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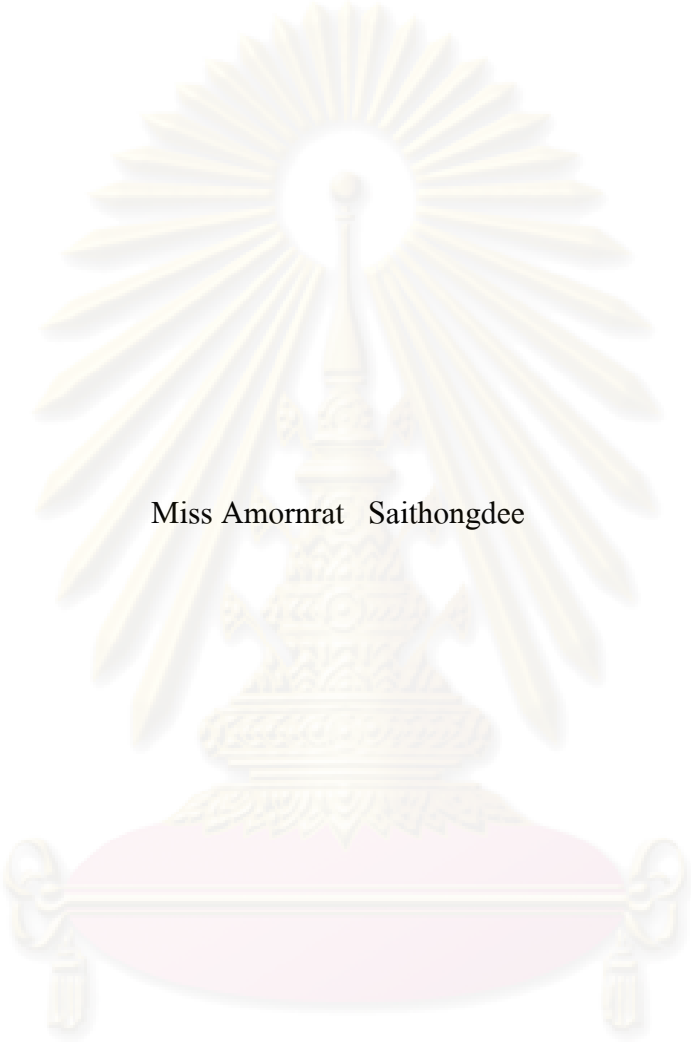
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ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

PREPARATION OF POLY[N-ISOPROPYLACRYLAMIDE-CO-(MALEIC ACID)]  
HYDROGEL MEMBRANE BY ELECTROSPINNING



Miss Amornrat Saithongdee

ศูนย์วิทยุโทรพักร  
A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Petrochemistry and Polymer Science

จุฬาลงกรณ์มหาวิทยาลัย  
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Thesis Title            PREPARATION OF POLY[N-ISOPROPYLACRYLAMIDE-CO-(MALEIC ACID)] HYDROGEL MEMBRANE BY ELECTROSPINNING

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Field of Study            Petrochemistry and Polymer Science

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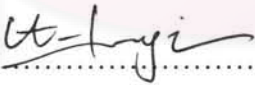
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อมรรัตน์ สายทองดี : การเตรียมเมมเบรนไฮโดรเจลพอลิ[เอ็น-ไอโซโพรพิลอะคริลาไมด์-โค-(มาลิกแอซิด)] โดยการปั่นเส้นใยด้วยไฟฟ้า. (PREPARATION OF POLY[N-ISOPROPYLACRYLAMIDE-CO-(MALEIC ACID)] HYDROGEL MEMBRANE BY ELECTROSPINNING) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ดร.อภิชาติ อิมข้ม, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: อ.ดร.พุทธรักษา วรานุกุล, 84 หน้า.

สังเคราะห์โพลีเมอร์ระหว่างเอ็น-ไอโซโพรพิลอะคริลาไมด์กับกรดมาลิกด้วยกระบวนการเกิดพอลิเมอร์แบบอนุโมลติสระ กรดมาลิกใช้เป็นตำแหน่งสำหรับการเชื่อมขวาง ศึกษาพอลิเมอร์ที่สังเคราะห์ได้คือ การเกิดปฏิกิริยาการเชื่อมขวางกับไดเอทิลีนไกลคอลที่เหนียวทำให้เกิดปฏิกิริยาการเชื่อมขวางแบบเอสเทอร์ฟิเคชัน ด้วยความร้อนที่อุณหภูมิ 145 องศาเซลเซียส เตรียมแผ่นฟิล์มแบบคาสติงแล้วทดสอบการละลาย พบว่าโพลีเมอร์ที่มีการเชื่อมขวางเตรียมได้จากภาวะที่สัดส่วนการเติมโคมอนอเมอร์กรดมาลิก 35 เปอร์เซ็นต์โดยโมลต่อโมล จากสารละลายที่ความเข้มข้น 10 เปอร์เซ็นต์โดยน้ำหนักต่อปริมาตรเอทานอล มีสัดส่วนการผสมสารเชื่อมขวาง ไดเอทิลีนไกลคอล 5 เปอร์เซ็นต์โดยน้ำหนักต่อน้ำหนักแล้วผ่านการเหนียวทำให้เกิดปฏิกิริยาการเชื่อมขวางด้วยความร้อน เป็นวัสดุที่ไม่ละลายน้ำ พอลิเมอร์ที่สังเคราะห์ได้มีผลึกถ่วงเท่ากับ 55 เปอร์เซ็นต์ พิสูจน์เอกลักษณ์ของพอลิเมอร์ได้ด้วยเทคนิคอินฟราเรดและนิวเคลียร์แมกเนติกเรโซแนนซ์สเปกโทรสโกปี และวิธีกรด-เบสไทเทรชัน จากนั้นเตรียมเมมเบรนไฮโดรเจลพอลิ[เอ็น-ไอโซโพรพิลอะคริลาไมด์-โค-(มาลิกแอซิด)] โดยการปั่นเส้นใยด้วยไฟฟ้าจากสารละลายพอลิเมอร์ที่มีการเติมสารเชื่อมขวาง ไดเอทิลีนไกลคอล ศึกษาตัวแปรในการปั่นเส้นใยด้วยไฟฟ้าได้แก่ ค่าศักย์ไฟฟ้า และระยะทางระหว่างหัวเข็มถึงแผ่นรองรับที่มีผลต่อสัณฐานวิทยาและขนาดเส้นผ่านศูนย์กลางของเส้นใยไฮโดรเจลเมมเบรนพอลิ[เอ็น-ไอโซโพรพิลอะคริลาไมด์-โค-(มาลิกแอซิด)] ด้วยกล้องจุลทรรศน์อิเล็กตรอนแบบส่องกราด โดยทำการเปลี่ยนแปลงค่าศักย์ไฟฟ้าที่ใช้ตั้งแต่ 15 ถึง 30 กิโลโวลต์ และระยะห่างระหว่างหัวเข็มถึงแผ่นรองรับตั้งแต่ 10 ถึง 25 เซนติเมตร ภาวะที่เหมาะสมในการผลิตเมมเบรนไฮโดรเจลคือใช้ศักย์ไฟฟ้า 25 กิโลโวลต์ และระยะทางระหว่างหัวเข็มถึงแผ่นรองรับ 25 เซนติเมตร โดยใช้หัวเข็มขนาดเส้นผ่านศูนย์กลาง 0.80 มิลลิเมตร ที่อัตราการไหล 1 มิลลิลิตรต่อชั่วโมง ได้ขนาดเส้นผ่านศูนย์กลางของเส้นใย  $117 \pm 33$  นาโนเมตร พิสูจน์เอกลักษณ์ของเมมเบรนไฮโดรเจลที่มีการเชื่อมขวางแบบเอสเทอร์ฟิเคชันได้ด้วยเทคนิคอินฟราเรดสเปกโทรสโกปี เมมเบรนไฮโดรเจลมีสมบัติการดูดซึมน้ำที่ตอบสนองต่อการเปลี่ยนแปลงอุณหภูมิ มีค่าการดูดซึมน้ำต่ำสุดและสูงสุด เท่ากับ  $4 \pm 0$  กรัมต่อกรัมน้ำหนักพอลิเมอร์แห้งที่อุณหภูมิ 50 องศาเซลเซียส และ  $17 \pm 4$  กรัมต่อกรัมน้ำหนักพอลิเมอร์แห้งที่อุณหภูมิ 34 องศาเซลเซียส โดยที่อุณหภูมิต่ำกว่าอุณหภูมิที่ทำให้พอลิเมอร์ไม่รวมตัวกับน้ำ (34 องศาเซลเซียส) เมมเบรนละลายในน้ำ ซึ่งแตกต่างจากแผ่นฟิล์มที่เตรียมแบบคาสติง ซึ่งไม่ละลายน้ำ

จุฬาลงกรณ์มหาวิทยาลัย

สาขาวิชาปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์ ลายมือชื่อนิสิต อมรรัตน์ สายทองดี

ปีการศึกษา 2552

ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก 

ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์ร่วม 

# # 507 25569 23 : MAJOR PETROCHEMISTRY AND POLYMER SCIENCE

KEY WORD : POLY[*N*-ISOPROPYLACRYLAMIDE-*CO*-(MALEIC ACID)]/ HYDROGEL/  
ELECTROSPINNING

AMORN RAT SAITHONGDEE: PREPARATION OF POLY[*N*-ISOPROPYLACRYLAMIDE-*CO*-(MALEIC ACID) HYDROGEL MEMBRANE BY ELECTROSPINNING.  
THESIS ADVISOR: ASST.PROF. APICHAT IMYIM, Ph.D., THESIS CO-ADVISOR:  
PUTTARUKSA VARANUSUPAKUL, Ph.D., 84 pp.

