment was dried and fire-heated under dynamic vacuum. All the experiments have been carried out under inert atmosphere, N_2. The solvent, which is toluene, was purified using distillation process and polystyrene lithium was added to purified toluene as an impurities tracking agent. D,L-lactide monomer (LA) (Alfa-Aesar) was recrystallized two times in purified toluene. ε-caprolactone monomer (CL) (Alfa-Aesar) was purified by freeze-drying over CaH_2 under nitrogen and dynamic vacuum. Stannous octoate ($SnOct_2$) 95 % (Sigma-Aldrich) and isopropanol (iPrOH) (Lancester) have been diluted by purified toluene solvent and were prepared according to desired concentration (Huang et al., 2004).

Synthesis of poly(D,L-lactide-co-ε-caprolactone)

All copolymers (Table 1-3) were synthesized by coordination-insertion ring-opening polymerizations (ROP) (Figure 2) in bulk from 24 hours until 1 week with (50 % LA : 50 % CL) (Veld et al., 1997). Three different reaction temperatures (130 ^{0}C, 150 ^{0}C and 200 ^{0}C) were used in these experiments in order to study its effect on the monomer conversion and microstructure of the fabricated PLCL copolymer. The molar ratio of [$SnOct_2$]/ [iPrOH] is 0.01 in all experiments. Polymerization started at the moment when $SnOct_2$ was added and stopped exactly on 1 week by using acidified ethanol. The obtained PLCL product was then precipitated using cold ethanol. After that, the PLCL was dried under vacuum at 40 ^{0}C over several days before proceed with characterization process (Baimark & Molloy, 2005; Nalampang et al., 2007).

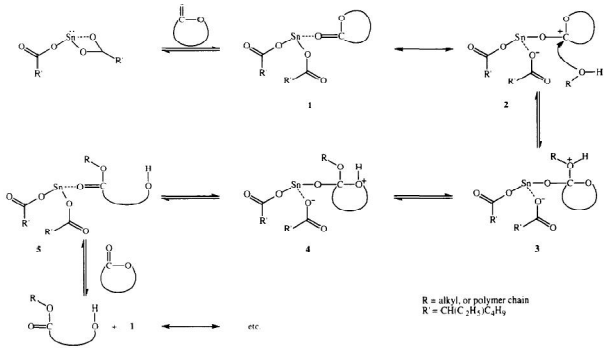

Figure 2: ROP of PLCL initiate by isopropanol and activated by $SnOct_2$ catalyst.

Characterization

Copolymers of poly (D,L-lactide-co-ε-caprolactone) were characterized using 300 MHz ^{1}H-NMR (nuclear magnetic resonance) Brucker Avance 300 in order to study its chemical composition and monomer conversion. Monomer average sequence lengths, degree of randomness and transesterification coefficients were determined using ^{13}C NMR. All proton and carbon NMR spectras were obtained from copolymer solutions in chloroform at room temperature. SEC-MALLS was performed by using a setting composed of Merck L6200 pump with the flow rate 0.7 mL/min and a degasser (Degazys DG 310, Uniflow). Columns used consisted of PLgel 5 µm 1000 Å and 100 Å, 300 x 75 mm and precolumn of PLgel 5 µm Guard, 500 x 7.5 mm. The samples have been prepared by solubilized in THF to get 3 mL of sample solution with concentration of 10 mg/mL for each samples. The average number of molecular weight (Mn) and polydispersity, PDI were determined through this method. The refractive index value (dn/dc) of PLA and PCL in THF are 0.054 and 0.074 (Gottlieb et al., 1997; Jeong et al., 2004).

