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SEMI-INTERPENETRATION OF POLY(ETHYLENE GLYCOL) INTO POLY(L-  
LACTIC ACID) NETWORK

Mr. Worapob Kitpanitch

A Thesis Submitted in Partial Fulfillment of the Requirements  
for the Degree of Master of Science Program in Petrochemistry and Polymer Science

Faculty of Science

Chulalongkorn University

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Thesis Title                   SEMI-INTERPENETRATION    OF    POLY(ETHYLENE  
  GLYCOL) INTO POLY(L-LACTIC ACID) NETWORK  
By                                 Mr. Worapob Kitpanitch  
Field of Study                 Petrochemistry and Polymer Science  
Thesis Advisor                Assistant Professor Varawut Tangpasuthadol, Ph.D.

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วรภพ กิจพาณิชย์ : การกึ่งสอดไขว้พอลิ(เอทิลีน ไกลคอล)ภายในร่างแหพอลิ(แอล-แล็กติกแอซิด). (SEMI-INTERPENETRATION OF POLY(ETHYLENE GLYCOL) INTO POLY(L-LACTIC ACID) NETWORK) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ดร.วราวุฒิ ตั้ง พสุธาคล, 44 หน้า.

ได้เตรียมร่างแหพอลิเมอร์แบบกึ่งสอดไขว้ของพอลิ(แอล-แล็กติกแอซิด)/พอลิ(เอทิลีน ไกลคอล) ที่มีสมบัติชอบน้ำ โดยกระบวนการเชื่อมขวางแบบเรดิคัลของ PLLA ที่มีเมทาคริเลตอยู่ที่ปลาย (PLLA-Meth) โดยมี PEG กระจายตัวอยู่ในร่างแหของ PLLA เริ่มแรกได้สังเคราะห์ PLLA จาก แอล-แล็กติกแอซิด โดยวิธีการเกิดพอลิเมอร์แบบควบแน่น เพื่อให้ได้น้ำหนักโมเลกุลในช่วง 3,000-5,000 ดาลตัน จากนั้นจึงนำ PLLA มาทำปฏิกิริยากับ เมทาคริลิกแอนไฮไดรด์ เพื่อให้ปลายสายโซ่ของ PLLA มีหมู่เมทาคริเลต ซึ่งปริมาณการเข้าแทนที่ของ เมทาคริเลต บน PLLA ตรวจสอบด้วยโปรตอนเอ็นเอ็มอาร์พบว่ามีค่าสูงกว่า 90% เมื่อเติมเมทาคริเลตเป็นปริมาณ 40 เท่าของ PLLA เมื่อเชื่อมขวางด้วยความร้อนโดยใช้เบนโซอิลเปอร์ออกไซด์เป็นตัวริเริ่มปฏิกิริยา มีปริมาณเจล 62% ในขณะที่การเชื่อมขวางด้วยยูวีโดยใช้ 2-ไฮดรอกซี-2-เมทิลโพรพิโอฟีโนนเป็นตัวริเริ่มปฏิกิริยา ไม่พบการเกิดเจล ในส่วนของการเตรียมร่างแหพอลิเมอร์แบบกึ่งสอดไขว้ทำได้โดยผสม PLLA-Meth, PEG ( $M_w = 20,000$  ดาลตัน), และ 10% เบนโซอิลเปอร์ออกไซด์ เข้าด้วยกัน แล้วให้ความร้อนที่ 150 °C ซึ่งจากผลการทดลองพบว่า ค่าการดูดซับน้ำของร่างแหพอลิเมอร์แบบกึ่งสอดไขว้ ของพอลิ(แอล-แล็กติกแอซิด)/พอลิ(เอทิลีน ไกลคอล)ที่ได้ มีค่าเพิ่มขึ้น 9% ที่ปริมาณการผสม PEG 40% โดยน้ำหนัก

สาขาวิชา.....ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์.....ลายมือชื่อนิสิต.....  
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# # 5272520423: MAJOR PETROCHEMISTRY AND POLYMER SCIENCE

KEYWORDS: POLY(LACTIC ACID)/ SEMI-INTERPENETRATING NETWORK/  
POLY(ETHYLENE GLYCOL)/ CROSSLINKED POLYMER

WORAPOB KITPANITCH: SEMI-INTERPENETRATION OF  
POLY(ETHYLENE GLYCOL) INTO POLY(L-LACTIC ACID)  
NETWORK. ADVISOR: ASST. PROF. VARAWUT TANGPASUTHADOL,  
Ph.D., 44 pp.

Radical crosslinking of methacrylate-endcapped PLLA (PLLA-Meth) with PEG dispersed in the crosslinked PLLA network was carried out in order to prepare hydrophilic PLLA/PEG semi-interpenetrating network (semi-IPN). PLLA was first prepared by direct condensation polymerization from L-lactic acid. The number average molecular weight of PLLA was around 3,000-5,000 Da. PLLA with one or two methacrylate end groups were prepared by reacting PLLA or PLLA-diol chain with methacrylic anhydride. The degree of substitution of methacrylate on PLLA as determined by  $^1\text{H}$  NMR was over 90% when 40 equivalents (relative to PLLA chains) of methacrylate was added in the reaction. The gel content of thermal cure using benzoyl peroxide as an initiator was 62% while no crosslinking occurred by 2-hydroxy-2-methylpropiophenone initiator induced by UV. The PLLA/PEG semi-IPN was carried out by heating the PLLA-Meth mixed with PEG ( $M_w = 20,000$  Da) at 150 °C in the presence of 10% of benzoyl peroxide. Water uptake of the prepared PLLA/PEG semi-IPN was as high as 9% for the composite having 40% (by weight) of PEG.

Field of Study: Petrochemistry and Polymer Science Student's Signature: \_\_\_\_\_  
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## LIST OF ABBREVIATIONS

LLA	: L-lactic acid
PLA	: Poly(lactic acid), poly(lactide)
PLLA	: Poly(L-lactic acid), poly(L-lactide)
ROP	: Ring-opening polymerization
PC	: Polycondensation
PEG	: Poly(ethylene glycol)
Meth	: Methacrylic anhydride
MA <sub>n</sub>	: Maleic anhydride
BD	: 1,4-butanediol
TNBT	: Titanium(IV) n-butoxide
BPO	: Benzoyl peroxide
Darocure 1173	: 2-hydroxy-2-methylpropiophenone
IPN	: Interpenetrating polymer network
Semi-IPN	: semi-interpenetrating polymer network
PLLA-Meth	: Methacrylated-endcapped PLLA
PLLA-diMeth	: Dimethacrylated-endcapped PLLA
PLLA-MA	: Maleate-endcapped PLLA
NMR	: Nuclear magnetic resonance spectroscopy
GPC	: Gel permeation chromatography
SEM	: Scanning electron microscopy
ATR-FTIR	: Attenuated total reflectance fourier transform infrared
$\overline{M}_n$	: Number-average molecular weight
$\overline{M}_w$	: Weight- average molecular weight
PDI	: Polydispersity index
DS	: Degree of substitution
%Gel	: Percentage of gel content
%w	: Degree of water uptake
%m	: Degree of mass loss

# CHAPTER I

## INTRODUCTION

### 1.1 Statement of Problem

Since 1968, poly(L-lactic acid) (PLLA) was introduced in the market for medical sutures. And nowadays it has become one of the leading biodegradable and biocompatible polyesters commercially used in biomedical and household product industries. PLLA can be prepared from lactic acid that was produced from renewable resources (such as corn, potato, and cane molasses) through two synthesis routes, ring-opening polymerization (ROP) from lactide and polycondensation (PC) from lactic acid [1, 2].

The structure of PLLA contains no double bond, making it somewhat difficult to crosslink. Therefore, there were a number of studies reporting the attachment of double bond on the PLLA chain. This was usually done through the esterification reaction between PLLA and diacid [3], diol [4], acid anhydride [5], or acid halide [6], that had at least one double bond in the structure. Those double bonds bearing PLLA were further crosslinked to prepare high molecular weight of PLLA, or hydrogel copolymer networks, for example.

Regarding the structure of PLLA, it is rather hydrophobic, which limited its use in application where water absorption into the polymer network was required. Thus, hydrophilic polymer such as poly(ethylene glycol) or PEG was often chosen to combine with PLLA with the aim to increase the polymer hydrophilicity through simple blending [7, 8], interpenetrating (IPN), or semi-interpenetrating process (semi-IPN) [9, 10]. The focus of this work was to prepare PLLA/PEG semi-IPN with the aim to create water absorbable polymer matrix that was biodegradable and biocompatible. Previously, Chad *et al.* reported the preparation of PLLA-PEG semi-IPN in which PLA chain interpenetrated in the matrix of PEG crosslinked network. But in this work, PEG was simply blended into the network of crosslinked PLLA which was prepared from PLLA chains that carried the crosslinkable carbon-carbon double bonds. Subsequent crosslinking would result in PLLA network having PEG trapped in it. By doing this,

PEG could have a tendency to leak out of the polymer matrix after long water-contacting time. This would increase the degradation rate of the crosslinked PLLA.

## **1.2 Objectives**

The goal of this work was to prepare the semi-IPN of PLLA and PEG. The structure of PLLA was modified by reacting with methacrylic anhydride or maleic anhydride to obtain double bond-endcapped PLLA, which was used in the preparation of crosslinked PLLA having PEG blended inside. Crosslinking by peroxide initiator activated by heat and UV were studied. The properties of the semi-IPN produced were investigated for degree of water uptake and mass loss. The resulting material was aimed to be used as new biocompatible water absorbing device, and might potentially be developed further for biomedical application.

## **1.3 Scope of Investigation**

1. Synthesis of PLLA by condensation polymerization from lactic acid
2. Synthesis of double bond-endcapped PLLA by esterification reaction between PLLA and acid anhydride
3. Crosslinking of PLLA by thermal and UV crosslinking
4. Preparation of PLLA/PEG semi-IPN
5. Structure characterization of PLLA, double bond-endcapped PLLA, and PLLA network by using nuclear magnetic resonance spectroscopy ( $^1\text{H}$  NMR), attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy, and gel permeation chromatography (GPC)
6. Property characterization of PLLA/PEG semi-IPN



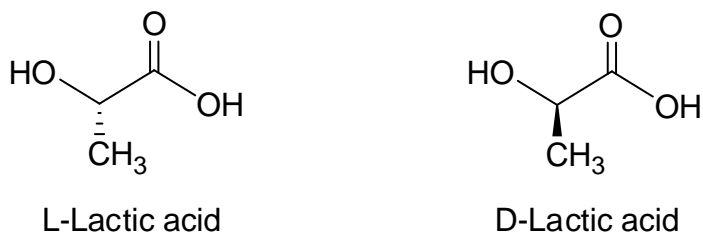
## CHAPTER II

### THEORY AND LITERATURE REVIEW

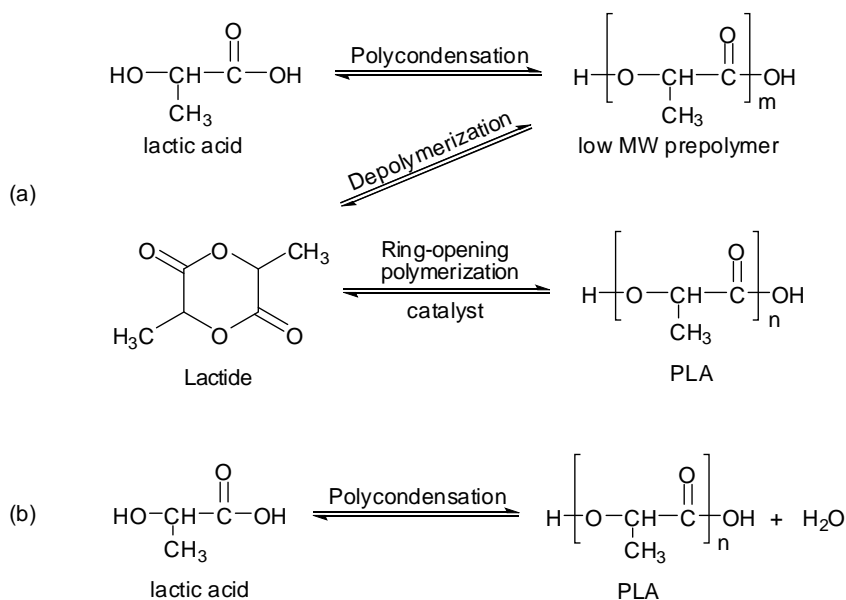
#### 2.1 Poly(lactic acid)

Poly(lactic acid) (PLA) is a biodegradable and biocompatible thermoplastic which can be produced by fermentation from renewable resources such as corn, potato, beet sugar, and cane molasses. Lactic acid had two optically active configurations, L-lactic acid (as high as 90 to 99%) and D-lactic acid (Figure 2.1). PLA can be prepared through two synthesis routes, ring-opening polymerization (ROP) and direct polycondensation (PC) (Scheme 2.1).

The ROP method can produce high molecular weight PLA (20,000 to 600,000 Da) without water by-product. But the cost of ROP process is high in the synthesis and purification steps of lactide, a cyclic dimer of lactic acid. The cost of PC method is lower than the ROP. But the molecular weight of PLA obtained was usually low (10,000 to 100,000 Da) [1, 2, 11]. In this work, PC method was chosen to synthesize PLA with molecular weight in the range of 3,000 to 5,000 Da.



**Figure 2.1** Two configurations of lactic acid



**Scheme 2.1** Synthesis of PLA via (a) ring-opening polymerization and (b) direct polycondensation polymerization

## 2.2 Poly(ethylene glycol)

Poly(ethylene glycol) (PEG) is a biocompatible and hydrophilic polymer which can be produced by the reaction of ethylene oxide with water, or ethylene glycol. Moreover, PEG is a flexible polymer and efficient plasticizers. Thus, PEG was used to attach with many polymers to improve their properties.