A copolymer of *N*-isopropylacrylamide (NIPA) and maleic acid (MA) acting as sites for the crosslinking was synthesized via free radical polymerization. Copolymer films of the synthesized copolymer by casting technique were fabricated, and then crosslinked with diethylene glycol DEG acting as crosslinker by a heat-induced esterification crosslinking reaction at 145 °C. The solubility in water of the films was tested. The crosslinked copolymer film synthesized from molar feed ratio of 35%mol/mol (MA comonomer/NIPA monomer) in copolymerization process and 10%wt/v (synthesized copolymer in ethanol) with 5%wt/wt (crosslinking agent DEG/copolymer), followed by a heat-induced crosslinking reaction was water-insoluble material. The yield of the synthesized copolymer was 55%. The copolymer was characterized by infrared and nuclear magnetic resonance spectroscopy and acid-base titration. Consequently, a new poly[*N*-isopropylacrylamide-*co*-(maleic acid)], poly(NIPA-*co*-MA) hydrogel membrane was fabricated by electrospinning the polymer solution. The effects of electrospinning parameters (e.g. applied voltage and distance between the needle and the collection screen) on the morphology and diameter of poly(NIPA-*co*-MA) hydrogel fibrous membranes were investigated by scanning electron microscopy. The range of the applied voltage studied was from 15 to 30 kV and the distance between the needle and the collection screen studied was from 10 to 25 cm. The optimal condition for fabrication of hydrogel membrane was the applied voltage at 25 kV and distance between the needle and the collection screen at 25 cm using a diameter of needle at 0.80 mm and the flow rate of 1 mL hour<sup>-1</sup>. The average diameter of electrospun fibers was 117±33 nm. The hydrogel membrane which has esterification crosslinked was characterized by Infrared spectroscopy. The hydrogel membrane showed temperature sensitive property. Its minimum and maximum water absorption ratio was 4±0 g g<sup>-1</sup> at 50 °C and 17±4 g g<sup>-1</sup> at 34 °C, respectively. The electrospun membrane dissolved in water at the temperature below the lower critical solution temperature (LCST, 34°C), while the cast film did not.

Field of Study : Petrochemistry and Polymer Science Student's Signature Amornrat Saithongdee

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# CONTENTS

	<b>page</b>
ABSTRACT (IN THAI).....	iv
ABSTRACT (IN ENGLISH).....	v
ACKNOWLEDGEMENTS.....	vi
CONTENTS.....	vii
LIST OF TABLES.....	x
LIST OF SCHEMES.....	xi
LIST OF FIGURES.....	xii
LIST OF SYMBOLS AND ABBREVIATIONS.....	xiv
<b>CHAPTER I INTRODUCTION.....</b>	<b>1</b>
1.1 Statement of the Problem.....	1
1.2 Objectives.....	3
1.3 Scope of the Research.....	3
1.4 The Benefits of This Research.....	4
<b>CHAPTER II THEORY AND LITERATURE REVIEW.....</b>	<b>5</b>
2.1 Hydrogels.....	5
2.1.1 Smart Hydrogels.....	8
2.1.2 Hydrogel Nanofibers.....	11
2.2 Poly( <i>N</i> -isopropylacrylamide) and its Copolymer.....	15
2.2.1 Chemical and Physical Properties.....	15
2.2.2 Preparation Poly( <i>N</i> -isopropylacrylamide) and its Copolymer.....	18
2.2.2.1 Non-Crosslinked Poly(NIPA) and its Copolymer.....	18
2.2.2.2 Crosslinked Poly(NIPA) and its Copolymer.....	21

	<b>page</b>
2.3 Electrospinning Technique.....	23
2.3.1 Basic Setup and Mechanisms.....	23
2.3.2 Factors Affecting Morphology of Electrospun Fibers.....	27
2.3.3 Crosslinked Nanofibers.....	28
2.4 Literature Review.....	29
<b>CHAPTER III EXPERIMENTAL SECTIONS.....</b>	<b>33</b>
3.1 Chemicals.....	33
3.2 Apparatuses.....	34
3.3 Synthesis of Poly[ <i>N</i> -isopropylacrylamide- <i>co</i> -(maleic acid)].....	35
3.4 Investigation of Monomer Feed Ratios of Copolymer on Crosslinking Reaction with Diethylene Glycol.....	36
3.5 Characterization of Copolymer.....	37
3.5.1 Fourier Transforms Infrared Spectrometer (FT-IR).....	37
3.5.2 Nuclear Magnetic Resonance Spectrometer (NMR).....	37
3.5.3 Acid-base Titration.....	37
3.6 Electrospinning and Esterification Crosslinking of Copolymer.....	38
3.6.1 Preparation of Copolymer Solution in the Presence of Diethylene Glycol.....	38
3.6.2 Electrospinning Process and Esterification Crosslinking Reaction..	39
3.7 Characterization of Electrospun Copolymer Hydrogel Membrane.....	40
3.7.1 Scanning Electron Microscope (SEM).....	40
3.7.2 Fourier Transforms Infrared Spectrometer (FT-IR).....	40
3.8 Water Absorption Measurement.....	41
<b>CHAPTER IV RESULTS AND DISCUSSION.....</b>	<b>42</b>
4.1 Synthesis of Copolymer.....	42



	<b>page</b>
4.2 Characterization of Copolymer.....	51
4.2.1 Fourier Transforms Infrared Spectroscopy (FT-IR).....	51
4.2.2 Nuclear Magnetic Resonance Spectroscopy (NMR).....	53
4.2.3 Acid content.....	54
4.3 Electrospun Copolymer Hydrogel Membrane.....	58
4.3.1 Morphology of Copolymer Hydrogel Membrane.....	59
4.3.2 FT-IR Spectrum of Copolymer Hydrogel Membrane.....	65
4.4 Water Absorbing Behavior of Copolymer Hydrogel Membrane in Different Temperatures.....	68
<b>CHAPTER V CONCLUSION AND SUGGESTIONS.....</b>	<b>71</b>
5.1 Conclusion.....	71
5.2 Suggestions for Future Work.....	73
<b>REFERENCES.....</b>	<b>74</b>
<b>VITA.....</b>	<b>84</b>

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF TABLES

<b>Table</b>	<b>page</b>
2.1 Factors affecting polymer hydrogels swelling.....	7
2.2 Comparison of processing techniques for obtaining nanofibers.....	14
2.3 Advantages and disadvantages of various processing techniques.....	14
3.1 Chemicals list.....	33
3.2 Apparatuses list.....	34
3.3 Synthesis conditions of copolymers.....	35
3.4 Parameters of mixture solutions.....	36
4.1 Solubility of crosslinked poly(NIPA- <i>co</i> -MA) film with varying the proportion of mixture solutions after water immersion at room temperature for 24 hours.....	45
4.2 Yield of synthesized poly(NIPA- <i>co</i> -MA) with 35%mol/mol MA in feed.....	48
4.3 Composition of MA in poly(NIPA- <i>co</i> -MA) by acid-base titration...	57
4.4 Quantitative analysis of electrospun poly(NIPA- <i>co</i> -MA) fibers containing DEG.....	64
4.5 Analysis of FT-IR absorption peaks of the crosslink poly(NIPA- <i>co</i> -MA) membrane in comparison with those of the cast film.....	67
4.6 Temperature-responsive water absorption ratio of poly(NIPA- <i>co</i> -MA) hydrogel membrane and film.....	70

จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF SCHEMES

<b>Scheme</b>		<b>page</b>
2.1	Mechanism of phase transition inversion of poly(NIPA) in aqueous solutions by temperature.....	16
2.2	Mechanism of initiator by the redox couple of APS and TEMED for free radical polymerization.....	20
4.1	Synthesis of poly(NIPA-co-MA).....	43
4.2	Crosslinking of poly(NIPA-co-MA) with DEG.....	44