Result and Discussion

^{1}H-NMR analysis

Chemical composition and monomer conversion

The ^{1}H-NMR spectrum of PLCL copolymer L (Figure 3) shows signals characteristic of lactidyl monomer unit at 1.53 ppm (CH_3, H^a), 5.15 ppm (CH, H^b). Proton of ε-caproyl units have also been observed at 1.38-1.65 ppm ($CH_2CH_2CH_2$, H^g, H^l, H^h H^f, H^m, H^k), 2.30 ppm (CH_2CO, H^n) and 4.10 ppm (CH_2O, H^e). Proton (CH_2O,$H^{e'}$) of CL monomer was observed at 4.35 ppm. Meanwhile there were no signals detected for proton (CH_2, $H^{i'}$, $H^{h'}$, $H^{g'}$, $H^{f'}$) because the percent of monomer CL inside this copolymer is too low. There was also no signal detected around 5.0 ppm for (CH, $H^{b'}$) and around 1.67 ppm (CH_3, $H^{a'}$) because all the LA monomer finished reacts with CL monomer. Signals characteristic to LA-CL junctions in PLCL copolymer were detected at 2.38 ppm (CH_2, H^i) and 4.05 ppm (CH_2, H^j) in the NMR spectrum (Garkhal et al., 2007). Other PLCL copolymer showed similar patterns like this ^{1}H-NMR spectrum except for variation in their intensity for each previously mentioned peaks. The peaks of CH_3 and CH_2 for ethanol were still observed at 1.25 ppm and 3.75 ppm (Gottlieb et al., 1997). The conversion of LA and CL comonomer in PLCL can be calculated by ^{1}H-NMR using equation (1) and (2) below and also refer to Figure 3 below (Nouvel, 2000).

Conversion for LA units;

$$X_{LA} = A_b/A_b+A_{b'} \quad (1)$$

Conversion for CL units;

$$X_{CL} = A_e+A_j/A_{e'}+A_e+A_j \quad (2)$$

Where, A_b = Area of peak H^b (lactidyl unit inside copolymer chain), $A_{b'}$ = Area of peak $H^{b'}$ (lactide monomer), A_e = Area of peak $H^{e'}$ (caprolactone monomer), $A_e + A_j$ = Area of peak ($H^e + H^j$) (caproyl unit inside copolymer chain).

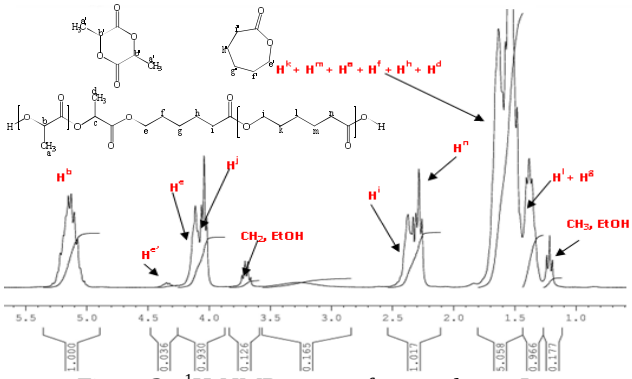

Figure 3 : ^{1}H-NMR spectra for copolymer L

Conversions for LA and CL for each experiment are summarized in Table 1-3. Based on Table 1-3 and Figure 4-5, conversion for LA in PLCL is relatively high (70-100 %) and this LA conversion increased as the reaction temperature increased from 130 ^{0}C to 200 ^{0}C. If we compared the CL conversion at temperature 130 ^{0}C, the overall conversion is relatively low (0-3.36 %) but the CL conversion started to increase until 96% as the reaction temperature increased to 200 ^{0}C. Apart from that, at same reaction temperature for example 130 ^{0}C, the LA conversion took place rapidly compare to CL conversion as the polymerization increased. This is due to the CL monomer reactivity itself. CL monomer needs a long time to homopolymerize compare to LA monomer. This is because LA monomer has higher reactivity compare with CL (Table 4) (Grijpma & Pennings, 1991). Based on Grijpma & Pennings (1991), one can concluded that when the r_{LA} » 1, r_{CL} « 1, the initial stage of the copolymerization monomer LA is incorporated faster and the copolymer is rich in monomer LA (Kricheldorf et al., 2000). When this monomer LA gets depleted, more monomer CL

units are added. According to Grijpma & Pennings (1991), the conversion for LA was almost ≥ 98 % after 24 hr of polymerization while the CL conversion was almost ≥ 98 % after the polymerization until 330 hours in bulk condition, however in our case the overall monomer conversion mainly influenced by the reaction temperature and polymerization time respectively.