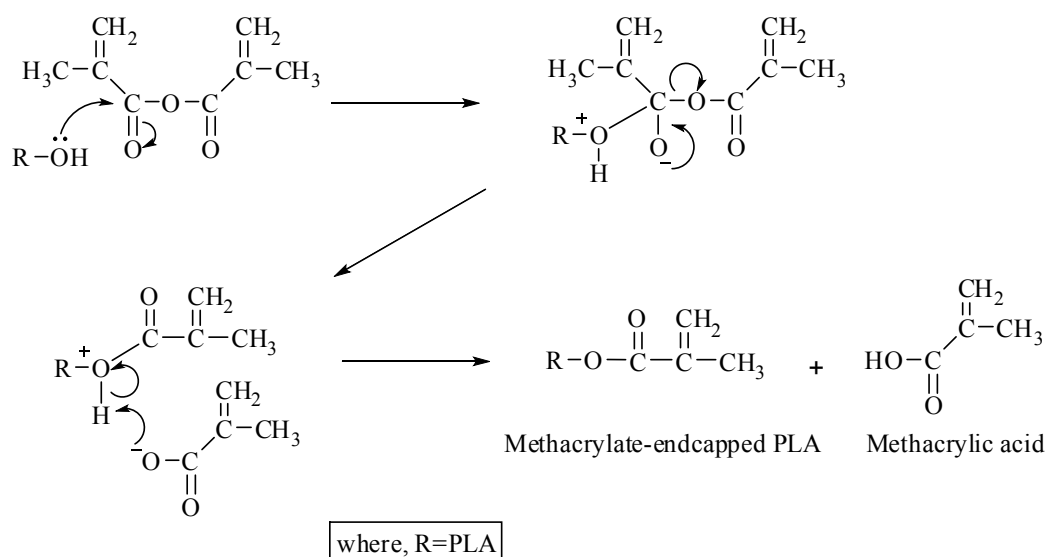
For example, Park *et al.* [12] were prepared high molecular weight PEG and mixed with a PLA to improve ductility of PLA. The melt blending polymer of PLA and high molecular weight PEG were obtained 540% of elongation at break and 40 times of relative ductility, compared with neat PLA. The synthesis of polylactide-b-polyethylene glycol (PEG) linear block copolymers were studied by Taskin *et al.* [13]. The copolymers were synthesized through transesterification reaction. Then the copolymers were blended with neat PLA to improve mechanical. The product polymer had better film properties than neat PLA.

Gui *et al.* [8] was tried to produce polyester-toughened polylactide from PLA and poly(ethylene glycol)-co-citric acid (PEGCA). PLA/PEGCA blended with the addition of 15% PEGCA was prepared and its elongation at break reached 242%, whereas the impact resistance reached 103 J/m. The applications in drug delivery of PEG-PLA nanoparticles were reported by Sunoqrot *et al.* [14]. The targeted dendrimers

were encapsulated into PEG-PLA blended. The encapsulation efficiencies were 69-85% and the release rate of the dendrimers from the nanoparticles depend on the molecular weight of the PEG-PLA blended.

### 2.3 Modification of PLA

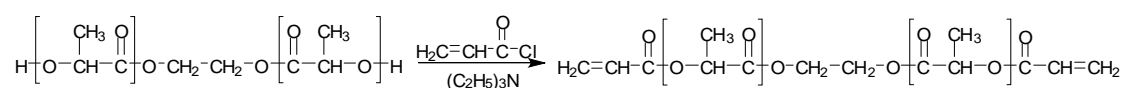
PLA is a biodegradation and biocompatible polyester that can be processed and fabricated quite readily similar to many petroleum-based polymers. Requirements for special functional groups on polymer are increasing in order to produce more advanced materials. For PLA, one side of the polymer chain end is a carboxylic group and the other side is a hydroxyl group. These two groups are quite reactive and thus provide several possibilities for derivatization. Scheme 2.2 show a mechanism of the reaction between chain end hydroxyl group of PLA and methacrylic anhydride through esterification reaction.



**Scheme 2.2** Mechanism of functionalization of PLA chain end with methacrylic anhydride

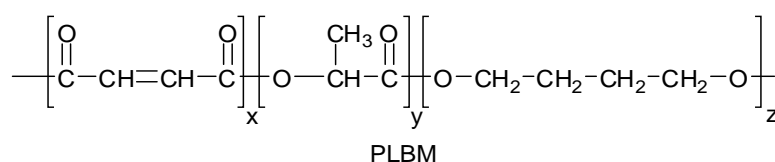
Successful crosslinking of a linear polymer requires unsaturated carbon-carbon double bonds in the polymer structure. This double bond therefore becomes an attacking point of a radical initiator. With chain reaction of the radical, a crosslinked network can be produced. One way to couple the double bond groups into the PLLA is

to allow the hydroxyl chain end reacting with a carboxylic acid compound possessing the double bond. In 1997, Lee *et al.* [6] functionalized PEG-co-poly(D,L-lactide) with acryloyl chloride to obtain a macromer in which two unsaturated double bonds were attached on both chain ends of the copolymer (Figure 2.2). The macromer was then crosslinked with a macromolecule,  $\beta$ -chitin, to prepare semi-interpenetrating polymer network hydrogels through UV irradiation method.



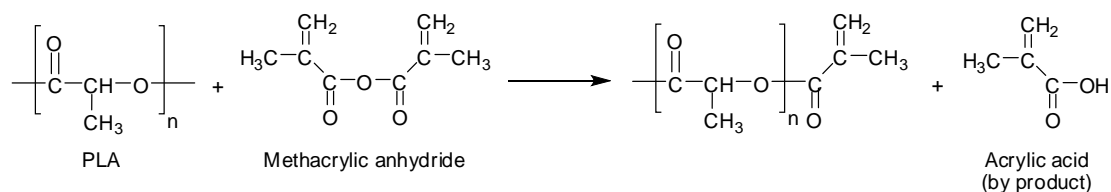
**Figure 2.2** Functionalization of PEG-co-poly(D,L-lactide) with acryloyl chloride

In 2003, Park *et al.* [3] reported the preparation of copolyester having unsaturated double bonds randomly scattered along the copolymer chain. It was created by copolymerization of lactic acid, 1,4-butanediol, and maleic acid in order to carry out polymer chain extension (Figure 2.3). Benzoyl peroxide (BPO) was used as the radical initiator activating the chain connection at the double bonds during hot pressing. The degree of chain linking depended on the temperature used. The biodegradation rate of the polymer product was much slower than that of PLLA and lowered further by the chain extension.

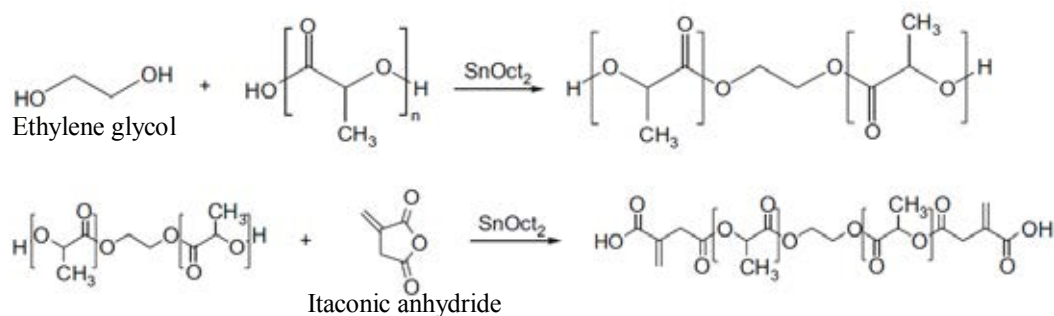


**Figure 2.3** The structure of poly(L-lactic acid) with unsaturated groups (PLBM)

The anhydride with double bond group such as methacrylic anhydride [5, 15, 16] and itaconic anhydride [17] were reportedly used to prepare double bond-terminated PLA (Figure 2.4 and 2.5).

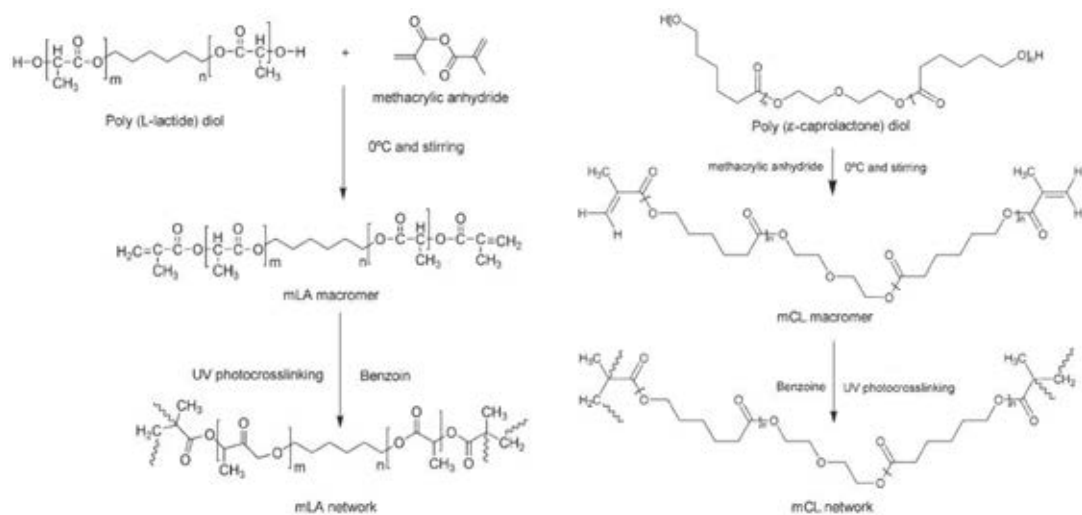


**Figure 2.4** Functionalization of PLA with methacrylic anhydride



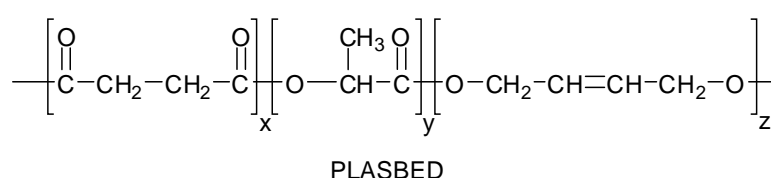
**Figure 2.5** Synthesis of PLA end-capping with itaconic anhydride

In 2009, Serra *et al.* [18] was tried to produce the PLA network. L-lactide and 1,6-hexanediol were reacted to produce the PLA-diol, which were functionalized with methacrylic anhydride to produce methacrylate-endcapped lactide macromer. Then the methacrylate-endcapped lactide macromer was copolymerized with the methacrylate-endcapped caprolactone macromer by UV polymerization using benzoin as a photoinitiator (Scheme 2.3).



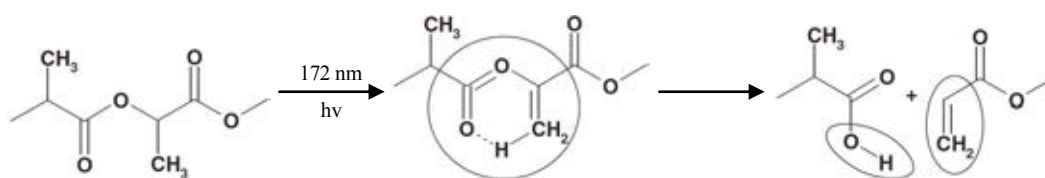
**Scheme 2.3** Synthesis and crosslink process for methacrylate-endcapped PLA and methacrylate-endcapped caprolactone macromer

The copolymerization of PLA with a diol molecule that contained the double bond was reported by Lee *et al.* [4]. Lactic acid, succinic acid, and 1,4-butenediol were copolymerized to produce poly(LA-co-SA-co-1,4-BED) (PLASBED) (Figure 2.6). The chain extension by intermolecular linking reaction through the unsaturated 1,4-BED units in PLASBED with benzoyl peroxide under a hot press further increased the molecular weight and made PLASBED more ductile and flexible. Its biodegradability was nearly independent of the content of 1,4-BED.



**Figure 2.6** The structure of poly(LA-co-SA-co-1,4-BED) (PLASBED)

In 2012, Sato *et al.* [19] modified the surface of PLA membranes by using vacuum UV irradiation at 172 nm to improve water vapor permeability through the membranes. Its surface hydrophilicity increased but the water vapor permeability was not enhanced. The interesting finding in this research is the chain scission changing the PLA chemical structure to C=C double bonds and hydroxyl group at newly formed chain end (Scheme 2.4). This reaction was a new pathway to generate C=C by itself. However, the main problem of this reaction was low molecular weight PLA was obtained.



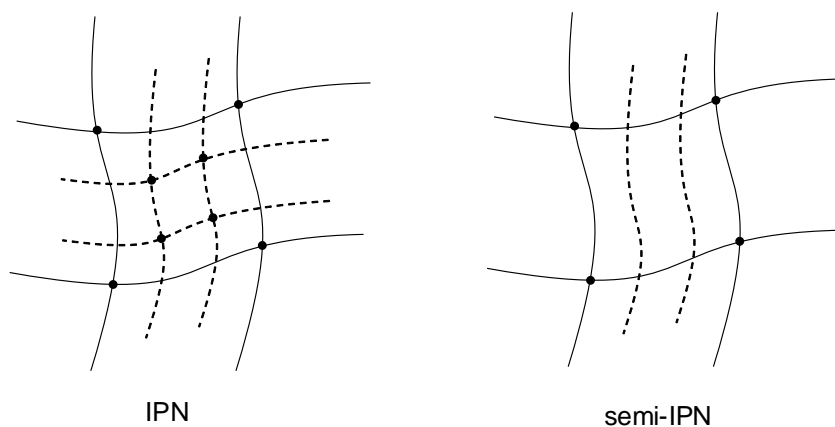
**Scheme 2.4** The scission reaction in PLA chains under UV exposure

From these selected literatures, the unsaturated carbon-carbon double bonds were attached to PLA chain in order to use in chain extension application or to prepare

polymer networks. The double bond groups in the chain (or chain end) of polymer were initiated by thermal and photo-initiator via radical chain addition.