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คุฑาลงคอรณัฑมหาวิทฑยาลัย

## LIST OF FIGURES

<b>Figure</b>		<b>page</b>
2.1	Schematic routes for synthesis of hydrogels.....	6
2.2	The swelling mechanism of polymer hydrogels.....	7
2.3	Typical response of smart hydrogels to swell variations in environmental conditions on a change in the swelling ratio.....	10
2.4	The structure and the physical/chemical properties of <i>N</i> -isopropylacrylamide monomer.....	15
2.5	The structure and the physical/chemical properties of maleic acid monomer.....	17
2.6	The basic setup for electrospinning.....	23
2.7	Trajectory of the jet in the instable area.....	25
2.8	The bending perturbations of the jet.....	26
2.9	The effect of process parameters on fiber diameters.....	28
3.1	Schematic of the electrospinning process.....	40
4.1	Images of crosslinked poly(NIPA- <i>co</i> -MA) film cast from mixture solution at 35%mol/mol MA in feed, 5%wt/wt DEG and 10%wt/v of copolymer (A) before, (B) after immersing in water at room temperature for 24 hours.....	47
4.2	The weight loss of crosslinked poly(NIPA- <i>co</i> -MA) film prepared from 35%mol/mol MA in feed solution with varying amount of DEG and concentration of copolymer in EtOH after water immersion at room temperature for 24 hours.....	50
4.3	FT-IR spectrum of poly(NIPA- <i>co</i> -MA).....	52
4.4	FT-IR spectrum of poly(NIPA).....	52
4.5	<sup>1</sup> H-NMR spectrum of poly(NIPA- <i>co</i> -MA).....	54

<b>Figure</b>		<b>page</b>
4.6	SEM images of electrospun poly(NIPA- <i>co</i> -MA) fibers containing DEG, original magnifications of 3,500.....	62
4.7	SEM images of electrospun poly(NIPA- <i>co</i> -MA) fibers containing DEG, original magnifications of 20,000.....	63
4.8	FT-IR spectrum of crosslinked poly(NIPA- <i>co</i> -MA) membrane.....	66
4.9	FT-IR spectrum of crosslinked poly(NIPA- <i>co</i> -MA) film.....	66
4.10	Images of crosslink-poly(NIPA- <i>co</i> -MA) hydrogel membrane containing 5%wt/wt DEG; (A) at 34 °C, (B) at 35 °C and (C) at 50 °C	70



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF SYMBOLS AND ABBREVIATIONS

APS	Ammonium peroxodisulfate
°C	Degree Celsius
cm	Centimeter
DEG	Diethylene glycol
EtOH	Ethanol
FT-IR	Fourier transforms infrared spectroscopy
g	Gram
kV	Kilovoltage
LCST	Lower critical solution temperature
MA	Maleic acid
mg	Milligram
mL	Milliliter
min	Minute
μL	Microliter
NIPA	<i>N</i> -Isopropylacrylamide
nm	Nanometer
NMR	Nuclear magnetic resonance spectroscopy
%	Percent
SEM	Scanning electron microscopy
SD	Standard deviation
TEMED	<i>N,N,N',N'</i> -Tetramethylethylenediamine
wt/v	Weight by volume
wt/wt	Weight by weight

# CHAPTER I

## INTRODUCTION

### 1.1 Statement of the Problem

Hydrogel is a crosslinked polymer. It is capable of swelling and absorbing much water to maintain within its structure which remains three-dimension polymer networks. In recent year, many research considered and paid attention to smart hydrogel which can alter its swelling behavior with only small changes of external environment such as temperature [1-3], pH [4-5], ionic strength [6-7], solvent [8], light [9] and electric field [10], *etc.* Much attention has been focused especially on the temperature-sensitive character of hydrogel since it is controlled only by physical environmental stimuli. Because unrequirement of any addition of chemical or extra materials, it is environmentally friendly.

Poly(*N*-isopropylacrylamide) or poly(NIPA) is the most popular of the temperature-responsive hydrogel. It has a lower critical solution temperature (LCST) in water around 31–34 °C [11]. Below the LCST, the gel is swelling caused by favorable polymer-water interaction *via* hydrogen bonding as the hydrophilic state. Above the LCST, the gel is shrinking caused by breaking of hydrogen bonds as the hydrophobic state. Consequently, it can potentially applied for many applications such as chemical separation process [12-13], sensors [14], drug delivery devices [15] and tissue engineering scaffold [16-17]. Recently, many researches on poly(NIPA) have been studied and the innovation of the smart hydrogels materials have been developed [18-21]. The good shape material has a large specific surface which response quickly to external stimuli, and easy to handle. Therefore, the production of the good shape materials is the important key for the most successful application of smart hydrogel.

Electrospinning or electrostatic spinning is a simple technique but versatile to produce nanofiber with diameters ranging from sub-micrometers down to nanometers. The fibers are intervene each other and cause non-woven fabric or membrane. Therefore, it has very large surface-to-volume, length-to-diameter ratios and porosity. Besides, the size of the porous that are produced between non-woven fabric are very small [22-23]. It can produce the good shape of a hydrogel. The electrospinning process uses the electrostatic force which is the main driving force for fiber formation. In the process, a high voltage power supply is used to charge between a polymer solution or melt through a metal contact. When the electrostatic repulsion on the surface of the fluid overcomes the surface tension, a jet is ejected from the tip of syringe to the collection screen. After the solvent evaporates, solid nanofibers are produced. When it produces continuously on the surface of the collection screen, the non-woven fabric or membrane is obtained. However, hydrogel membrane is impossible to generate directly hydrogel nanofibers by electrospinning because it is crosslinked polymer network which are neither soluble nor meltable. Therefore, the crosslinking membrane has to apply with special treatment techniques such as Heat-induced crosslinking [24-25], UV-visible radiation-induced crosslinking [26] and an *in-situ* photo-induced polymerization [27]. Heat-induced crosslinking attracts more and more interest because it is an inexpensive and simple method. Esterification is a very common and thermoreactive reaction. It is much popular used to crosslinking reaction post-fabricated membrane. It has been reported that carboxylic acid groups on the polymer backbone of copolymers work as a site crosslink that react with diol as a crosslinking agent. A crosslinking agent can be along with the copolymer by electrospining. Afterwards membrane is activated by heat at 145 °C in order to induce esterification crosslinking reaction [28-29]. It also calls “heat-induced esterification crosslinking reaction”. The hydrogel membranes are obtained as a result.



Therefore, this research is aimed to prepare poly[*N*-isopropylacrylamide-*co*-maleic acid)] hydrogel membrane by electrospinning, followed by a heat-induced esterification crosslinking reaction at 145 °C for 10 min that consisted of the maleic acid moieties in the polymer backbone as sites for the crosslinking, diethylene glycol as a crosslinker and heat as activator for the crosslinking reaction.

## 1.2 Objectives

1.2.1 To prepare poly[*N*-isopropylacrylamide-*co*-(maleic acid)] hydrogel membrane by electrospinning.

1.2.2 To investigate morphology of electrospun fibers.

1.2.3 To study the water absorbing behavior of copolymer hydrogel membranes in different temperature.

## 1.3 Scope of the Research

The scope of this research includes:

1.3.1 Synthesis of poly[*N*-isopropylacrylamide-*co*-(maleic acid)] *via* free radical polymerization in aqueous solution by varying the monomer feed ratios of copolymer.

1.3.2 Investigation of suitable conditions for crosslinking reaction as to obtain water insoluble material by casting film, followed by a heat-induced esterification crosslinking reaction. The following parameters were studied: the effect of feed molar ratio of maleic acid in the copolymerization process, the effect of the amount of crosslinking agent diethylene glycol and the effect of concentration of polymer solution.

1.3.3 Characterization of the synthesized copolymer by Fourier Transforms Infrared Spectroscopy (FT-IR), Nuclear Magnetic Resonance Spectroscopy (NMR) and Acid-base titration.

1.3.4 Preparation of electrospun copolymer hydrogel membrane by electrospinning and a subsequent heat-induced crosslinking reaction. Finding suitable electrospinning processing on the morphology and diameter of poly(NIPA-co-MA) hydrogel fibrous membrane and studying the following parameters: the effect of electric potential and the effect of distance between needle and collection screen.

1.3.5 Characterization of electrospun copolymer hydrogel membrane by Scanning Electron Microscopy (SEM), Fourier Transforms Infrared Spectroscopy (FT-IR) and Water Absorption Measurement.

## 1.4 The Benefits of This Research

In this research, the new copolymer membrane which has hydrogel nanofibers property was achieved.