Table 1: Monomer conversion and microstructure result of PLCL at 130 ^{0}C

CP	A	B	C	D
PT (day)	1	3	5	7
X_{LA} [a]	70	74	76	83.65
X_{CL} [b]	1.09	2.01	3.36	3.07
l^e_{LL} [c]	2.016	2.579	2.789	3.041
l^e_{Cap} [d]	0.082	0.095	1	1
$T_{(I)}$ [e]	0.325	0.435	0.566	0.878
$T_{(II)}$ [f]	0	0	0	0
R_{LL} [g]	0	0.009	0.011	0.003
Mn [h]	35960	39780	43530	48312
Mn [i]	18270	19370	22670	30120
PD [j]	1.01	1.01	1.02	1.03

Table 2: Monomer conversion and microstructure result of PLCL at 150 ^{0}C

CP	E	F	G	H
PT (day)	1	3	5	7
X_{LA} [a]	84.62	85.40	86.00	88.00
X_{CL} [b]	16.00	17.50	18.00	18.72
l^e_{LL} [c]	2.035	2.145	2.345	2.458
l^e_{Cap} [d]	1.367	1.454	1.589	1.589
$T_{(I)}$ [e]	0.389	0.546	0.667	0.718
$T_{(II)}$ [f]	0.000	0.000	0.000	0.000
R_{LL} [g]	0.025	0.027	0.031	0.027
Mn [h]	39834	42119	45389	55008
Mn [i]	18989	19456	22567	16780
PD [j]	1.02	1.01	1.02	1.03

Table 3: Monomer conversion and microstructure result of PLCL at 200 ^{0}C

CP	E	F	G	H
PT (day)	1	3	5	7
X_{LA} [a]	90.10	98.60	99.50	99.80
X_{CL} [b]	80.00	85.00	95.40	96.00
l^e_{LL} [c]	1.101	1.233	1.367	1.481
l^e_{Cap} [d]	1.998	2.090	2.110	2.117
$T_{(I)}$ [e]	0.234	0.323	0.551	0.556
$T_{(II)}$ [f]	0.000	0.000	0.000	0.000
R_{LL} [g]	0.198	0.220	0.221	0.228
Mn [h]	42678	65799	99367	101448
Mn [i]	13830	13899	14098	14080
PD [j]	1.02	1.00	1.10	1.10

Where; [a] Conversion of D,L-lactide determined by ^{1}H-NMR, [b] Conversion of ε-caprolactone determined by ^{1}H-NMR, [c] Number-average length of lactidyl unit by experiment, [d] Number-average length of caproyl unit by experiment, [e] Yield of transesterification (first mode), [f] Yield of transesterification (second mode), [g] Degree of randomness for lactidyl unit, [h]Total average molecular weight determined by theory, [i] Total average molecular weight determined by SEC, [j] Polydispersity index of copolymer obtained

Table 4: Reactivity ratio of LA and CL copolymerized with $SnOct_2$ at different temperature.

Polymerization Temperature (^{0}C)	Reactivity Ratio LA (r_{LA})	Reactivity Ratio CL (r_{CL})
80	57.10	0.39
110	42.00	0.36
130	34.70	0.24

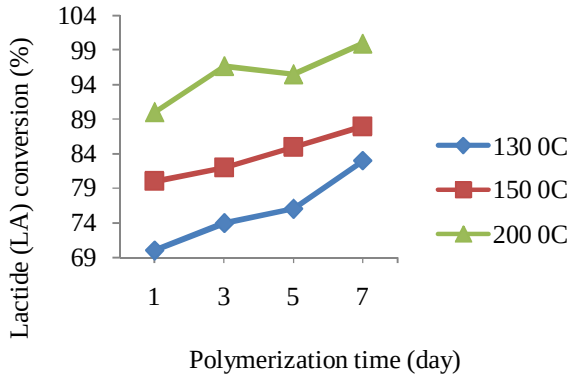

Figure 4 : Lactide (LA) monomer conversion (%) versus polymerization time (day)