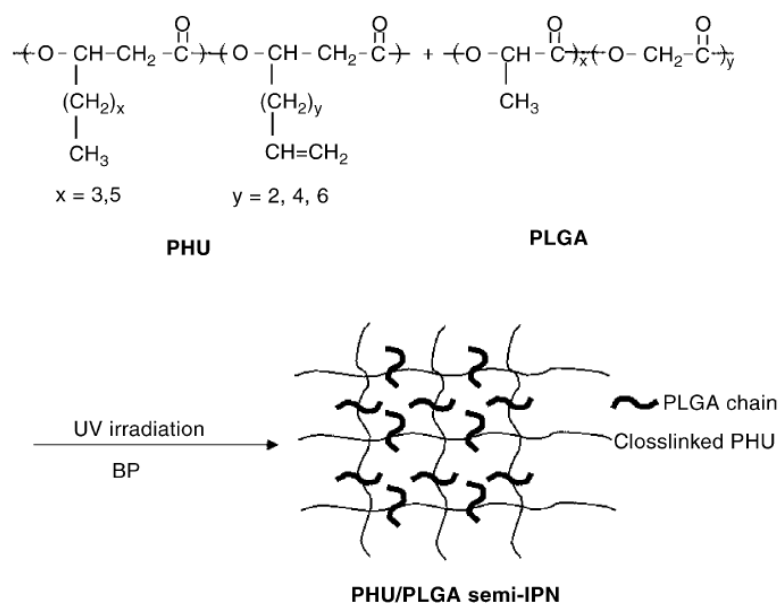
#### 2.4 Interpenetrating polymer network (IPN) and semi-interpenetrating polymer network (semi-IPN)

George Odian explained the definitions of IPN and semi-IPN in the *Principles of Polymerization* [20] as: “The interpenetrating polymer network is a blend of two different polymer networks without covalent bonds between the two networks. An IPN is obtained by the simultaneous or sequential crosslinking of two different polymer systems, IPN synthesis is the only way of achieving the equivalent of a physical blend for systems containing crosslinked polymers. A simultaneous IPN, referred to as SIN, is produced by reacting a mixture of the monomers, crosslinking reagents, and catalysts for the two crosslinking systems. A sequential IPN (SIPN) is produced by reacting a mixture of one crosslinked polymer and the ingredients for the other crosslinking system. Semi-IPN and pseudo-IPN refer to sequential and simultaneous synthesis, respectively, of interpenetrating polymer networks in which one of the polymers is not crosslinked. Interpenetrating polymer networks are possible for a pair of step polymerization systems, a pair of chain polymerization systems, or the combination of step and chain polymerization systems.” The structure of IPN and semi-IPN were shown in Figure 2.7.



**Figure 2.7** The structure of interpenetrating (IPN) and semi-interpenetrating (semi-IPN) polymer networks

The IPN and semi-IPN were often used to prepare copolymer network. For example, Kim *et al.* [21] prepared the semi-IPN of poly(3-hydroxyundecenoate) (PHU) and poly(lactide-co-glycolide) (PLGA) by irradiation of UV light with benzophenone (as a photoinitiator) to the homogeneous solutions of PHU and PLGA in chloroform. After the crosslinking process, the PLGA chains were entrapped in the crosslinked networks of PHU having unsaturated double bonds in its structure (Scheme 2.5). The result show that the mechanical strength of semi-IPN was enhanced as the PLGA content increased. And the degradation rate of the obtained semi-IPN was faster than crosslinked PHU.

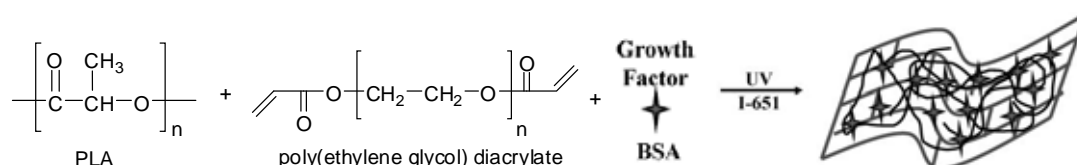


**Scheme 2.5** Synthesis pathway of PHU/PLGA semi-IPN

One way to increase the hydrophilicity of PLLA was to blend or attach a hydrophilic molecule to the polymer. For example, water-soluble PEG has drawn many researchers attention to ‘merge’ this macromolecule to PLLA. The semi-interpenetrating network of poly(ethylene glycol) and poly(D,L-lactide) (PEG/PLA IPN) were prepared by Chad *et al.* [10]. The poly(D,L-lactide) chain and bovine serum albumin (BSA) were entrapped into the poly(ethylene glycol) diacrylate networks through photopolymerization (Scheme 2.6). The PEG component drew water into its matrix to form a hydrogel, which was used to controlled release protein

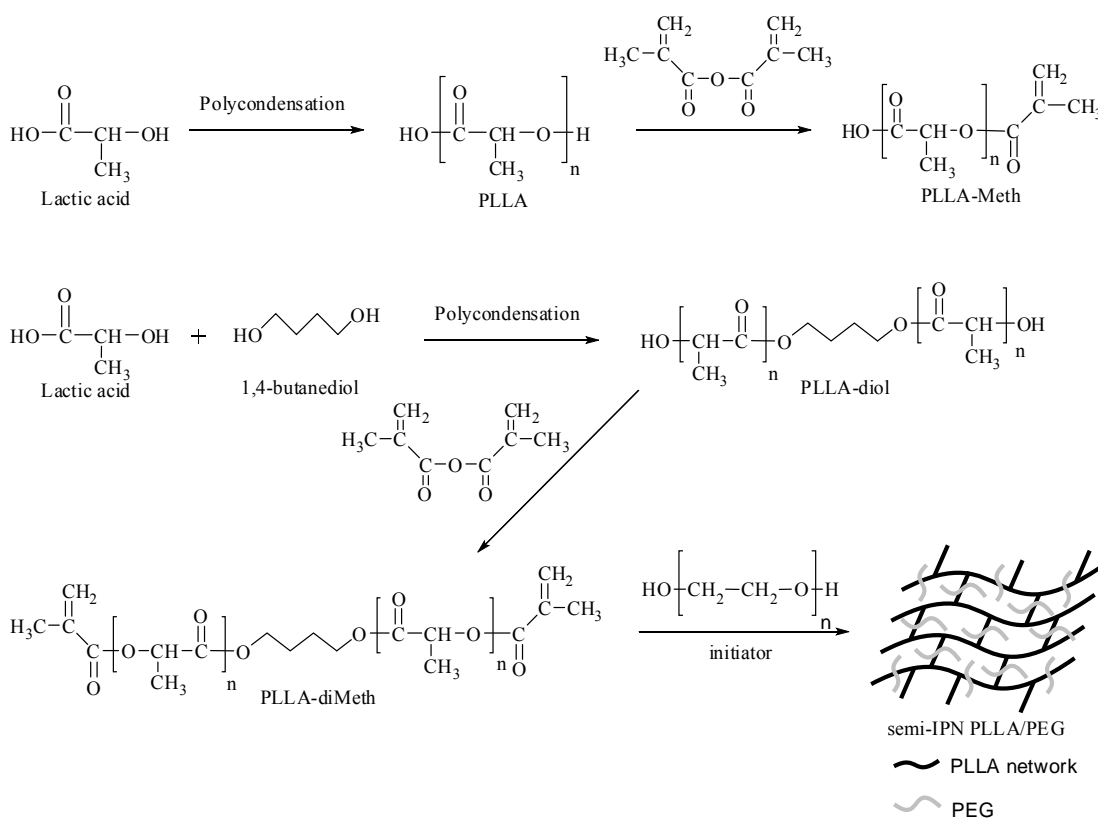


drug. The PLA component both strengthens the hydrogel and enhances the degradation of the network.



**Scheme 2.6** Synthesis pathway of PEG/PLA IPN

In this research, semi-IPN of PLLA and PEG was prepared through the crosslinking of double bond-terminated PLLA (such as methacrylated-endcapped PLLA). Two radical initiators and methods for crosslinking of PLLA were studied; benzoyl peroxide as a thermal initiator and 2-hydroxy-2-methylpropiophenone as a photoinitiator. The synthesis pathway of semi-IPN in this research is shown in Scheme 2.7.



**Scheme 2.7** Synthesis pathway of semi-IPN PLLA/PEG

## **CHAPTER III**

### **EXPERIMENTAL**

#### **3.1 Materials**

L-lactic acid (LLA) (minimum assay as lactic acid total 88% by weight) was purchased from Carlo Erba Reagent (France). Titanium(IV) butoxide (TNBT) (reagent grade 97%), methacrylic anhydride (Meth) (contains 2,000 ppm topanol A as inhibitor, 94%), maleic anhydride (MAn) (purity  $\geq 98.0\%$ ), poly(ethylene glycol) (PEG) (BioUltra,  $M_w = 20,000$ ), 1,4-butanediol (BD), and 2-hydroxy-2-methylpropiophenone 97% (Darocure 1173) were purchased from Sigma-Aldrich (USA). Methanol (MeOH), toluene and benzoyl peroxide (BPO) (with 25% H<sub>2</sub>O) were purchased from Merck (Germany). Chloroform and tetrahydrofuran (THF) (HPLC grade) were purchased from RCI Labscan Limited (Thailand).

#### **3.2 Equipments**

##### **3.2.1 Nuclear Magnetic Resonance (NMR) Spectroscopy**

<sup>1</sup>H NMR spectra were recorded in solution of CDCl<sub>3</sub> using a Varian, model Mercury-400 nuclear magnetic resonance spectrometer (USA) operating at 400 MHz. Chemical shifts were reported in part per million (ppm) relative to tetramethylsilane (TMS) or using the residual protonated solvent signal as a reference.

##### **3.2.2 Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy**

The PLLA samples were determined by Attenuated total reflectance-Fourier transform infrared spectrometer in the range of 4000-400 cm<sup>-1</sup>. IR spectra were collected using a Nicolet 6700 FT-IR spectra. The IR spectra were acquired by using the Omnic ESP in a range of 4000-500 cm<sup>-1</sup>.

##### **3.2.3 Gel Permeation Chromatography (GPC)**

Gel permeation chromatograms of PLLA were obtained from Waters 600 controller chromatograph equipped with two HR (Waters) columns (HR1 and HR4)

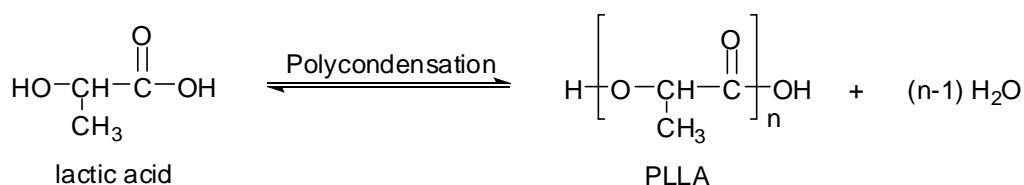
(MW resolving range = 100-500,000 Da) at 35 °C and a refractive index detector (Waters 2414). THF (HPLC grade) was used as an eluent with the flow rate of 1.0 mL/min. Sample injection volume was 50 µL. Polystyrenes (996-188,000 Da) were used as standards for calibration.

### 3.2.4 Scanning Electron Microscopy

A scanning electron microscope (SEM) was used to analyze the cross section surface of polymer network. The samples were cut by scalpel and sputter-coated with gold. The photographs were taken on a JOEL JSM-5410 SEM. The SEM photographs were used to investigate the morphology and homogeneity of polymer network. Measurements were done at 30 kV at 1,000 and 5,000 magnifications.

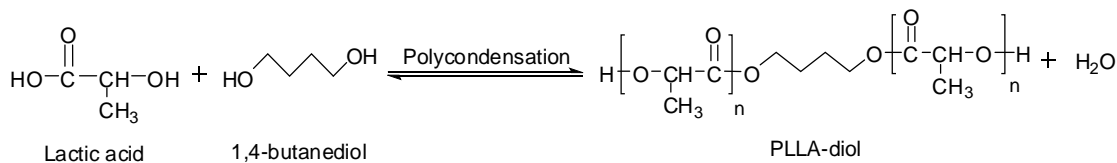
## 3.3 Methods

### 3.3.1 Synthesis of PLLA by condensation polymerization



L-lactic acid was heated to 80 °C under reduced pressure for 4 h to remove free water. Next, N<sub>2</sub> was purged into the reaction vessel which was heated up to 170 °C, followed by the addition of 0.1 mol% TNBT as a catalyst. After 1 h, pressure was reduced slowly to avoid the bumping of solution and the polycondensation was carried out for 5 h at high vacuum. The resulting polymer was cooled down to room temperature and purified 3 times by dissolving in chloroform and precipitated in MeOH. The white product of PLLA was obtained and dried by vacuum at room temperature.

### 3.3.2 Synthesis of PLLA-diol by condensation polymerization



The method used followed the work reported by Zeng *et al.* [22]. L-lactic acid was heated to 80 °C. The pressure was reduced to remove free water for 3 h. Then, 1.5 mol% 1,4-butanediol and 0.1 mol% TNBT were added. The reaction was heated up to 160 °C for 5 h and then continued at 180 °C for 5 h. The resulting PLLA-diol was purified and collected by the same method as for PLLA.