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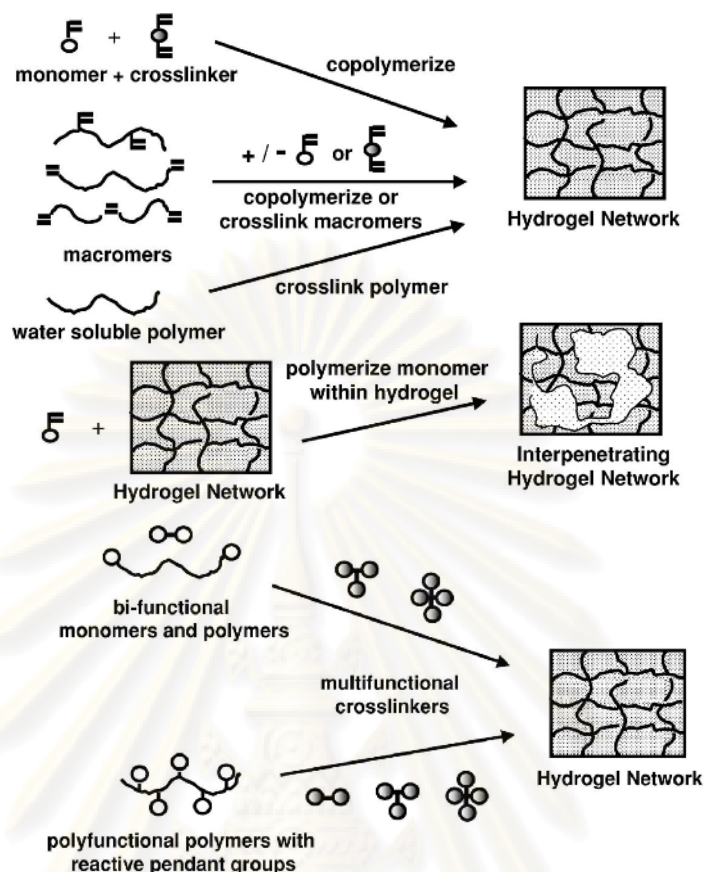
## CHAPTER II

### THEORY AND LITERATURE REVIEW

#### 2.1 Hydrogels

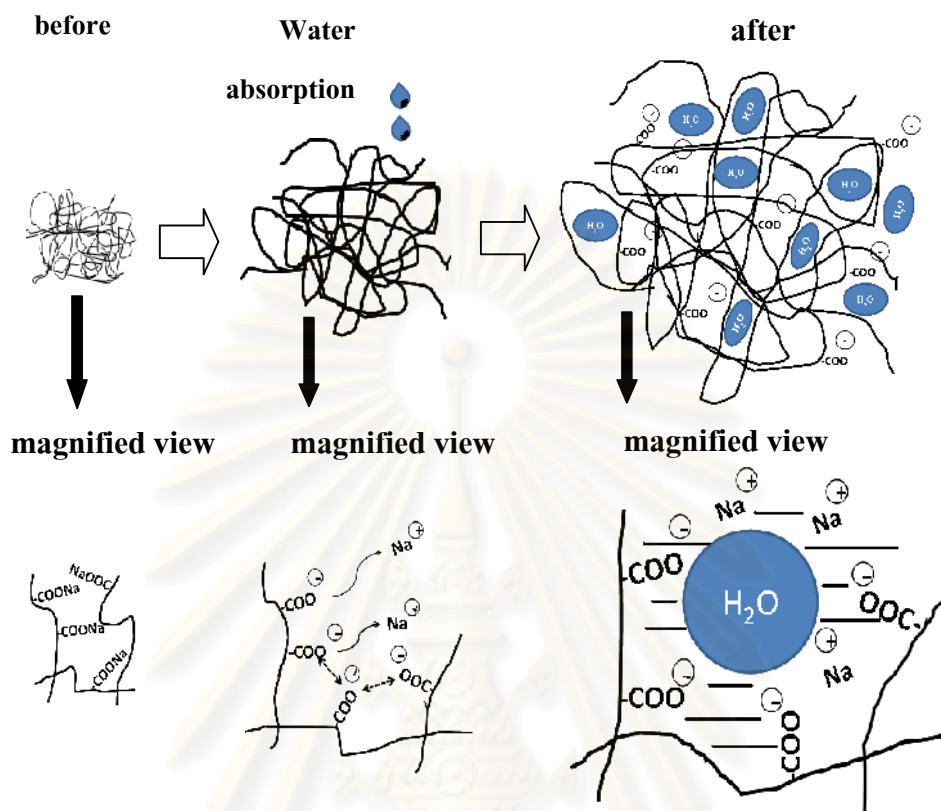
Hydrogels are hydrophilic polymer networks that absorb water in quantities that cause macroscopic volume changes while maintaining the structure [30]. The hydrophilicity of the gels is due to the presence of water-solubilizing groups such as -OH, -COOH, -CONH<sub>2</sub>, -CONH-, -SO<sub>3</sub>H, and so on, along the polymer chains. The stability of the gels is due to the presence of three-dimensional network which comes from connecting of polymer chains by crosslinking. Chemically cross-linked hydrogels or chemical gels are cross-linked by covalent bonds and do not dissolve in water in any conditions while physically cross-linked hydrogels can be reversible in shape because they are cross-linked through noncovalent bonds such as hydrogen bonds, physical entanglements, charged complexes, or vander Waals or hydrophobic interactions. These physical hydrogels can show sol-gel reversibility [31]. The volume phase transition of the gels has drawn significant attention since their discovery.

Hydrogels which are produced either from monomers or macromers or polymers can be prepared by various methods which have been synthesized both in solution and in bulk state such as copolymerizing a hydrophilic monomer with crosslinker, polymerizing a monomer within hydrogel network and crosslinking water soluble polymer by chemical, irradiation or thermal treatments, *etc* [31]. Many different routes have been used to synthesize hydrogels (physical or chemical gels) and they are summarized in Figure 2.1. The product of hydrogels can be in the form of particle, powder, fiber, membrane, beads and even liquid or emulsion, *etc*.



**Figure 2.1** Schematic routes for synthesis of hydrogels [31].

Swelling in water is one of the inherent properties hydrogels. Figure 2.2 shows the swelling mechanism of polymer hydrogels. In contact with water, the hydrophilic backbone interacts through hydration and hydrogen bonding leading to the molecular chain expansion, as well as energy decrease and entropy increase. After the hydrophilic backbones have interacted and bound with water molecules, the network will imbibe water due to the osmotic driving force of the network. As the hydrophilic backbones are hydrated that lead to the swollen network. However this swelling is opposed by the crosslink which possesses an elastic network retraction force. When there is a balance between the trend toward infinite dilution of the chains and the retraction forces, the hydrogel will reach an equilibrium swelling level which has a balance between dispersive (repulsive) and cohesive (attractive) force acting simultaneously [32]. Factors affecting the swelling of polymer hydrogels are listed in Table 2.1.



**Figure 2.2** The swelling mechanism of polymer hydrogels [32].

**Table 2.1** Factors affecting polymer hydrogels swelling [33]

<i>Increase swelling</i>	<i>Decrease swelling</i>
Repulsive forces	Attractive forces
Hydrophilic groups	Hydrophobic groups
Low crosslinking density	High crosslinking density
High chain flexibility	Low chain flexibility
High free volume	Low free volume
Osmotic pressure	Dipole-dipole interaction
Electrostatic repulsion	Impurities in the fluid

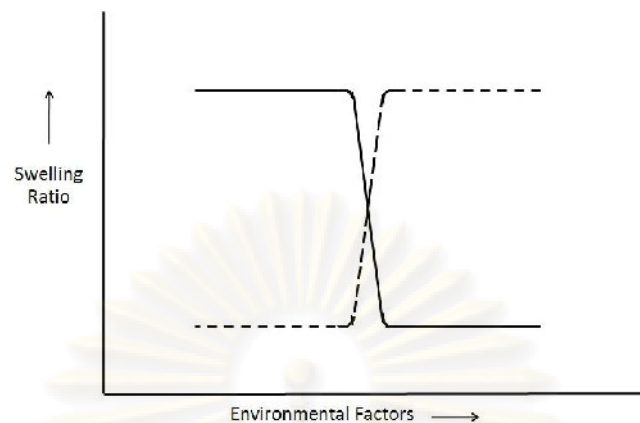
### 2.1.1 Smart Hydrogels

Smart (or intelligent) hydrogels are the types of environmentally sensitive hydrogels. They can reversibly change volume in response to slight external change in some environmental conditions. Many different stimuli have been applied to produce various responses of the smart hydrogel systems. These stimuli can be classified as either physical or chemical stimuli [34]. Chemical stimuli, such as pH, ions and chemical agents, will change the interactions between polymer chains or between polymer chains and solvents at the molecular level. The physical stimuli, such as temperature, electric or magnetic fields, light and pressure, will affect the level of various energy sources and alter molecular interactions at critical onset points. For convenience, smart hydrogels are called according to the types of stimuli. The most commonly studied smart hydrogels are focused on temperature- and pH- sensitive hydrogels.