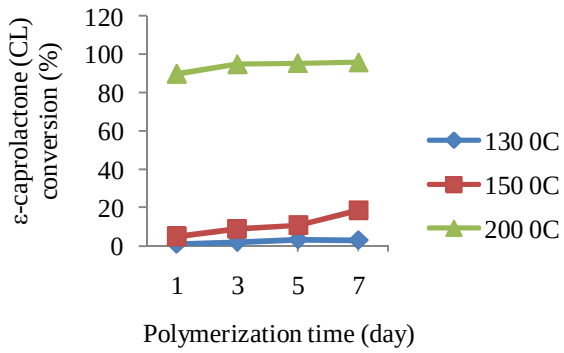

Figure 5 : ε-caprolactone (CL) monomer conversion (%) versus polymerization time (day)

Molar fraction determination

Molar fraction for LA unit (F_{LA}) and molar fraction for CL unit (F_{CL}) can be determined by the ^{1}H-NMR spectrum (Figure 3) after precipitation process. The molar fraction, F_{LA} and F_{CL} can be calculated by using equations (3-8) below (Nouvel, 2000):

Intensity of lactidyl unit (proton H^b) :

$$A_{CHLA} = A_{1H} \quad x \quad 2n_{LArepeating\ unit} \qquad (3)$$

Intensity of caproyl unit (proton $H^e + H^j$) :

$$A_{OCH2CL} = A_{1H} \quad x \quad 2 \quad x \quad n_{CLrepeating\ unit} \qquad (4)$$

Then,

Molar fraction of LA, $F_{LA,}$

$$F_{LA} = \frac{[LA]}{[LA] + [CL]} = \frac{A_{CHLA}/2A_{1H}}{A_{CHLA}/2A_{1H} + A_{OCH2CL}/2A_{1H}} \qquad (5)$$

$$F_{LA} = \frac{[LA]}{[LA] + [CL]} = \frac{A_{CHLA}}{A_{CHLA} + A_{OCH2CL}} \qquad (6)$$

Molar fraction of CL, $F_{CL,}$

$$F_{LA} = \frac{[CL]}{[LA] + [CL]} = \frac{A_{CH2CL}/2_{A1H}}{A_{CHLA}/2A_{1H} + A_{OCH2CL}/2A_{1H}} \qquad (7)$$

$$F_{LA} = \frac{[CL]}{[LA] + [CL]} = \frac{A_{OCH2CL}}{A_{CHLA} + A_{OCH2CL}} \qquad (8)$$

Where; A_{CHLA} = area of peak CH (H^b) (lactidyl unit inside copolymer chain), A_{OCH2CL}= area of peak CH_2 ($H^e + H^j$) (caproyl unit inside copolymer chain).

From the analysis of ^{1}H-NMR spectrum, we can conclude that molar fraction for LA unit is superior to the molar fraction for CL unit for copolymer D and H. Besides that, we should obtain the same result for the molar fraction in copolymer with the molar fraction in feed; unfortunately they are not the same. Only copolymer L has the same molar fraction in both cases (feed and copolymer). This proofed that, at reaction temperature = 200 ^{0}C, monomer CL and LA can polymerize at the same rate and produce molar fraction same as molar fraction in feed.

Table 5: Molar feed ratio of comonomer in PLCL at polymerization time = 7 days

Copolymer	D	H	L
Reaction temperature (^{0}C)	130	150	200
fLA : fε-CL[c]	50.10 : 49.90	49.00 : 51.00	48.71 : 51.29
FLA : Fε-CL[d]	96:4	81:19	52:48
FLA : Fε-CL[e]	96:4	82:18	50:50

Where; [k]Molar fraction ratio of comonomers in feed, [l] Molar fraction ratio of comonomers in the chain determined by ^{1}H-NMR, [m]Molar fraction of comonomer inside copolymer determined by theory