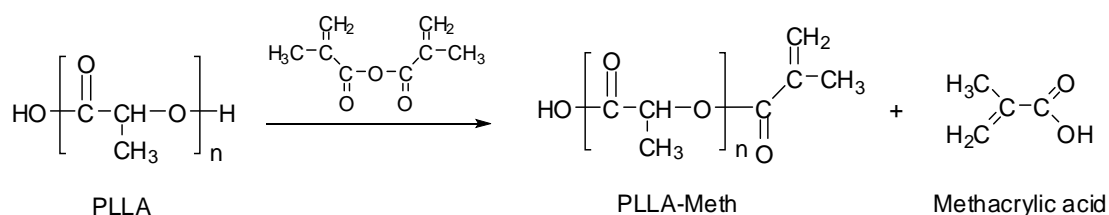
### 3.3.3 Synthesis of functionalized PLLA and PLLA-diol

In this step, methacrylic anhydride and maleic anhydride were used to prepare double bond-endcapped PLLAs. The degree of substitution (DS) was determined from <sup>1</sup>H NMR and calculated by Eq. (1):

$$DS = \frac{\int H_{before} - \int H_{after}}{\int H_{before}} \times 100 \qquad \text{Eq. (1)}$$

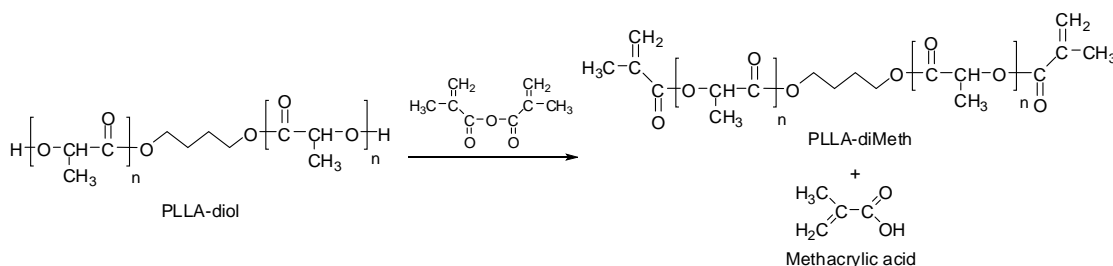
where  $H_{before}$  and  $H_{after}$  are peak areas of a proton signal (at  $\delta = 4.36$  ppm) belonging to the methine (-CH-) proton of terminal repeat unit of PLLA *before* and *after* double bond encapping reaction, respectively. The proton signal of the methine proton in PLLA repeat units at 5.18 ppm was used as the reference peak for normalizing the intensity of the peak area of the terminal unit.

#### 3.3.3.1 Methacrylate-endcapped PLLA



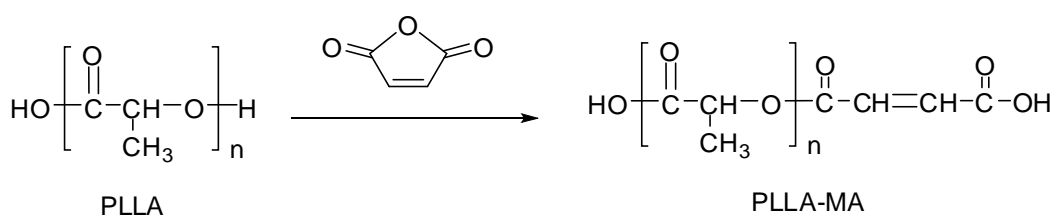
PLLA and a predetermined amount of Meth were dissolved in toluene in a round bottomed flask. Then the reaction was stirred and heated at 80 °C for 24 h. The product was purified 3 times by dissolving in chloroform and precipitated in MeOH. After vac drying at room temperature, the product obtained as white powder.

### 3.3.3.2 Methacrylate-endcapped PLLA-diol



The synthesis of PLLA-diMeth was prepared by the same process except that PLLA-diol was used as the starting material instead of PLLA.

### 3.3.3.3 Maleate-endcapped PLLA



The synthesis of PLLA-MA was performed by using similar approach for synthesizing PLLA-Meth except that maleic anhydride was used as the starting material instead of methacrylic anhydride.

## 3.3.4 Preparation of polymer network

### 3.3.4.1 Thermal crosslinking

The functionalized PLLA was mixed with 10 wt% BPO, a peroxide curing agent, in chloroform (BPO was purified by dissolution in chloroform and re-precipitation in methanol prior to use [23]). Then the mixture was poured into a

circular mold (3 mm high and 6 mm in diameter) and kept at room temperature for 24 h to let the solvent evaporate. The dry-mixture was heated at 150 °C for 1 h in an electric oven to initiate the crosslinking and dry the polymer matrix. The translucent pellet of PLLA network was obtained. The efficiency of crosslinking of PLLA network was verified by percentage of gel content (%Gel) [24, 25], Eq. (2):

$$\%Gel = \frac{m_{final}}{m_{initial}} \times 100 \quad \text{Eq. (2)}$$

where  $m_{initial}$  and  $m_{final}$  are the weight of initial sample and insoluble gel, respectively.

#### 3.3.4.2 UV crosslinking

The functionalized PLLA was mixed with 10 wt% Darocure 1173 in chloroform. The mixture was poured into a mold and UV-irradiated (253.7 nm, 10 watts) for 10 min to initiate the crosslinking. Then the mixture was dried under vacuum at room temperature for 24 h. The opaque pellet of PLLA network was obtained. And the efficiency of crosslinking of PLLA network was verified by the same above equation.

#### 3.3.5 Preparation of PLLA/PEG semi-IPN

The functionalized PLLA was mixed with 0-40 wt% PEG and 10 wt% BPO in chloroform. Then the mixture was poured into a mold and heated at 150 °C for 1 h in an electric oven to initiate the crosslinking and dry the polymer matrix. The translucent pellet of PLLA/PEG semi-IPN was obtained. The degree of water uptake (%W) of PLLA/PEG semi-IPN was determined by immersing the polymer pellet in deionized water for 24 h and calculated using Eq. (3):

$$\%W = \frac{m_{wet} - m_{dry}}{m_{dry}} \times 100 \quad \text{Eq. (3)}$$

where  $m_{dry}$  and  $m_{wet}$  are the weight of the pellet before and after immersed in deionized water, respectively. And the degree of mass loss (%m) of PLLA/PEG semi-IPN was calculated by Eq. (4):

$$\%m = \frac{m_{before} - m_{after}}{m_{before}} \times 100 \quad \text{Eq. (4)}$$

where  $m_{before}$  and  $m_{after}$  are the weight of dried pellet before and after immersed in deionized water, respectively.

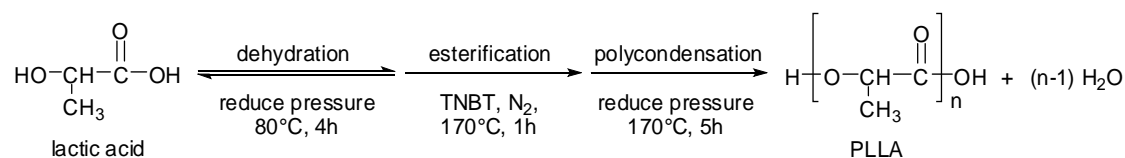
## CHAPTER IV

### RESULTS AND DISCUSSION

This chapter was divided into three parts. The first part is the synthesis of polymer. PLLA and PLLA-diol which were synthesized through polycondensation polymerization. Then the polymers were functionalized through the reactions between the -OH on the polymer chain end and an anhydride compound that has a double bond. In the second part, PLLA network was prepared. The functionalized PLLA was crosslinked through thermal and UV crosslinking while PEG was blended in the crosslinked matrix. And in the last part, water uptake, mass loss, and morphology of PLLA/PEG semi-IPN were investigated.

#### 4.1 Synthesis of polymer

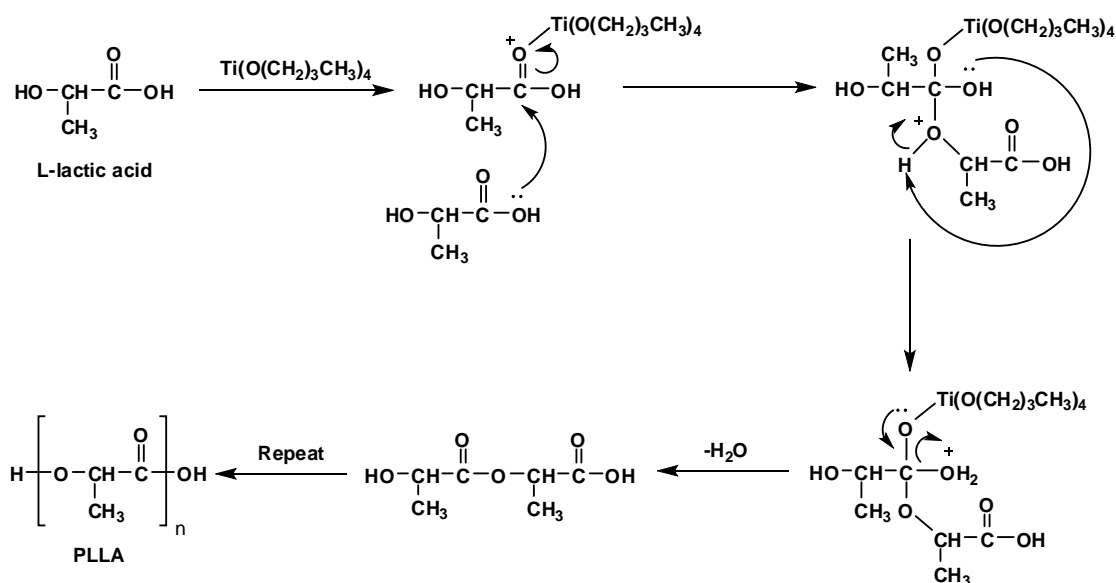
##### 4.1.1 Synthesis of PLLA and PLLA-diol by condensation polymerization



**Scheme 4.1** Synthesis of PLLA from lactic acid

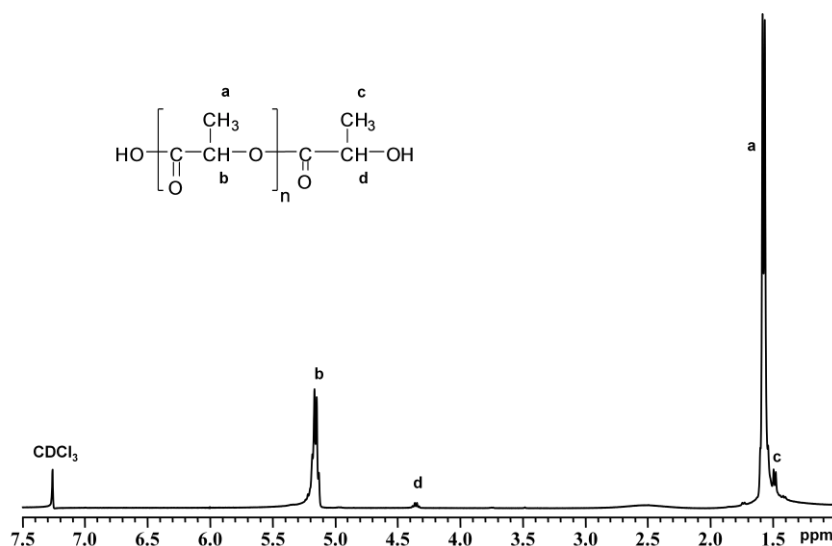
The synthesis method of PLLA followed the work reported by Chen *et al.* in 2006 [1], with some modification in dehydration step in which performed in vacuum in order to remove higher amount of water from the reaction as suggested by Zeng *et al.* [22] (Scheme 4.1). Because the dehydration at 100 °C under N<sub>2</sub> atmosphere resulted in poor water removal from the reaction (the water condensed at still head and dropping back to the reaction flask in the distillation setup). The mechanism of PLLA synthesis in the presence of TNBT Lewis acid catalyst is shown in Scheme 4.2.





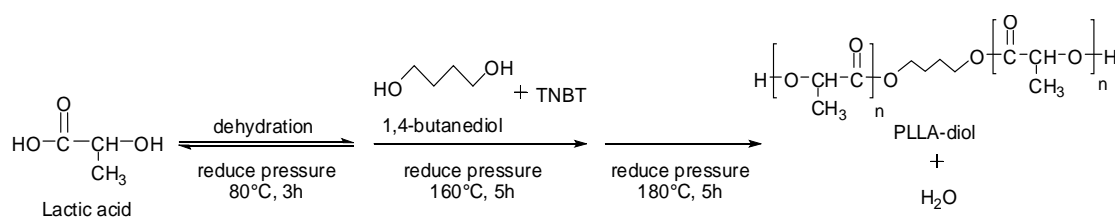
**Scheme 4.2** Condensation reaction mechanism of L-lactic acid to form PLLA in the presence of TNBT catalyst

Figure 4.1 shows  $^1\text{H}$  NMR spectrum of the obtained PLLA. The proton signals at 1.58 and 5.18 ppm were assigned to methyl (a) and methine (b) protons of the lactide repeat unit, respectively. The methyl (c) and methine (d) protons at the chain end were found at 1.48 and 4.36 ppm, respectively.

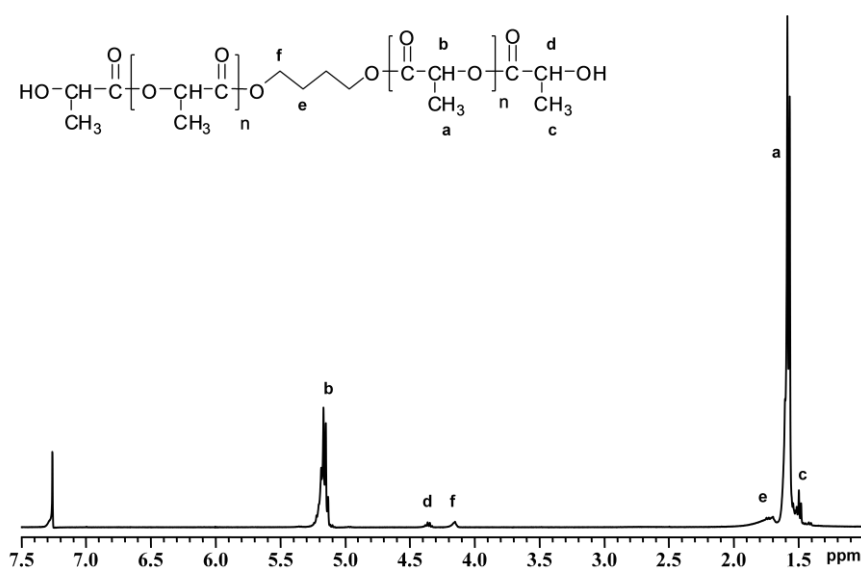


**Figure 4.1**  $^1\text{H}$  NMR spectrum of PLLA in  $\text{CDCl}_3$

The synthesis of PLLA-diol followed Zeng's work [22]. The PLLA-diol that had one -OH group on each chain end was obtained from the condensation of L-lactic acid with 1,4-butanediol as the initiator and TNBT as catalyst (Scheme 4.3). Proton signals of PLLA-diol is similar to PLLA, except for low intensified signals at 1.68 and 4.11 ppm referring to methylene protons of butanediol part in polymer chain (Figure 4.2). As expected, the molecular weight of PLLA and PLLA-diol were obtained in the range of 3,000-5,000 Da. And the molecular weight results are shown in Table 4.1.