**Temperature-sensitive hydrogels.** The temperature-sensitive (also called thermosensitive or thermoresponsive) hydrogels undergo volume collapse (or shrinkage) upon heating above a certain temperature. The thermosensitive property comes from the monomers that have the lower critical solution temperature (LCST) phenomenon in the uncrosslinked homopolymer form in aqueous solution. The most commonly used LCST monomers are *N*-substituted acrylamide derivatives, such as *N*-isopropylacrylamide, *N,N*-diethylacrylamide, and *N*-cyclopropylmethacrylamide because they are easy to obtain or prepare. The main interaction during LCST monomers is hydrophobic in nature, and it is enhanced as the temperature increases due to the breaking of hydrogen bonds among water molecules surrounding the hydrophobic moieties [34]. Thus, the hydrogels are made of LCST monomers. The hydrogels collapse at temperatures higher than the LCST and swell again at temperature lower than the LCST.

**pH-sensitive hydrogels.** The pH-sensitivity of hydrogels results from the presence of weak acid or base functionality on the polymer backbone. Commonly used weak acids are acrylic acid, methacrylic acid, and styrene sulfonate. A frequently used weak base is dimethylaminoethyl methacrylate [30]. The window of pH-sensitive hydrogels shows substantial volume change that depends on the type of weak acid and base used. If hydrogels contain weak acid functionality, they will swell in a weakly alkaline medium but collapse in an acidic medium. On the other hand, hydrogels containing weak bases, they will swell in an acid medium but collapse in alkaline medium. Polyampholytic hydrogel, with both acidic and basic groups, swell at the maximum extent at neutral pH, and shrink in acidic or alkaline medium [35].

The response of smart hydrogels to environmental changes is usually measured by changes in the hydrogel volume. The volume change of hydrogels is commonly measured by the swelling ratio which is the ratio of the volume (or weight) of the swelling hydrogel to the volume (or weight) of the dried hydrogel. When weight is used to calculate the swelling ratio, it is referred to the weight degree of swelling [30]. Figure 2.3 shows a typical response of smart hydrogels to swell under variations in environmental conditions on a change in the swelling ratio. It is an unique qualification of smart hydrogels to be applied in various disciplines, such as in the separation processes (including microfiltration, ultrafiltration, gas permeation, pervaporation, dialysis, and reverse osmosis), in the biomedical field (including diagnostic, therapeutic, and implantable devices), and in the biomedical and pharmaceutical field (including controlled drugs delivery, tissue culture substrates, enzyme activity controlling systems, and implantable devices).



**Figure 2.3** Typical response of smart hydrogels to swell under variations in environmental conditions on a change in the swelling ratio [30].

Although smart hydrogels have many exciting properties but these properties hydrogels will be developed continuously especially the responses time of hydrogels since the responses of whose hydrogels to changes in environmental factors are too slow but most applications of smart hydrogels require fast response times [30]. It is very important to manipulate the smart hydrogels to respond as quickly as possible upon receiving environmental signals. The fast response time is the key for the successful application of smart hydrogels in various disciplines. The response time also depends on the size of the hydrogels; smaller hydrogels have faster responses to environmental factors [36]. Thus, the preparation of hydrogel on a nanometer or sub micrometer sizes are interesting to develop responses time of hydrogels. It is prime candidates for smart hydrogels use. In addition, in order to develop smart hydrogels, it is also necessary to consider other several factors such as structural rigidity, biocompatibility, handling and cost.



### 2.1.2 Hydrogel Nanofibers

Hydrogel nanofibers represent a fast-swelling class of hydrogel because of one-dimensional (1D) nanostructures in the form of fiber. A "fiber" from a geometry is generally defined as a slender, elongated, threadlike object or structure that has a high length/width ratio and a small cross-section [35]. A term "nano" used technically and it refers to physical quantities within the scale of a billionth ( $10^{-9}$ ) of the reference unit; for example nanometer, nanosecond and nanogram for describing a billionth of a meter (length), second (time) and gram (weight), respectively. Therefore the nanofiber is on a scale of nanometers in view of its diameter. It can be made several amazing characteristics such as very large surface area to volume and length-to-diameter ratios, a flexibility in surface functionalities, superior mechanical properties (e.g. stiffness and tensile strength) compared with conventional form of the material [37]. These outstanding properties make the hydrogel nanofibers to be optimal candidates for many important applications, especially in work highly requiring a super-large surface area material.

Polymeric nanofibers can be produced by a number of techniques such as drawing, template synthesis, phase separation, self-assembly and electrospinning.

**Drawing.** The drawing is a process which can make one-by-one very long single nanofibers. However, only a viscoelastic material that can undergo strong deformations while being cohesive enough to support the stress developed during pulling fabricating nanofibers through the process of mechanical drawing. A micropipette with a diameter of a few micrometers is dipped into the droplet near the contact line. The micropipette is then withdrawn from the liquid and moved at a speed of approximately  $1 \times 10^{-4} \text{ m s}^{-1}$ , resulting in a nanofiber by pulling [38]. The pulled fiber is deposited on the surface by touching it at the edge of the micropipette. The drawing of nanofibers is repeated several times on every droplet. The viscosity of the material at the edge of the droplet is increased by evaporation. In the final stage of evaporation

of the droplet, the solution is concentrated at the edge of the droplet and broken in a cohesive manner. Therefore the nanofibers are successfully drawn.

**Template synthesis.** The template synthesis, as the name suggests, uses a template or mold to obtain a desired material or structure. For nanofiber creation, the template refers to a metal oxide membrane with thickness pores of nano-scale diameter or a nanoporous membrane [38]. The application of water pressure on one side and restraining from the porous membrane causes extrusion of the polymer and then it becomes a solidifying solution and gives nanofibers whose diameters are determined by the pores. On the other hand, this method cannot make one-by-one continuously nanofibers.

**Phase separation.** The phase separation is another method for producing a nanofibrous foamed material. This procedure consists of several steps: raw-material dissolution, gelation, extraction using a different solvent, freezing and drying [38]. The main mechanism in this process is the separation of phases due to physical incompatibility. The first phase is solvent which is extracted, and then leaves behind the other remaining phase as the porous nanofibrous structure. However, this method takes relatively long period of time to transfer the solid polymer into the nano-scale porous foam.

**Self-assembly.** In general, self-assembly is a process in which molecules or supramolecular aggregates, organizes and arranges themselves into an ordered structure through weak and noncovalent bonds [39-40]. For obtaining nanofibers, self-assembly refers to the build-up of nano-scale fibers using smaller molecules as basic building blocks. A small molecule is arranged in a concentric manner that bonds can form among the concentrically arranged small molecules whose extension in the plane gives normally the longitudinal axis of a nanofiber [38]. The main mechanism for a generic self-assembly is the intermolecular forces that bring together the smaller units

or the shape of the smaller units of molecules which produce finally the complete shape of the macromolecular nanofiber.

**Electrospinning.** The electrospinning (also known as electrostatic spinning) is a process that utilizes electrical force to create nanofibers from polymer solutions or polymer melt [41]. When the electrical force overcomes the surface tension, fluid is thrown out in the form of fine jets. The jet is electrically charged and the charge permits the fibers to bend in such a way that every time the polymer fiber is looped and its diameter is reduced. Finally, the solvent evaporates or the melt solidifies. As result very long fibers are produced often in the form of a non-woven mat.

A comparison of the various issues relating to these processing techniques can be found in Table 2.2 and 2.3. Among these techniques, electrospinning is the simplest and versatile way to fabricate very fine continuous polymer fibers that form a non-woven structure. The electrospun nanofibrous membrane exhibits several attractive attributes such as high porosity, pore sizes ranging from sub-micron to several micrometers, a large surface area per unit volume and light weight. The high porosity is due to the entanglement of nanofibers where all the pores (or the void space) are fully interconnected [42-43]. Moreover, electrospinning offers not only a clear path to industrial scale up but also low cost effect. In conclusion, nanofibers can assure that they develop highly efficiently smart hydrogel properties on the basic of shape and they can be produced by electrospinning.