Size Exclusion Chromatography (SEC) analysis

Molecular weights of copolymers estimated by SEC are reported in Table 1-3. The polydispersity indexes (PDI) were lower than 1.2. The targeted total average molecular weight (M_n) of fabricated copolymer PLCL is 100,000 g/mol. This value was chosen because it will make the scaffold fabrication by electrospinning method become easy (Eda & Shivkumar, 2006). Unfortunately, as shown in Table 1-3, M_n was in the range of 13830-30120 g/mol by SEC. A significant difference does exist between M_n calculated by theory and M_n obtained by SEC (Figure 6-7). This phenomenon occurs because of a transesterification process. Transesterification process is the exchange reaction of groups between two esters, is a well-known process described in organic chemistry. Therefore,

during the copolymerization of PLCL, we always have to take the possibility of inter- and intra-molecular transesterifications into consideration, which affect the molecular weight of copolymer obtained. Although the degree of transesterification T_I is still low and T_{II} is negligible, we observed that there was existence of transesterification process affecting the total average molecular weight of copolymer obtained (Kasperczyk & Bero, 1993).

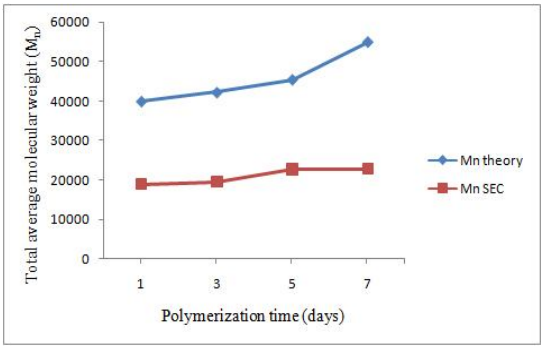

Figure 6 : Total average molecular weight (Mn) at temperature = 130 ^{0}C

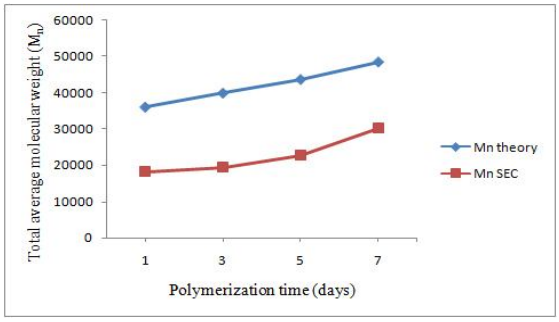

Figure 7 : Total average molecular weight (Mn) at temperature = 150 ^{0}C

^{13}C-NMR analysis

Chain microstructure and randomizing effects of transesterification reactions were studied by means of ^{13}C-NMR since this technique is very sensitive to monomer sequencing. All the values such as number average sequence lengths, degree of randomness and transesterification coefficients can be determined through this analysis. In particular, the carbonyl carbon signals (between 174 ppm and 169 ppm) are the most sensitive to the sequence distribution of the caproyl and lactidyl units (named Cap and LL) (Figure 8) (Nalampang et al., 2007; Baimark & Molloy, 2005).

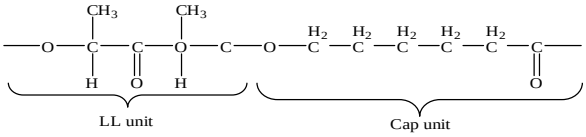

Figure 8: A chemical structure represents Cap = caproyl unit; LL = lactidyl unit.

The number average-lengths of the Cap and LL sequences were determined on the basis of the attribution of the peak in the ^{13}C-NMR spectrum, as previously described by (Kricheldorf et al., 2000; Karspercyzk & Bero, 1993). In addition, two types of transesterification reactions were discovered referred to as the first and second modes (Karspercyzk & Bero, 1993; Nalampang et al., 2007). In the first mode, there is a cleavage between one LL unit with another LL unit to obtain the formation without anomalous sequences of –CapLLCap–. While in the second mode, a LL unit undergoes bond cleavage leading to the formation of anomalous sequences of –CapLCap– and –CapLLLCap–, both with an odd number of half-lactidyl (L) units (Figure 9) (Karspercyzk & Bero, 1993; Nalampang et al., 2007).