**Scheme 4.3** Synthesis of PLLA-diol from lactic acid



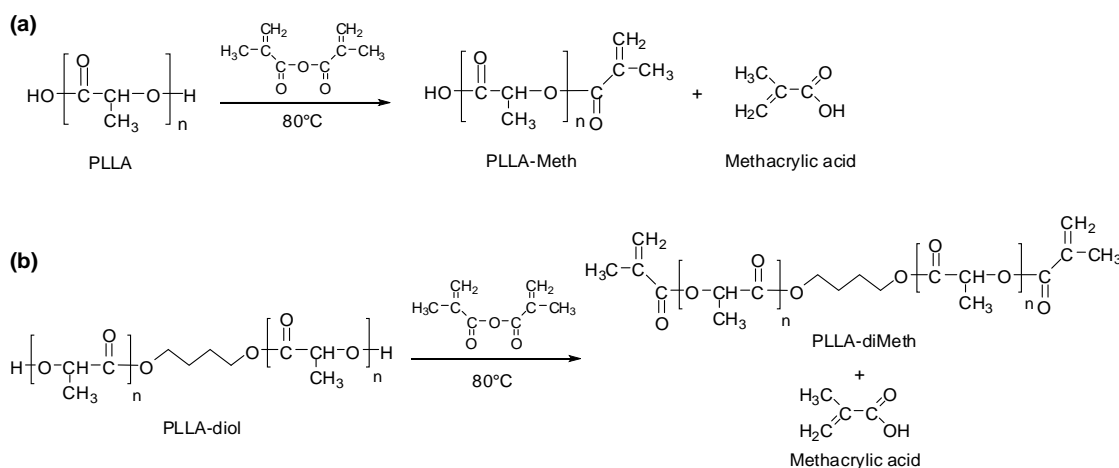
**Figure 4.2**  $^1\text{H}$  NMR spectrum of PLLA-diol in  $\text{CDCl}_3$

**Table 4.1** Molecular weight, polydispersity index, and yield of synthesise PLLA

Sample	by NMR	by GPC			Yield (%)
	$\bar{M}_n$ (Da)	$\bar{M}_n$ (Da)	$\bar{M}_w$ (Da)	PDI	
PLLA	2,574	3,156	3,623	1.15	40
PLLA-diol	3,976	5,376	6,471	1.2	62

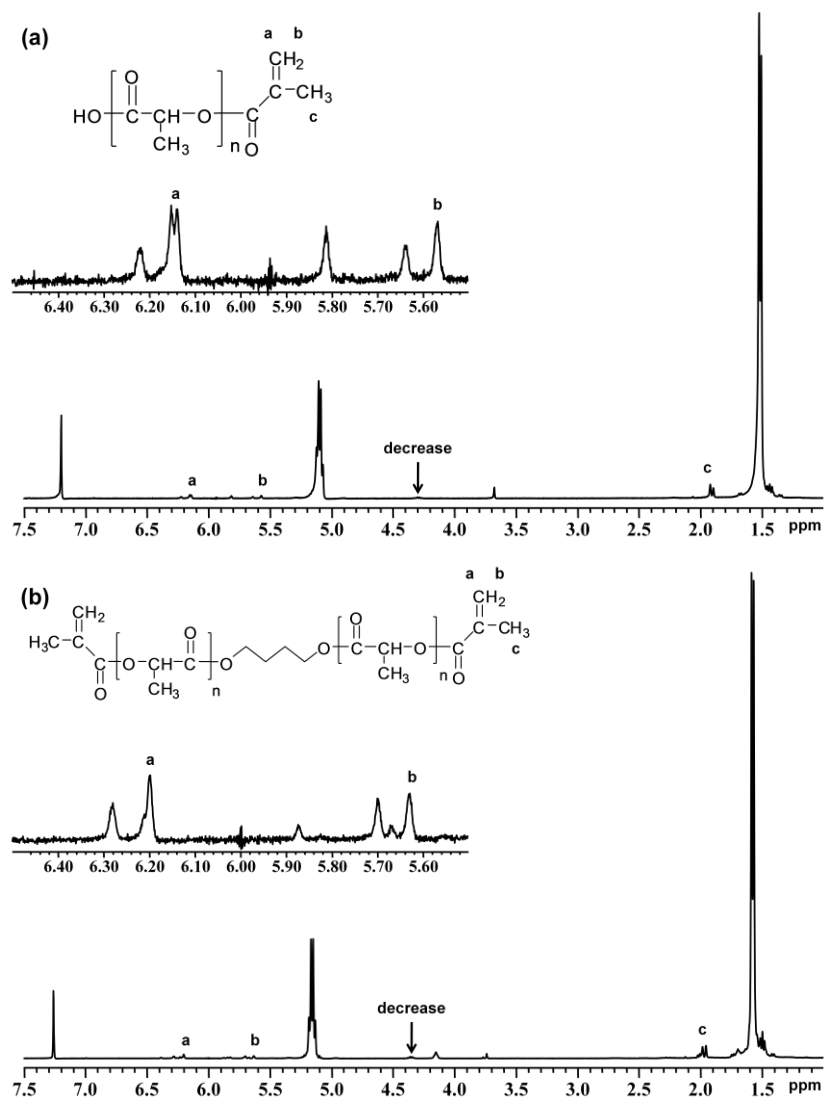
## 4.1.2 Synthesis of functionalized PLLA and PLLA-diol

### 4.1.2.1 Methacrylate-endcapped PLLA and PLLA-diol

**Scheme 4.4** Synthesis of (a) PLLA-Meth and (b) PLLA-diMeth

PLLA and PLLA-diol were reacted with methacrylic anhydride to obtain PLLA-Meth and PLLA-diMeth (Scheme 4.4). Reaction mixtures were monitored by  $^1\text{H}$  NMR (Figure 4.3a and 4.3b). After the methacrylation step, new proton signals from the methacrylate group at 1.93, 5.56, and 6.14 ppm, assigned to the methyl and two olefinic methylene protons, were clearly visible [5, 15, 26]. However, the proton signals at 5.82 and 6.22 ppm also appeared. It's the methylene protons of residual methacrylic anhydride monomer. And the proton signal at 5.64 ppm assigned to the methylene proton of methacrylic acid by-product. It was possible that the excess amount of methacrylic anhydride monomer ( $\geq 40$  times the moles of PLLA:Meth) could not be completely removed from the product. Attachment of the methacrylate group to the chain end of PLLA caused the reduction in signal intensity of protons in the terminal

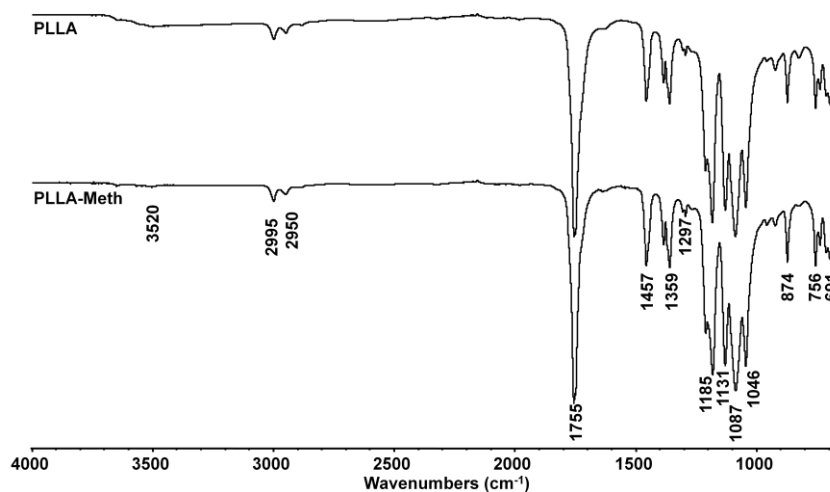
lactide unit, i.e. at 4.36 ppm. The fact that this signal did not completely disappear suggests that not all hydroxyl chain end unit was connecting to the methacrylate. And then this signal was used to calculate the degree of substitution.



**Figure 4.3**  $^1\text{H}$  NMR spectrum of (a) PLLA-Meth and (b) PLLA-diMeth in  $\text{CDCl}_3$

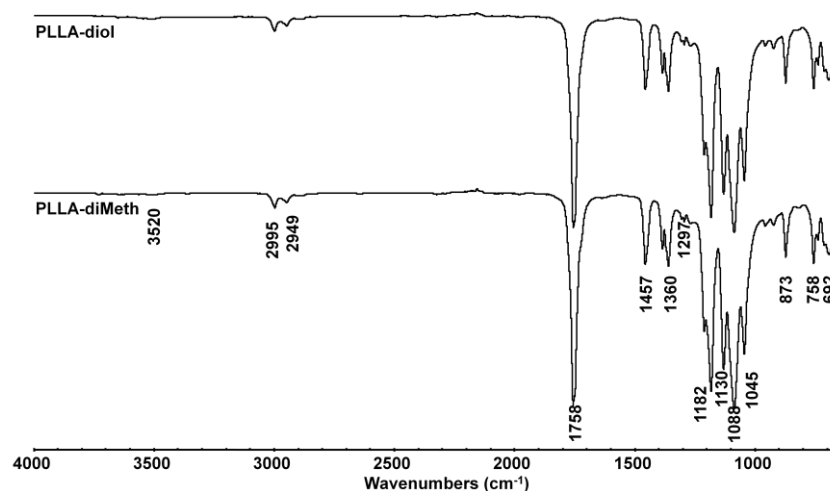
The attachment of methacrylic group on the PLLA chain end was also analyzed by ATR-FTIR (Figure 4.4). Weak absorption bands for hydroxyl groups (OH stretching vibrations) of PLLA chain end can be seen at  $3300\text{--}3600\text{ cm}^{-1}$ . After the reaction with methacrylic anhydride, the intensity of hydroxyl band reduced significantly due to the formation of ester linkage. However, characteristic signals for the double bond ( $\text{C}=\text{C}$ ) in PLLA-Meth did not appear at  $1640\text{ cm}^{-1}$  [5, 15, 25, 26],

possibly because of the relatively low contents compared to other functional groups. Other absorption signals are as follows. PLLA spectrum contains characteristic absorption bands at 2800-2995, 1300-1500 and 756  $\text{cm}^{-1}$  which can be assigned to methyl/methylene groups (stretching and bending vibrations, respectively). The peak at 1755  $\text{cm}^{-1}$  was assigned to carbonyls (C=O stretching) of ester group, and 1185, 1087  $\text{cm}^{-1}$  were attributed to C-O-C stretching.



**Figure 4.4** ATR-FTIR spectra of PLLA and PLLA-Meth

The ATR-FTIR spectra of PLLA-diol and PLLA-diMeth (Figure 4.5) are similar to those of PLLA and PLLA-Meth, respectively. Again the double bond absorption band at 1640  $\text{cm}^{-1}$  also did not appear in this result.



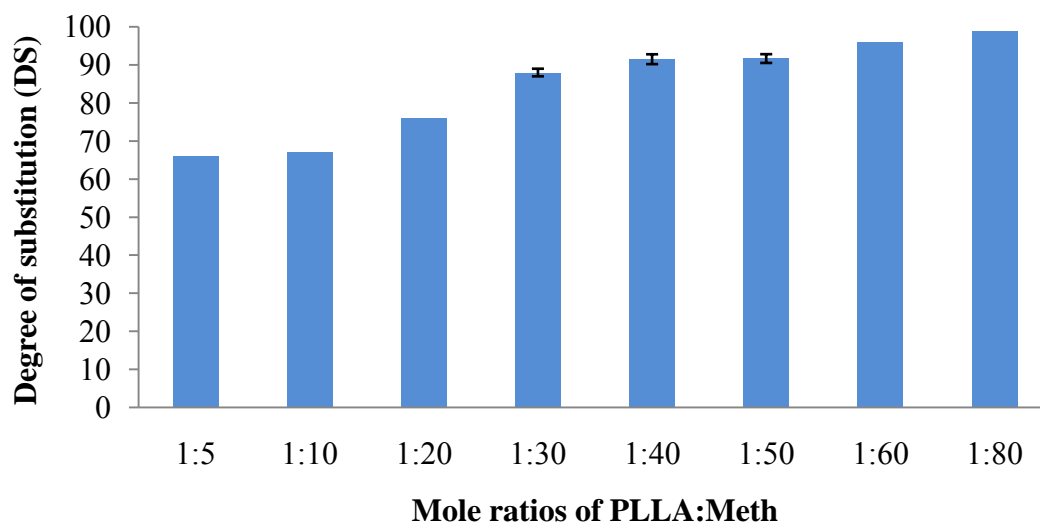
**Figure 4.5** ATR-FTIR spectra of PLLA-diol and PLLA-diMeth

The effect of temperature and catalyst were investigated. The degree of substitution (DS) in PLLA was shown in Table 4.2. It was also found that increasing the temperature from 60 to 80 °C resulted in higher DS and the use of catalyst (TNBT) did not enhance the DS.