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**Table 2.2** Comparison of processing techniques for obtaining nanofibers [38]

<i>Process</i>	<i>Technological advances</i>	<i>Can the process be scaled?</i>	<i>Repeatability</i>	<i>Convenient to proceed</i>	<i>Control on fiber dimensions</i>
Drawing	Laboratory	X	√	√	X
Template Synthesis	Laboratory	X	√	√	√
Phase Separation	Laboratory	X	√	√	X
Self-Assembly	Laboratory	X	√	X	X
Electrospinning	Laboratory, Industrial	√	√	√	√

X = No, √ = Yes

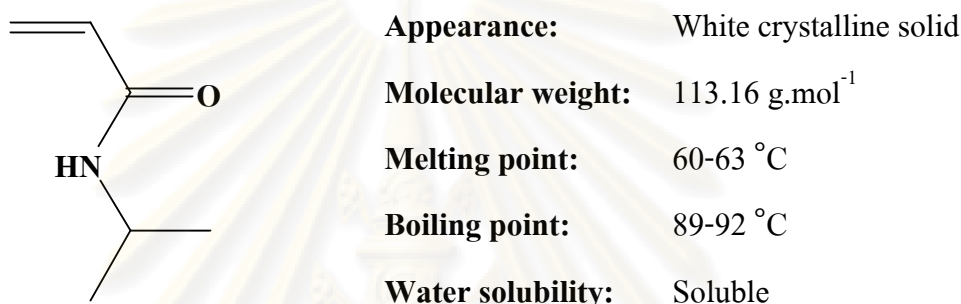
**Table 2.3** Advantages and disadvantages of various processing techniques [38]

<i>Process</i>	<i>Advantages</i>	<i>Disadvantages</i>
Drawing	Minimum equipment requirement	Discontinuous process
Template Synthesis	Fiber of different diameters can be easily achieved by using different templates.	Discontinuous process
Phase Separation	Minimum equipment requirement. Process can directly fabricate a nanofiber matrix. Batch-to-batch consistency is achieved easily.	Limited to specific polymers
Self-Assembly	Good for obtaining smaller nanofibers.	Complex process
Electrospinning	Cost effective. Long, continuous nanofibers can be produced.	Jet instability

## 2.2 Poly(*N*-isopropylacrylamide) and its Copolymer

### 2.2.1 Chemical and Physical Properties

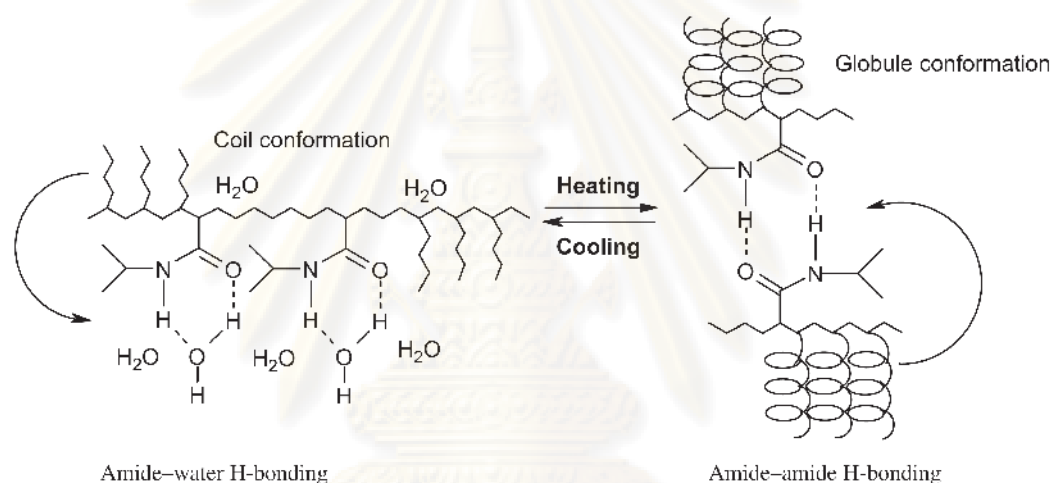
Poly(*N*-isopropylacrylamide) or poly(NIPA) is the most popular hydrogel of the temperature-sensitive hydrogels. The structure and the physical/chemical properties of *N*-isopropylacrylamide monomer are shown in Figure 2.4.



**Figure 2.4** The structure and the physical/chemical properties of *N*-isopropylacrylamide monomer [44].

Poly(NIPA) has a lower critical solution temperature (LCST) at the degree between 32-34 °C. It exhibits hydrophilicity and hydrophobicity in aqueous solution at temperature lower and higher than the LCST respectively. At low temperatures, a strong hydrogen bonding between hydrophilic groups (CO and NH) on the polymer backbone of poly(NIPA) and the surrounding water will cause the formation of a highly organized water layer around the polymer chains [45-46]. With increasing temperature, the weakened hydrogen bonding leads to a reduction in the structure of water around the hydrophobic (CH<sub>2</sub> and CH<sub>3</sub>) groups on the polymer backbone and on the side chain and it will make water released because the interactions between hydrophobic side groups of the polymer increase. Scheme 2.1 presents the mechanism of phase transition inversion of poly(NIPA) in aqueous solutions by temperature.

This mechanism explains that poly(NIPA) chains are extremely soluble in water and appear transparent when the temperature is lower than its LCST but they are precipitated from aqueous solution and appear turbid when the temperature is higher than its LCST. If poly(NIPA) possesses a three dimensional network structure, it is insoluble but it has characteristics of reversible swelling: at a temperature lower than the LCST, the poly(NIPA) hydrogel absorbs water in its network and exhibits a swollen state, but it shrinks and displays a decreased volume when the temperature is higher than the LCST [47-48].

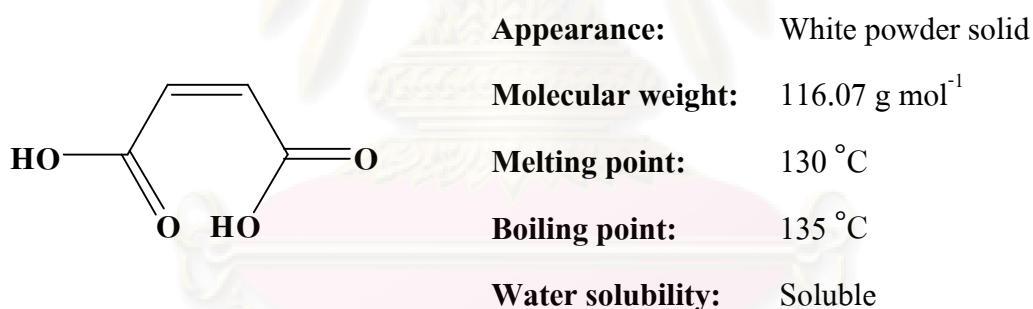


**Scheme 2.1** Mechanism of phase transition inversion of poly(NIPA) in aqueous solutions by temperature [17].

For poly(NIPA) copolymers, they are incorporation between NIPA monomer and various comonomers that may cause shift of LCST and swelling behavior since there is changing the critical hydrophilic/hydrophobic balance of NIPA [47]. Generally, incorporation of NIPA with a more hydrophobic comonomer leads to a decrease of LCST; contrarily, if incorporation of NIPA with a more hydrophilic or an ionizable comonomer leads to an increase of LCST. This shift can be controlled by the number of comonomer in the polymer. For example, Fares *et al.* (2008) [49]

synthesized thermosensitive *N*-isopropylacrylamide-*alt*-2-hydroxyethyl methacrylate copolymer. The lower critical solution temperatures (LCSTs) were verified and determined for different molar feed ratios on NIPA and HEMA monomers with ultraviolet spectroscopy and differential scanning calorimetry techniques. They found that the LCST of various Poly(NIPA-*alt*-HEMA) molar ratios first increased as result of increasing NIPA content from 35 °C [pure poly(HEMA)] to a maximum value of 36.7 °C at 50%mol/mol NIPA, and then it declined to 33 °C, the LCST of pure poly(NIPA). This behavior was attributed to the increase in the hydrophobicity as the NIPA content (%mol/mol) increased. Therefore, the LCST could be controlled by incorporation of hydrophobic or hydrophilic moieties.

In this work, maleic acid was selected as a comonomer. The structure and the physical/chemical properties of maleic acid monomer are shown in Figure 2.5.



**Figure 2.5** The structure and the physical/chemical properties of maleic acid monomer [50]

The maleic acid (MA) comonomer is available and representative of vinyl monomer with dicarboxylic acid groups. They are chemically active because carboxylic acid group can react with alcohols by dehydration. It is a heat-induced esterification crosslinking reaction. For example, poly(vinyl alcohol) (PVA) can react

with poly(styrene sulfonic acid-*co*-maleic acid) (PSSA\_MA) at 120-140 °C [51]. Thus it is believed that the introduction of a small percentage of maleic acid moieties into the backbone of poly(NIPA) may have two potential benefits for the preparation and properties of a poly(NIPA) hydrogel nanofiber. First, it provides sites for the crosslinking reaction with diols since as a rule, all multifunctional compounds capable of reacting with carboxylic acid groups can be used to obtain three-dimension network in poly(NIPA). Second, it can increase their swelling capacity that is increasing the number of ionic groups in the hydrogels which produces an additional osmotic pressure.