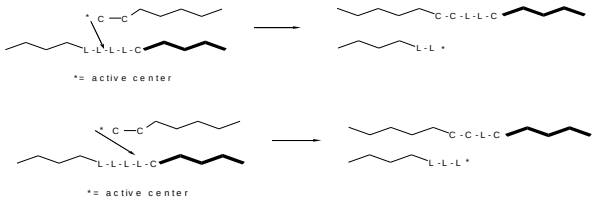

Figure 9 : First mode and second mode of transesterification.

Thus, transesterification plays an important role in the redistribution of monomer sequences, thereby influencing the microstructure. These odd number of L sequences cannot be formed by the opening of LA rings during the propagation. The yield of first mode transesterification can be calculated from the equation (9) below (Karspercyzk & Bero, 1993):

$$T_1 = \frac{l_{LL}^{\,r} - l_{LL}^{\,e}}{l_{LL}^{\,r} - l_{LL}^{\,T}} \quad \text{.....(9)}$$

With, $l_{LL}^{\,r}$ = the number-average length of lactidyl blocks calculated from the reactivity ratio of LA.

$$l_{LL}^{\,r} = 1 + r_{LA} * x \quad \text{.....(10)}$$

Here, we used the value of r_{LA} from Table 4 above. Value of x represents the ratio of [CL]/[LA], where [CL] and [LA] are the concentration of ε-caprolactone and lactide monomer inside feed. $l_{LL}^{\,e}$ is the experimental the number-average length of lactidyl blocks and we may express the number-average length of lactidyl blocks in completely random distribution, $l_{LL}^{\,T}$ by equation (11) below (Karspercyzk & Bero, 1993):

$$l_{LL}^{T} = (k + 1) / k \quad \ldots\ldots\ldots\ldots \qquad (11)$$

The value of k represents for the ratio of [Cap] / [LL], where [Cap] refer to the concentration of caproyl units and [LL] for lactidyl units in the copolymer chain.

Experimental number-average length of lactidyl and caproyl blocks may be calculated from the following equations (12) and (13) (Nalampang et al., 2007):

$$l^{e}_{LL} = 1/2 \left(\frac{I_{LLL} + (I_{LLCap} + I_{CapLL})/2}{I_{LLCap} + I_{CapLL})/2 + I_{CapLCap})} + 1 \right) \ldots\ldots (12)$$

$$l^{e}_{LL} = \frac{I_{CapCapCap} + I_{LCapCap} + 1}{I_{CapCapL} + I_{LCapL}} \quad \ldots\ldots\ldots \qquad (13)$$

Where, for example, $I_{CapCapCap}$ is the area of the peak attributed to CapCapCap triad (see Figure 11). The second mode of transesterification can be calculated from ^{13}C NMR spectrum by using equation below (Nalampang et al., 2007):

$$T_{II} = [CapLCap]/[CapLCap]_R \ldots\ldots\ldots\ldots\ldots\ldots (14)$$

Where, [CapLCap] = Experimental concentration of the CapLCap sequences determined from the ^{13}C-NMR spectrum. $[CapLCap]_R$ is theoretical concentration for completely random chains as calculated via Bernoullian statistics and can be calculated by using equation (15) below:

$$[CapLCap]_R = k^2 / (k + 1)^3 \ldots\ldots\ldots\ldots\ldots\ldots (15)$$

Where the k = [Cap]/[LL], which is the ratio of molar fraction CL monomer with LA monomer inside copolymer.