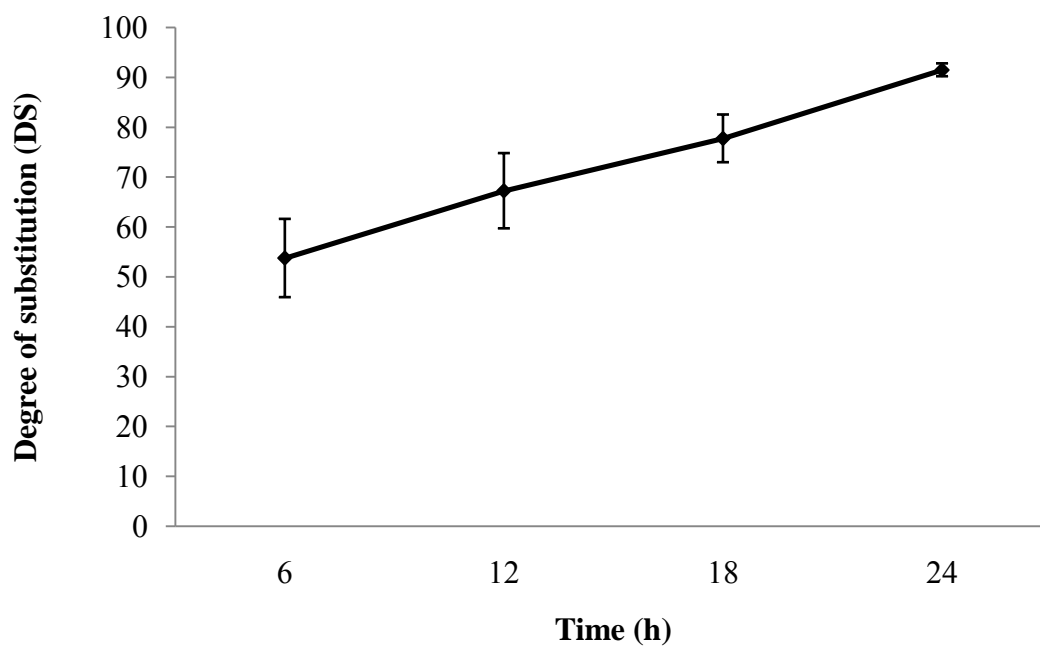
**Table 4.2** Degree of substitution of methacrylate group at the chain end of PLLA (reaction time = 24 h, PLLA:Meth = 1:80 by mole)

<b>Sample</b>	<b>Reaction temperature (°C)</b>	<b>Catalyst</b>	<b>DS (%)</b>
PLLA-Meth 1	60	-	56
PLLA-Meth 2	80	1 mol% TNBT	71
PLLA-Meth 3	80	-	99

Next, optimization the reaction between PLLA and Meth in terms of mole ratios and reaction times shown in Figure 4.6 and 4.7. The mole ratios of PLLA:Meth were varied between 1:5 to 1:80. The result indicated that the mole ratios of 1:40 and higher would give 90% and higher DS. And the reaction time of 24 h was long enough to achieve high degree of methacrylate end-capping. The yield of PLLA-Meth products obtained were 40-60%. This condition was also used to prepare PLLA-diMeth, except that the mole ratio of PLLA-diol to methacrylic anhydride was changed from 1:40 to 1:80, because of the amount of -OH group at the chain end of PLLA-diol were twice that of the PLLA.

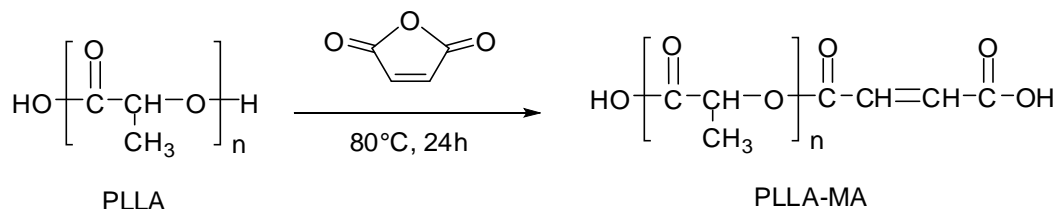


**Figure 4.6** Effect of mole ratios (PLLA:Meth) on the degree of methacrylate substitution on PLLA chain end (reaction time = 24 h, reaction temperature = 80 °C)



**Figure 4.7** Effect of reaction time on the degree of methacrylate substitution in PLLA-Meth (PLLA:Meth = 1:40 by mole, reaction temperature = 80 °C)

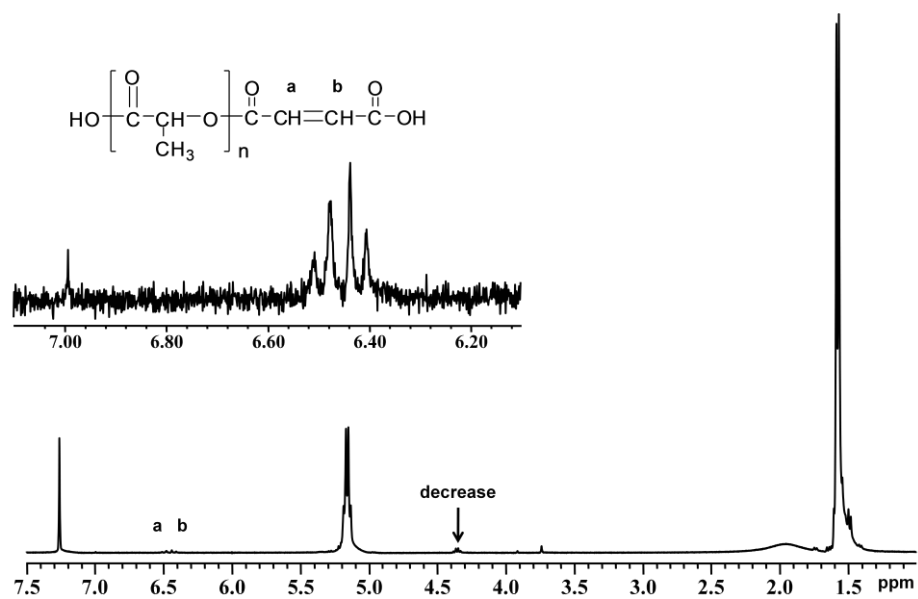
#### 4.1.2.2 Maleate-endcapped PLLA



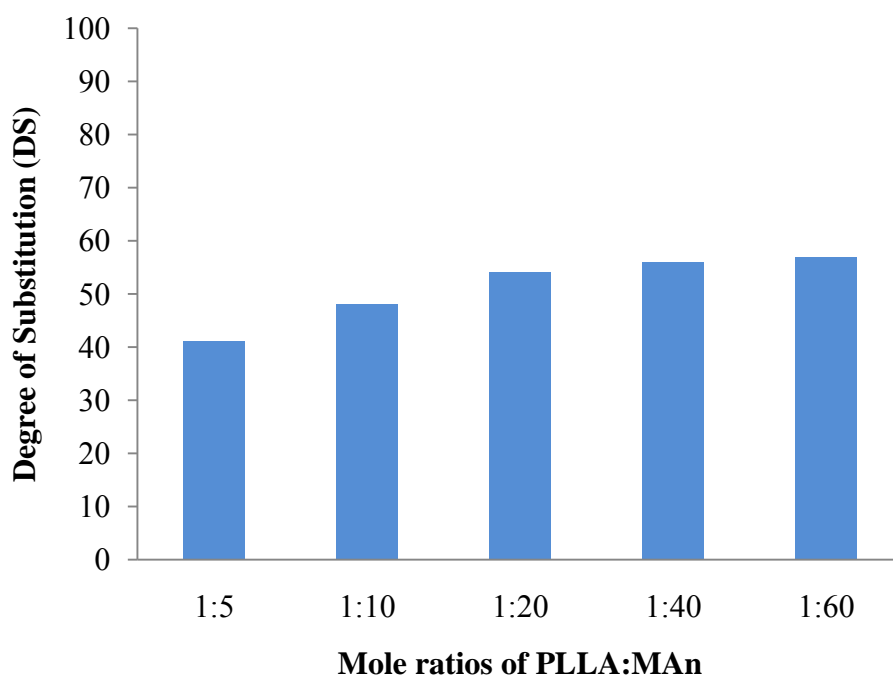
**Scheme 4.5** Synthesis of PLLA-MA from the reaction between PLLA and maleic anhydride

The synthesis of PLLA-MA was performed by using similar approach for synthesizing PLLA-Meth except that maleic anhydride was used as the starting material instead of methacrylic anhydride (Scheme 4.5). Figure 4.8 shows the methine proton of MAn appeared at 7.0 ppm, which is shifted to 6.5 ppm when MAn was end-capped into PLLA chain end as maleate groups. Multiplet proton signals were found as reported by Teramoto *et al.* [27]. The mole ratios of PLLA:MAn were preliminarily varied from 1:5 to 1:60 (Figure 4.9). The trend of DS was 40 to 60% depending on the amount of MAn added in the reaction. Nevertheless the DSs in the resulting PLLA-MA were lower than PLLA-Meth in every mole ratio at the same reaction condition. Therefore, maleic anhydride was not chosen to functionalize the PLLA. However, these condition maybe suitable for preparation of the PLLA-Meth but not for the PLLA-MA. Moreover, Seppälä *et al.* [16] earlier reported that the crosslinking of polyester oligomers with maleic double bond remained low at less than 10%.





**Figure 4.8** <sup>1</sup>H NMR spectrum of PLLA-MA in CDCl<sub>3</sub>



**Figure 4.9** Effect of mole ratios (PLLA:MAN) on the degree of maleate substitution on PLLA chain end (reaction time = 24 h, reaction temperature = 80 °C)

## 4.2 Preparation of polymer network

### 4.2.1 Crosslinking of PLLA

#### 4.2.1.1 Thermal crosslinking

The PLLA-Meth and PLLA-diMeth that have a nearby DS (93 and 92%, respectively) were crosslinked by using 10 wt% BPO as the thermally activated initiator at 150 °C for 1 h. Then the crosslinking was analyzed by dissolution technique in chloroform. After 24 h immersion, the BPO-treated PLLA-Meth was dissolved completely, while the BPO-treated PLLA-diMeth appeared as colorless gel that has 62% gel content (Table 4.3), suggesting crosslinking took place by the radical pathway at the double bonds from the two methacrylate groups at the PLLA chain ends. Interestingly only one double bond per chain in the case of PLLA-Meth did not seem to provide enough crosslinking points to become gel in chloroform.

**Table 4.3** The percentage of gel contents of PLLA-Meth and PLLA-diMeth after immersed in chloroform for 24 h

Sample	Degree of Substitution (DS)	Percentage of gel content (%Gel)
PLLA-Meth	93	Completely dissolved
PLLA-diMeth	92	62

The colorless PLLA-diMeth pellet after crosslinking was shown in Figure 4.10. Small air bubbles and voids caused by rapid solvent evaporation were observed in the polymer pellets. Figure 4.11 shows the colorless gel of PLLA-diMeth that is swollen after chloroform immersion for 24 h. Thus, only the PLLA-diMeth was used to prepare the UV crosslinking and PLLA/PEG semi-IPN.



**Figure 4.10** Photographs of PLLA-diMeth after thermal crosslinking



**Figure 4.11** A Photograph of PLLA-diMeth gel after immersed in chloroform for 24 h

#### **4.2.1.2 UV crosslinking**

The PLLA-diMeth was mixed with 10 wt% Darocure 1173 in chloroform. Then the mixture was poured into a mold and UV-irradiated (253.7 nm, 10 watts) for 10 min to initiate the crosslinking. After that, the mixture was dried under vacuum at room temperature for 24 h, obtaining opaque pellet of PLLA-diMeth (Figure 4.12). The pellet was then analyzed for crosslinking by chloroform immersion test. After 24 h the UV-treated PLLA-diMeth was dissolved in chloroform completely, suggesting that no crosslink was taken place by UV irradiation in the sample prepared. Anticipated that the power of UV lamp might not be enough to initiate the crosslinking, or the UV-irradiated time might be too short. Further investigation is required.

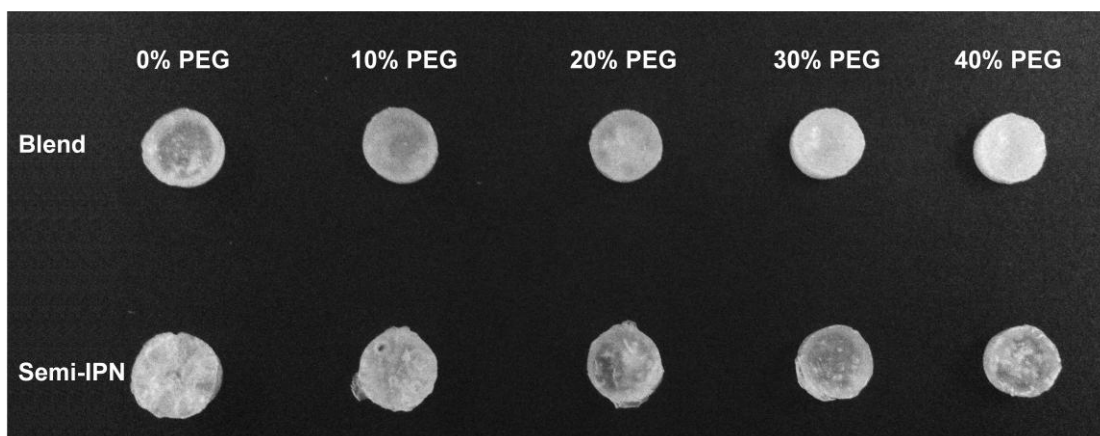


**Figure 4.12** Photographs of PLLA-diMeth after UV crosslinking

#### 4.2.2 Preparation of PLLA/PEG semi-IPN

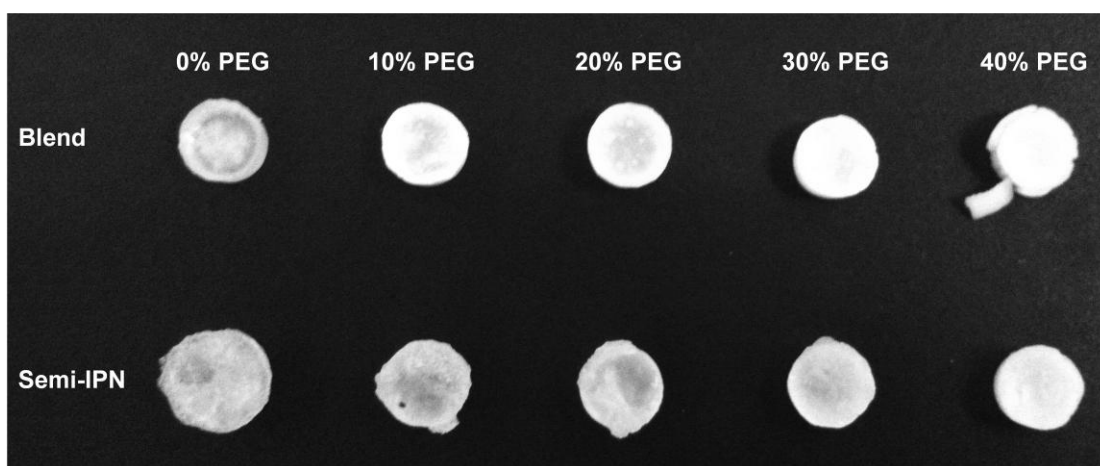
The PLLA-diMeth was mixed with 0-40 wt% PEG and 10 wt% BPO in chloroform to prepare PLLA/PEG semi-IPN. Beside, PLLA-diol was prepared as the same condition without BPO to prepare as PLLA/PEG blend. Then the mixture was poured into a mold and heated at 150 °C for 1 h in an electric oven to initiate the crosslinking and dry the polymer matrix. The pellet of PLLA/PEG semi-IPN and PLLA/PEG blend were obtained.