### **2.2.2 Preparation Poly(*N*-isopropylacrylamide) and its Copolymer**

There are many routes to prepare non-crosslinked and crosslinked poly(*N*-isopropylacrylamide) or poly(NIPA) and its copolymer

#### **2.2.2.1 Non-Crosslinked Poly(NIPA) and its Copolymer**

Preparation of linear poly(NIPA) and its copolymer can be used by several methods such as radical copolymerization, controlled living radical copolymerization and graft copolymerization, *etc.* For all these techniques, free-radical initiated polymerization is a widely used technique for the synthesis of poly(NIPA) and its copolymer [17]. It allows various vinyl comonomers, monomer contains a carbon double bond, to incorporate with the polymer backbone. The comonomers which have been synthesized *via* copolymerization of NIPA are unsaturated monocarboxylic acids, unsaturated dicarboxylic acids and their anhydrides, acrylamides, and heterocyclic monomer. This polymerization reaction occurs by polymerization chain growth mechanism and it has mainly three basic reaction types occurring simultaneously during polymerization: initiation reactions that generate continuously radicals, propagation reactions that are responsible for the growth of polymer chain by monomer addition to a radical center and termination reactions between the radical

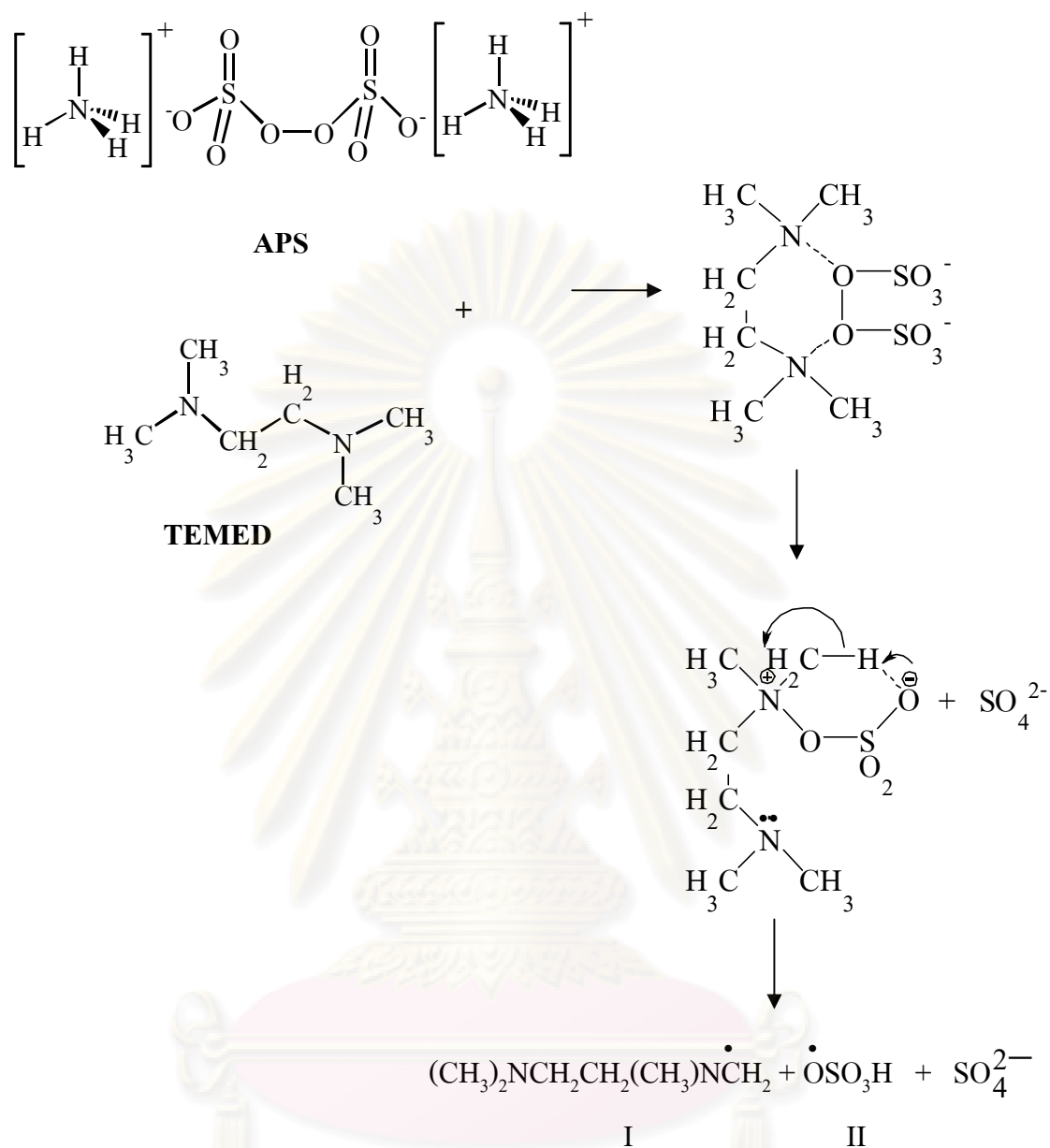


centers that give a net combination of radical [52]. Initiator provide free radicals that may come from thermal degenerator or reduction-oxidation (redox) reaction or a combination of these. Thermal initiators include peroxides and azo compounds that cleavage according to temperature. The redox systems compose of reducing agents such as *N,N,N',N'*-tetramethylenediamine (TEMED), ferrous salts, or sodium metabisulfite, and oxidizing agents such as ammonium persulfate or hydrogen peroxide. These polymerizations are usually performed in organic solvents using peroxide-type initiators or in aqueous solutions using redox initiation systems [53]. In aqueous systems, the poly(NIPA) and its copolymer can be synthesized by using the redox couple of ammonium peroxydisulfate (APS) and *N,N,N',N'*-tetramethylene diamine (TEMED) as typically initiated at room temperature (Scheme 2.2) and it can be carried out in aqueous media by elevating the temperature above the LCST [54-55].

Compared to other polymerization techniques, free radical polymerization presents several advantages such as less sensitive to impurities because it is not sensitive to water, easy to control *via* heat transfer and low cost for equipments.



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**Scheme 2.2** Mechanism of initiator by the redox couple of APS and TEMED for free radical polymerization [56].

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### 2.2.2.2 Crosslinked Poly(NIPA) and its Copolymer

Poly(NIPA) and its copolymer hydrogel can be prepared by a variety of methods. But they are divided into two main ways of making hydrogels or three dimension crosslinked structure: crosslinking during polymerization of monomer and post polymerization whose crosslinking is finished after linear polymer processing [57]. The crosslinking during polymerization by using divinyl crosslink agent which is added to obtain a three dimension crosslinked structure and which contains the double bonds such as ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, and tetraethylene glycol dimethacrylate. Alternatively, the crosslinking post polymerization, linear polymer can be crosslinked by an appropriate multifunctional chemical reagent or by gamma or electron beam irradiation or heat as activator to form hydrogels.

Compared to non-crosslinked poly(NIPA), crosslinked poly(NIPA) is of particular interest to make a poly(NIPA) hydrogel for many applications such as chemical separation process, sensors, drug delivery devices and tissue engineering scaffold but non-crosslinked poly(NIPA) is readily water soluble that limits the application of a poly(NIPA).

Although a conventional poly(NIPA) hydrogels that have basic shape (rod, dish, films) materials have shown swelling characteristics, they have exhibited a poor response and reversibility to changes in temperatures. The slow response to temperature variations associated with the differences in morphology and sizes of hydrogels are major restricts its application. A fast response is necessary for most applications. In recent years, many reports appear continuously in the literature on the study and modification of the innovation of the basic shape (rod, dish and film) materials used in several techniques in order to develop the response time of poly(NIPA) hydrogels.

Zhang *et al.* (2000) [18] prepared a new poly(*N*-isopropylacrylamide) [poly(NIPA)] gel by using polyethylene glycol with a molecular weight of 400 as the pore-forming agent during the polymerization reaction. This poly(NIPA) gel had a significant large swelling ratio at a temperature below the LCST and exhibits a fast deswelling rate as the temperature was increased above the LCST.

Choi *et al.* (2000) [21] prepared a novel separation system by using porous thermosensitive membranes. The pore surfaces of a porous substrate were covered with a thermosensitive *N*-isopropylacrylamide grafted polymer, which enabled the hydrophobicity of the pore surface to be dramatically varied by a slight change in temperature. The membrane was made by a plasma-graft-filling polymerization technique.

Kim *et al.* (2002) [58] prepared porous alginate/poly(NIPA) comb-type graft hydrogels using NaCl particles as a porogen in order to improve the swelling and deswelling rate.

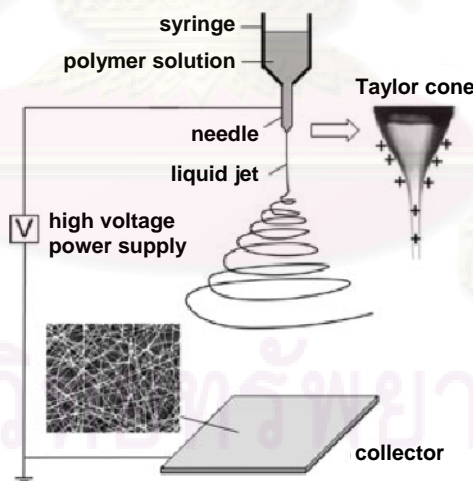
Varghese *et al.* (2008) [59] synthesized a fast, thermoresponsive hydrogel composed of poly(NIPA) and chondroitin sulfate (ChS) by using precipitation polymerization. ChS was introduced to increase the water absorption of the poly(NIPA) hydrogel, and the precipitation polymerization method was used to induce a porous network morphology to enhance the thermal response of the hydrogel. It was found that the swelling ratio of the poly(NIPA) hydrogel was greatly enhanced by semi-interpenetrating polymer network formation with ChS. The poly(NIPA)/ChS hydrogels showed a fast deswelling, due to the presence of a large free water content associated with the interconnected porosity and reduced hydrophobic skin effect from the hydrophilic ChS chains.