For comparison, the number-average lengths of the lactidyl and caproyl sequences in chains with a random distribution of units would be obtained by complete transesterification via the first and second modes. These sequences can be calculated from the following equations (16) and (17) (Nalampang et al., 2007):

$$l^{R}_{LL} = (k + 1)/2k \quad \ldots\ldots\ldots\ldots\ldots\ldots (16)$$

$$l^{R}_{Cap} = k + 1 \quad \ldots\ldots\ldots\ldots\ldots\ldots (17)$$

Consequently, the degree of randomness (R) of the copolymer chains is given by equations (18) and (19) below (Nalampang et al., 2007):

$$R_{LL} = l^{R}_{LL} / l^{e}_{LL} \quad \ldots\ldots\ldots\ldots\ldots\ldots (18)$$

$$R_{Cap} = l^{R}_{Cap} / l^{e}_{Cap} \quad \ldots\ldots\ldots\ldots\ldots\ldots (19)$$

Monomer sequencing inside PLCL was characterized from the ^{13}C-NMR spectra, more specifically from the expanded carbonyl carbon (C=O) region from 169-174 ppm (Baimark & Molloy, 2005). An example is shown in Figure 10. The various peaks were assigned to the various carbonyl carbons, C=O, located in the middle of the triad sequences as labelled in Figure 9.

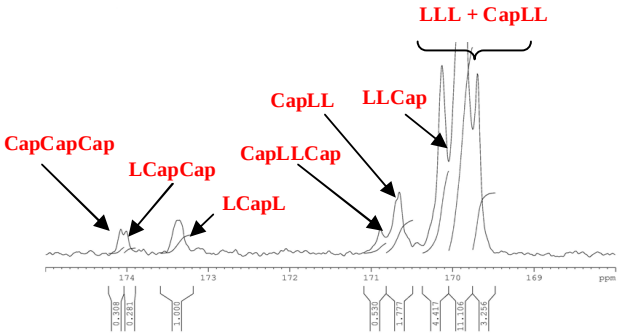

Figure 10: Expanded carbonyl regions of the ^{13}C-NMR spectrum of PLCL.

The most prominent peaks at 170.436 ppm and 174.626 ppm can be assigned to LLL and CapCapCap triad sequences, respectively. The ^{1}H-NMR spectrum of the PLCL copolymers in this work show not only peaks due to the LLL and CapCapCap sequences only, but also the intermediate peaks due to LCapCap, LCapL, CapLCap, CapLL and LLCap sequences, it confirms that copolymerization has indeed occurred (Baimark & Molloy, 2005). Furthermore, the reaction temperature has a profound influence on the values of l^{e}_{LL} and l^{e}_{Cap}. According to the Table 1-3, the number-average length of lactidyl increases proportionally with the molar fraction of lactide inside the copolymer, but in the case of CL, the number-average length of caproyl unit was not changed too much for the case of copolymers A-L. For the case of copolymer L, the number-average length of lactidyl is the lowest among other copolymer and the average length of caproyl unit is the highest value. This may be due to the molar fraction of comonomer observed in copolymer L which is almost 50:50 but also to the transesterification which occurred at high temperature. Consequently, we can conclude that the more CL units incorporated into copolymer chain, the shorter for the number-average length of lactide it will be, and the larger number-average length for caproyl. Coefficient R is a measure of the degree of randomness of the copolymer chain structure. From the Table 4, we can conclude that as the temperature and polymerization time increased, the degree of randomness also increased. This is because when the

temperature increases, these blocky structures may be randomized by transesterification reactions and probably because of more CL units incorporated inside copolymer chain. Besides that, the value of T_I is lower than 1 for every copolymer. This phenomenon indicates that there was still not a complete random distribution of comonomer units. In contrary, if the value of T_I is higher than 0, it proves that notable transesterification process occurred (Kasperczyk & Bero, 1993).

Conclusions

Conversion of the monomer unit in copolymer PLCL majorly influenced by the reaction temperature and polymerization time. As the temperature increase, the percentange of lactide (LA) and caprolactone (CL) monomer nearly approach 100%. Total average molecular weight is majorly depending on the reaction temperature. There was little deviation between total average molecular weight determined by SEC and calculated by theory due to the transesterification process. In conclusion, from this research, the microstructure of fabricated copolymer PLCL can be modified based on reaction temperature and polymerization time. As the reaction temperature increased, the microstructure of the copolymer PLCL became randomized. In future, the focus on study the mechanical and thermal properties can be done by using tensile test and Differential Scanning Calorimetry (DSC) machine.

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