Figure 4.13 shows photographs of PLLA/PEG semi-IPN and PLLA/PEG blend with varied PEG contents. The transparency of PLLA/PEG pellets were decreased when the PEG content increased. The shapes of semi-IPN were somewhat distorted from the original mold shape, expect to the shrinking effect when the polymer chains were crosslinked. And the mobility of the crosslinked polymers in the mold is more difficult than the non-crosslinked polymers.



**Figure 4.13** Photographs of PLLA/PEG pellets after thermal crosslinking

The photographs of PLLA/PEG after immersed in deionized water for 24 h are shown in Figure 4.14. The crosslinked PLLA and neat PLLA pellet (0 wt% PEG) did not show any change on the appearance. But in the semi-IPN and blend samples with PEG, the pellet becomes more opaque when the PEG content increased (PEG components become white when contact with water). Notice that the PLLA/PEG blend over 40 wt% PEG could not maintain the shape after immersed in deionized water for 24 h. On the other hand, PLLA/PEG semi-IPN remains as pellets because crosslinking can strengthen the PLLA networks.



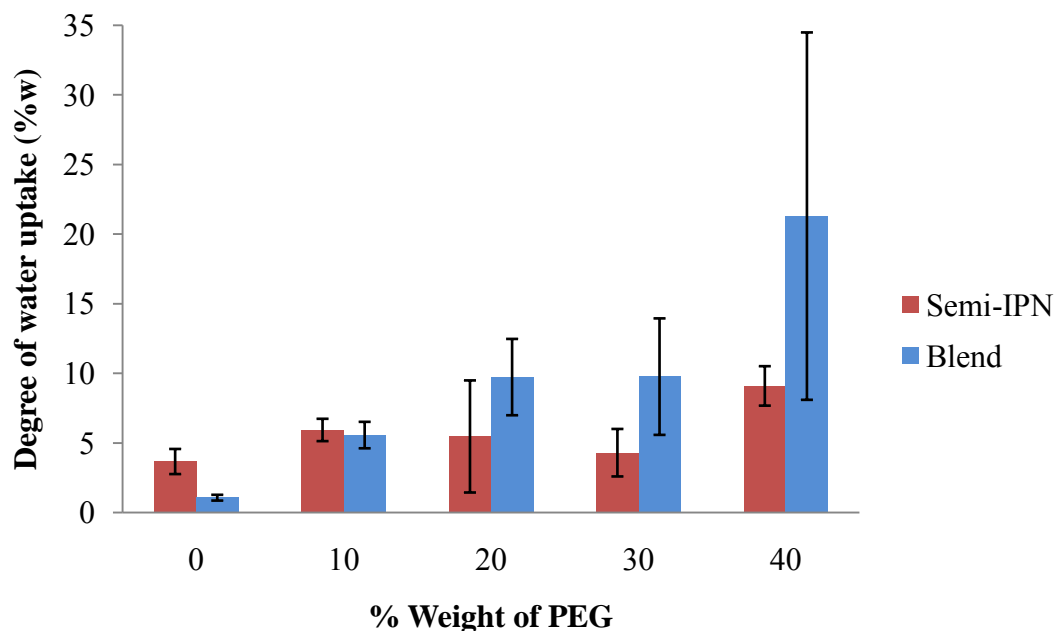
**Figure 4.14** Photographs of PLLA/PEG pellets after immersed in deionized water for 24 h

### 4.3 Properties of PLLA/PEG semi-IPN

#### 4.3.1 Degree of water uptake

PLLA/PEG semi-IPN was compared with PLLA/PEG blend for their water uptake ability (%w) (Figure 4.15). The %w values of the blended polymer increased when PEG content was increased, and was higher than that of semi-IPN polymer. On the other hand, the %w of semi-IPN was increased to a maximum of 9% for the sample containing 40 wt% PEG. Since the blended polymers show extensive cracks (as shown in SEM results), water can penetrate into the polymer matrix more than in the case of the semi-IPN. Although the blended polymers can absorb a large amount of water, it cannot maintain the pellet structure at over 40 wt% PEG, as shown in

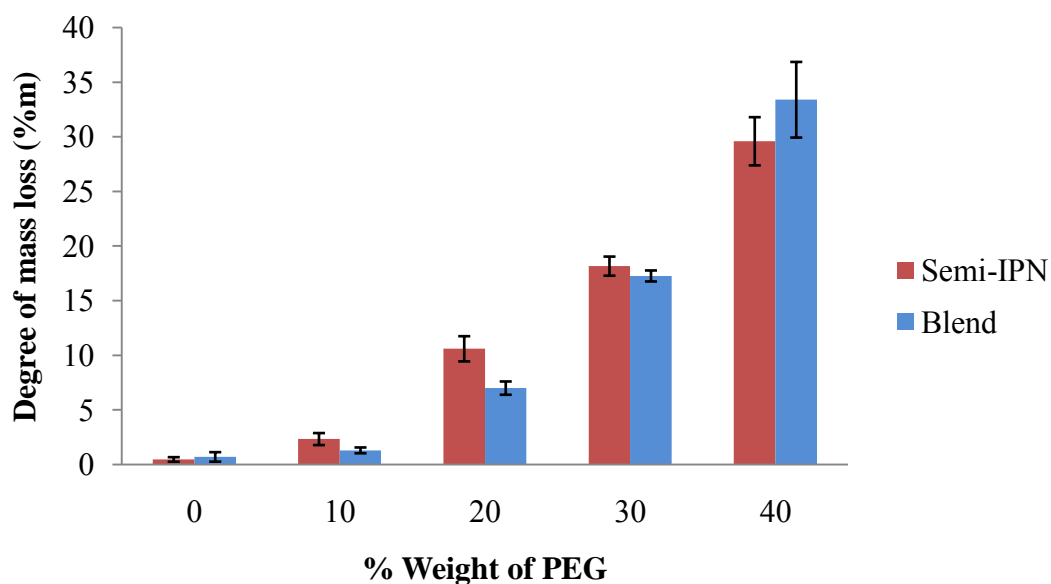
Figure 4.14. The %w of the semi-IPN is lower than that of the blended polymer, because the packing of PLLA networks is higher than the blend.



**Figure 4.15** Degree of water uptake of PLLA/PEG semi-IPN and PLLA/PEG blend after immersed in deionized water for 24 h

#### 4.3.2 Degree of mass loss

Figure 4.16 shows the degree of mass loss (%*m*), compared between the semi-IPN and blended polymer. The %*m* of both polymers increased when the PEG content was increased. The %*m* values of semi-IPN having 0-30 wt% PEG were almost equal to the %*m* of the blended polymers with the same PEG content. However, the %*m* of blended polymer at 40 wt% PEG is higher than that of semi-IPN. It can be explained that the PLLA crosslinked network can maintain the components in the semi-IPN more efficiently than the blended polymer. And the result can be supported by the microscopic result (SEM) in Figure 4.18.



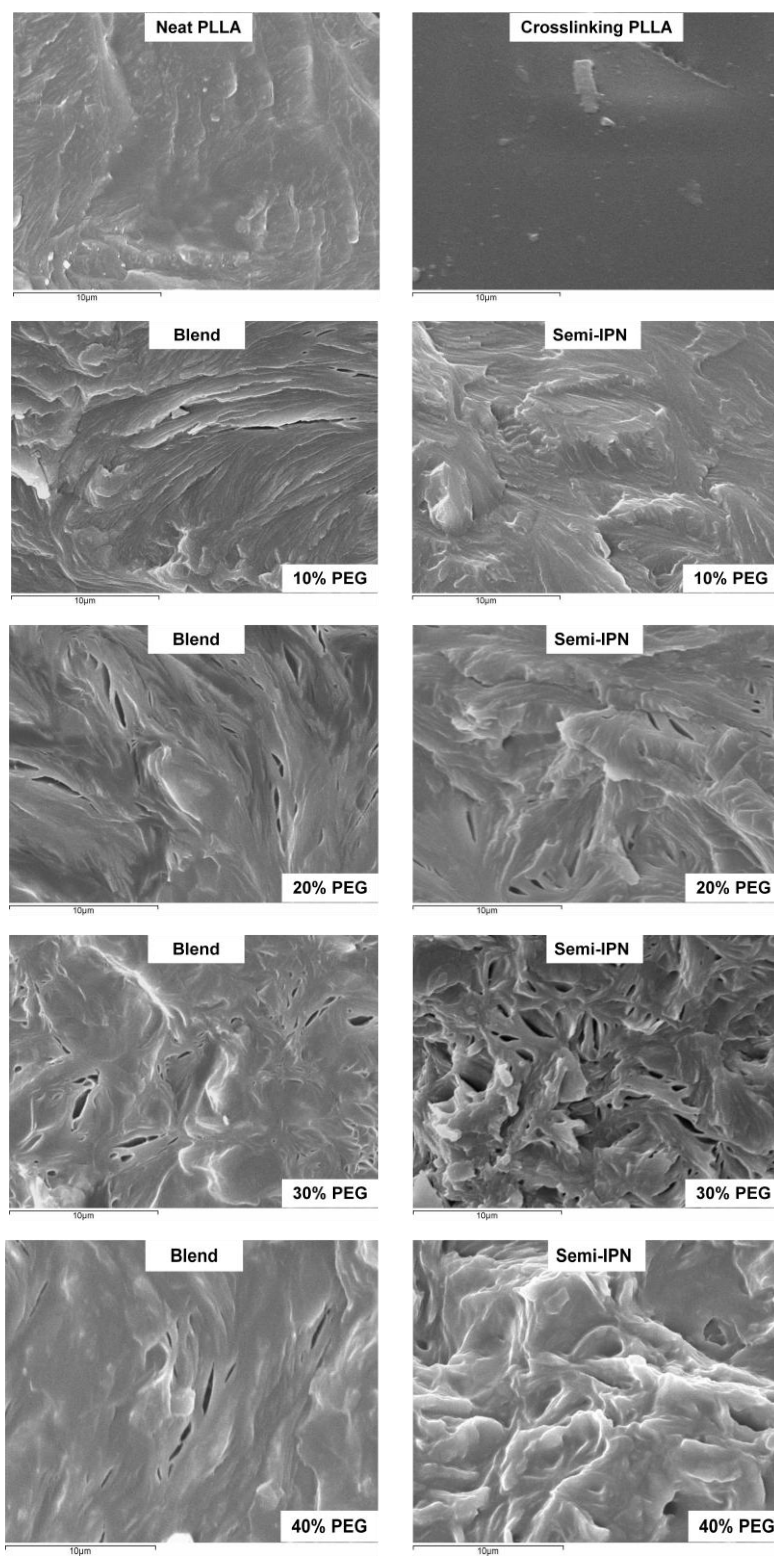
**Figure 4.16** Degree of mass loss of PLLA/PEG semi-IPN and PLLA/PEG blend after immersed in deionized water for 24 h

**Table 4.4** The degree of PEG loss after immersed in deionized water for 24 h

Sample	Degree of PEG loss (% PEG loss)			
	10 wt% PEG	20 wt% PEG	30 wt% PEG	40 wt% PEG
Semi-IPN	23	53	61	74
Blend	13	35	58	84

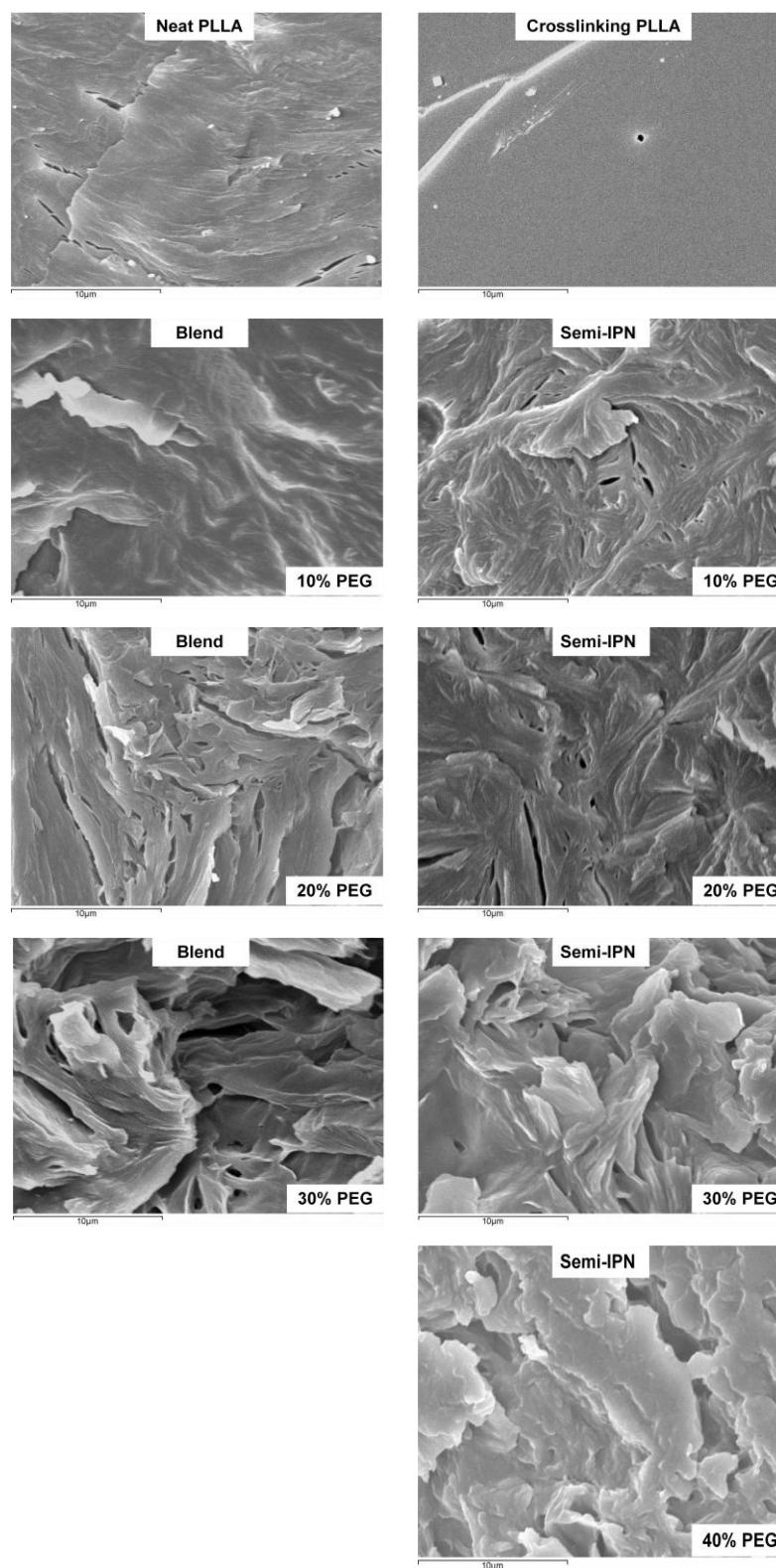
Assuming that the only PEG component was dissolved in deionized water, Table 4.4 shows the PEG content that leaked out of the polymer matrix after 24 h water-contacting time. The PEG content decreased as much as 74% for 40% blended PEG in semi-IPN sample. This indicates that the crosslinked PLLA could not maintain the blended PEG in the network due to high PEG solubility in water.

### 4.3.3 Morphology of polymers



**Figure 4.17** SEM images of PLLA/PEG semi-IPN and PLLA/PEG blend before immersed in deionized water (5,000×)





**Figure 4.18** SEM images of PLLA/PEG semi-IPN and PLLA/PEG blend after immersed in deionized water for 24 h (5,000 $\times$ )

Figure 4.17 shows SEM cross section images of PLLA/PEG semi-IPN and PLLA/PEG blend after thermal crosslinking (before immersed in deionized water). The crosslinked PLLA network formed homogeneous, typical for one component systems. After PEG was mixed with either neat or crosslinked PLLA, immiscibility between the two polymers was clearly observed and increased when the content of PEG was increased. The SEM cross-section images of the samples after immersed in deionized water for 24 h are shown in Figure 4.18. The crosslinked PLLA network did not show any change, but in the neat PLLA samples, small cracks and voids were observed. In the added PEG samples, both semi-IPN and blend of PLLA/PEG show more cracks and voids when the content of PEG was increased. At 40 wt% PEG, the blend sample could not maintain the shape and was shattered to tiny pieces during the cross section step before SEM analysis. Therefore no SEM was obtained from this sample. These results were consistent with the degree of PEG loss in the Table 4.4 which indicated that the semi-IPN could not maintain the PEG content in the network. However, the semi-IPN of PLLA and PEG was found to hold up its shape more than PLLA and PEG blend at high PEG content.

## **CHAPTER V**

### **CONCLUSION**

#### **5.1 Conclusions**

In this work, PLLA network was prepared by radical thermal crosslinking of PLLA-diol ( $M_n = 5,376$  Da) having methacrylate endcapping at both chain ends. The percentage of gel contents incurring after crosslinking of the 92% substitution PLLA-diMeth was 62%. The crosslinking was proceeded with PEG blend in the polymer, resulting in semi-interpenetrating network of crosslinked PLLA and PEG. Immiscibility between the two polymers was clearly observed by SEM images.

The degree of water uptake (%w) in the semi-IPN increased when PEG content was increased after 1-day of water immersion. Unfortunately evidence suggested that, after immersed in water for 1 day, the PEG content decreased as much as 74% (at 40 wt% PEG in the blend). The crosslinked PLLA could not maintain the blended PEG in the network due to high PEG solubility in water. The prepared semi-IPN of PLLA & PEG, however, was found to hold up its shape in water unlike PLLA & PEG blend with the same mass ratio which disintegrated after 1 days.

#### **5.2 Future Direction**

The percentage of gel content in this work is rather low (62%). The crosslinking efficiency should be higher so that PEG components can be entrapped in the PLLA network more efficiently. Thus, the direction to develop this system is to find a way to increase the crosslink (or gel content) by using different initiators, or increase the number of crosslinkable double bonds either on PLLA or PEG molecule.

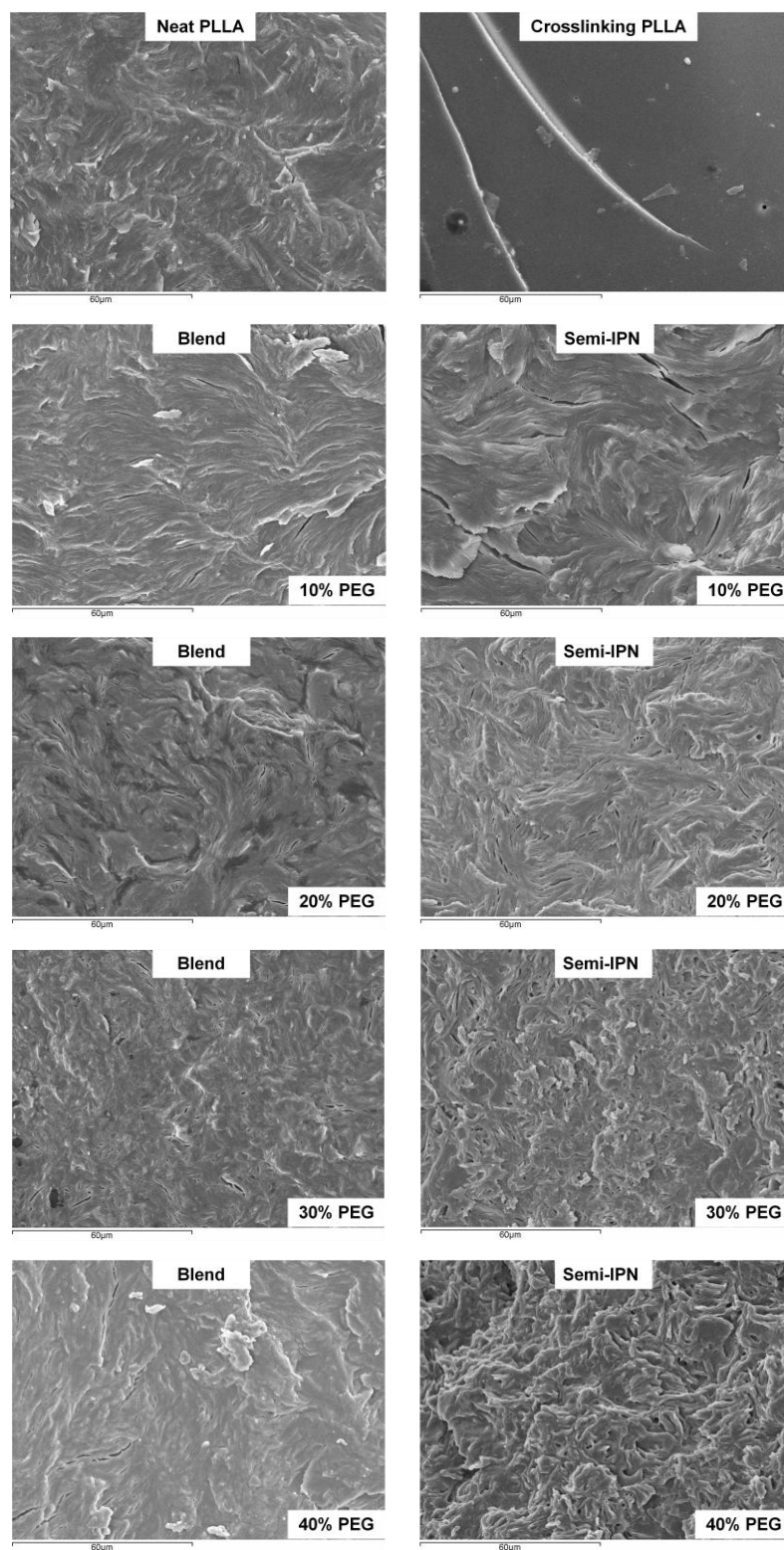
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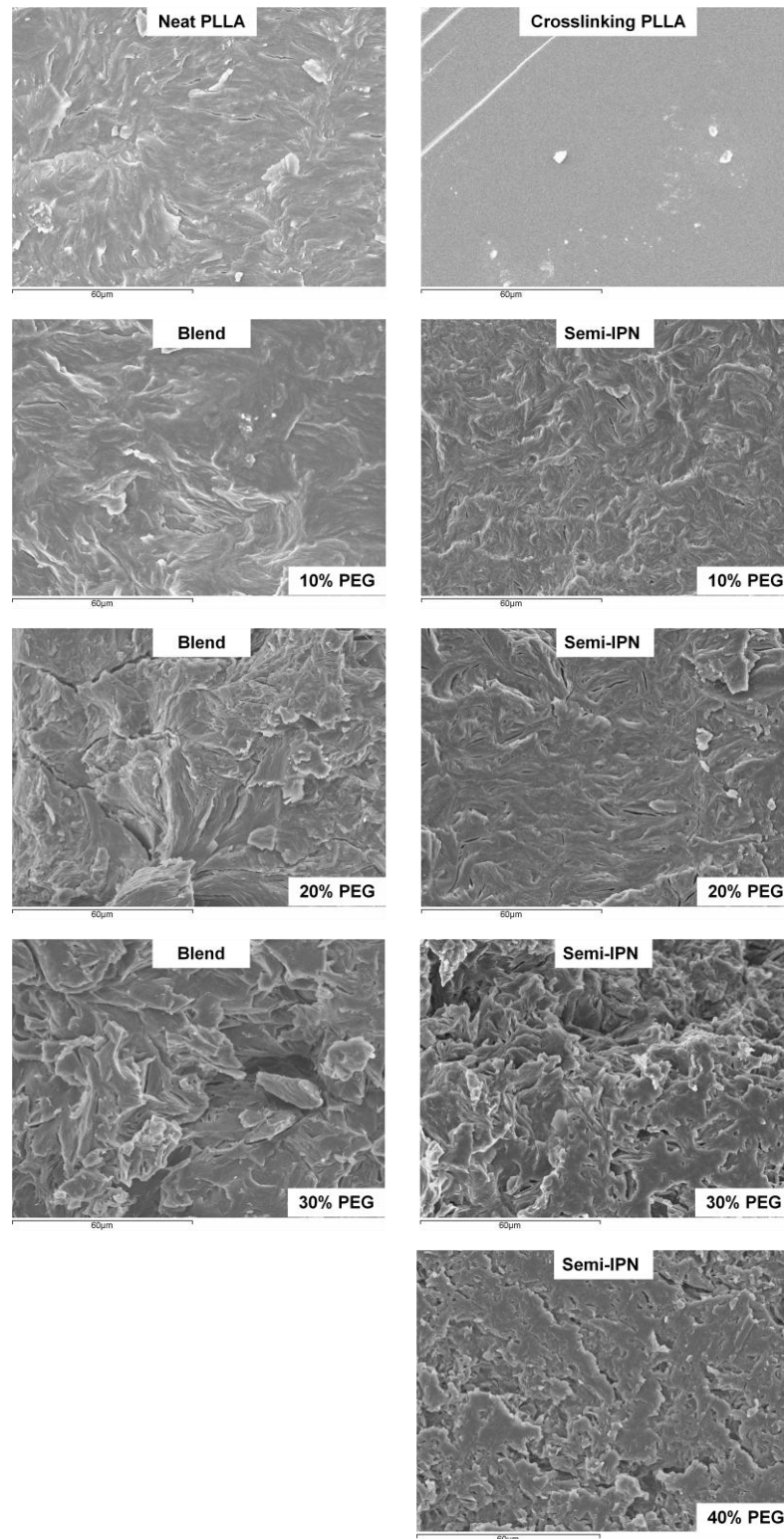
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## **APPENDIX**



**Figure A.1** SEM images of PLLA/PEG semi-IPN and PLLA/PEG blend before immersed in deionized water (1,000 $\times$ )





**Figure A.2** SEM images of PLLA/PEG semi-IPN and PLLA/PEG blend after immersed in deionized water for 24 h (1,000×)

## VITAE

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### **Presentation in Conference:**

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