Nowadays, there is no report on preparation of poly[*N*-isopropylacrylamide-*co*-maleic acid)] hydrogel nanofibrous membrane.

## 2.3 Electrospinning Technique

### 2.3.1 Basic Setup and Mechanisms

The first patent that described the operation of electrospinning appeared in 1934, when Formalas pioneered an apparatus for producing polymer filaments by using an electrostatic force [60]. The basic setup for electrospinning is shown in Figure 2.6. It consists of three major components: a high-voltage power supply, a spinneret (a metallic needle), and a collector (a metal collection screen). A high voltage power supply is used to create an electrically charged jet of a polymer solution or a polymer melt out of the spinneret. One electrode is attached at spinneret and the other at a collector. The spinneret is connected to a syringe in which the polymer solution (or melt) is contained. A syringe is used as the reservoir. A collector is used as targets to receive the charged jet. Before the charged jet reached the collector, the solution jet evaporates or solidifies and then is collected as an interconnected web of small fibers.

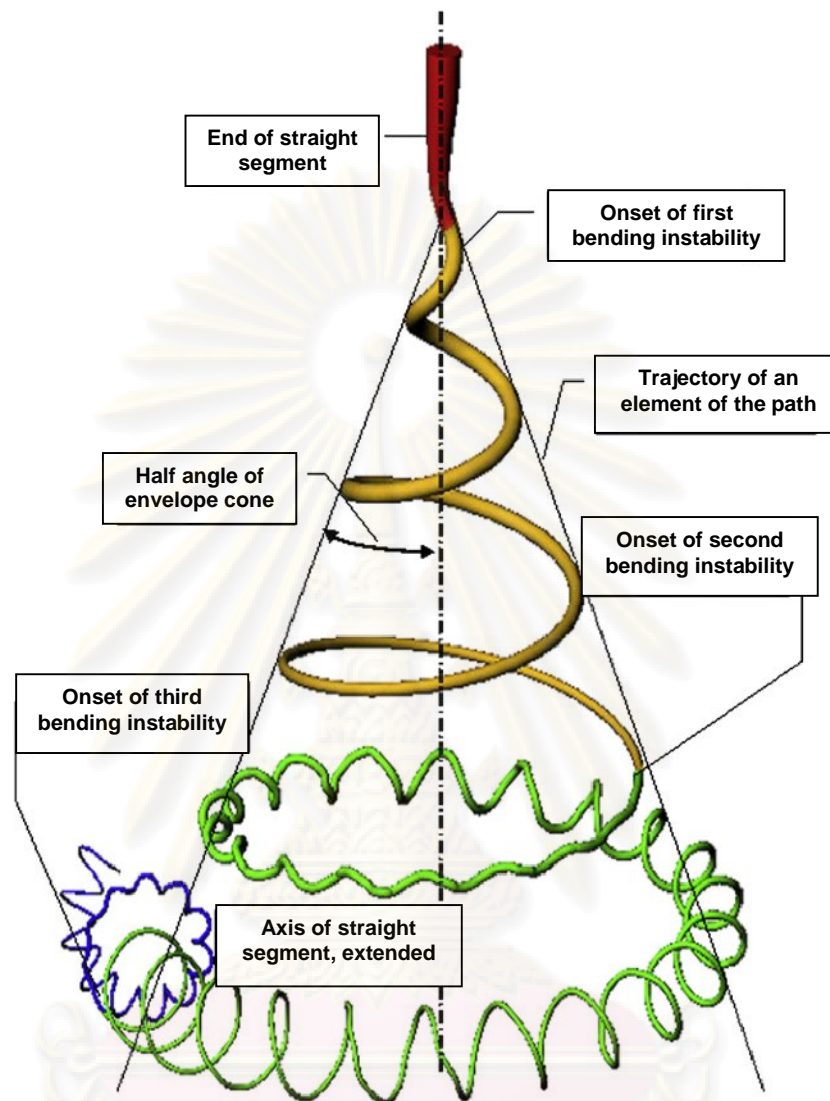


**Figure 2.6** The basic setup for electrospinning [23].

Although the setup for electrospinning is extremely simple, the spinning mechanism is rather complicated. The mechanism for the fiber formation in the electrospinning process is separated into three stages for convenience of description: (1) jet initiation and the extension of the jet along a straight line, (2) the growth of whipping instability and the further elongation of the jet which allows the jet to become very long and thin while it follows a looping and spiraling path and finally (3) solidification of the jet into nanofibers [61].

**Jet initiation.** The electric field is subjected to the end of a spinneret that contains the pendent droplet of polymer solution is supported by its surface tension. This induces a charge on the surface of the fluid. Mutual charge repulsion and the contraction of the surface charges to the counter electrode cause a force and an opposite way to the surface tension. As the intensity of the electric field is increased, the hemi-spherical surface of the fluid at the tip of the spinneret is elongated to form a conical shape known as the Taylor's cone [62-63]. Further increasing the electric field, a critical value is attained by which the repulsive electrostatic force overcomes the surface tension and then the charged jet of the fluid is ejected from the tip of the Taylor's cone.

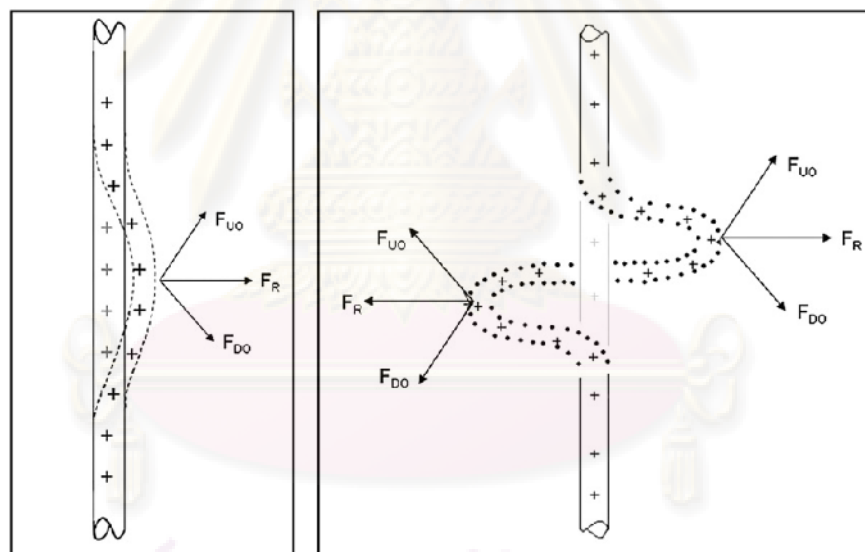
**Jet thinning.** The thinning of a jet during electrospinning is mainly caused by the bending instability associated with the electrified jet. After the jet fluid driven by the electric forces, it is unstable during its trajectory towards the collector [64]. The trajectory of the jet in the instable area is shown in Figure 2.7. The typical path of the jet is a straight segment followed by a coil of increasing diameter. After several turns are formed, a new electrical bending instability forms a smaller coil on a turn of the larger coil. The turns of the smaller coil transforms into an even smaller coil until the elongation is stopped usually by solidification of the thin jet.



**Figure 2.7** Trajectory of the jet in the instable area [64].

The bending instability driven by electricity which the jet rotates in a conical area whose vertex is the end of the straight jet. The continuing electrical bending generated a coil with many turns which expanded in diameter as the jet continued to elongate in response to the coulomb repulsion of the charge. The different forces acting on the bending charged jet during electrospinning [65]. Figure 2.8 shows the bending perturbations. In Figure 2.8, a segment of an electrospinning jet at the place where a

perturbed segment is shown in dotted lines. It began to grow in response to the repulsive electric forces between the uniformly distributed charges carried with the jet. The charge carried with the perturbed segment was forced downward and outward ( $F_{Do}$ ) by the charges above the perturbed region, at the same time this perturbed segment was forced upward and outward ( $F_{Uo}$ ) by the charge below the perturbation. The resultant of these forces  $F_R$  was in a radiation direction with respect to the straight jet and grew exponentially in time as the radiation displacement of the segment increased. At the same time the repulsion of adjacent charges moving with the jet caused all the bent and straight segments of the jet to continue to elongate along their local axes. The elongation increased more rapidly in the bending segment. The bent part of the path is elongated and reduced in diameter of the jet.



**Figure 2.8** Bending perturbations of the jet[65].

**Jet solidification.** The available duration of the jet to undergo whipping instability is also governed by the rate of evaporation of the solvent. Yarin *et al.* [66] derived a quasi-one-dimensional model that describes the decreasing mass and volume variation of the fluid jet due to evaporation and solidification by assuming that there is



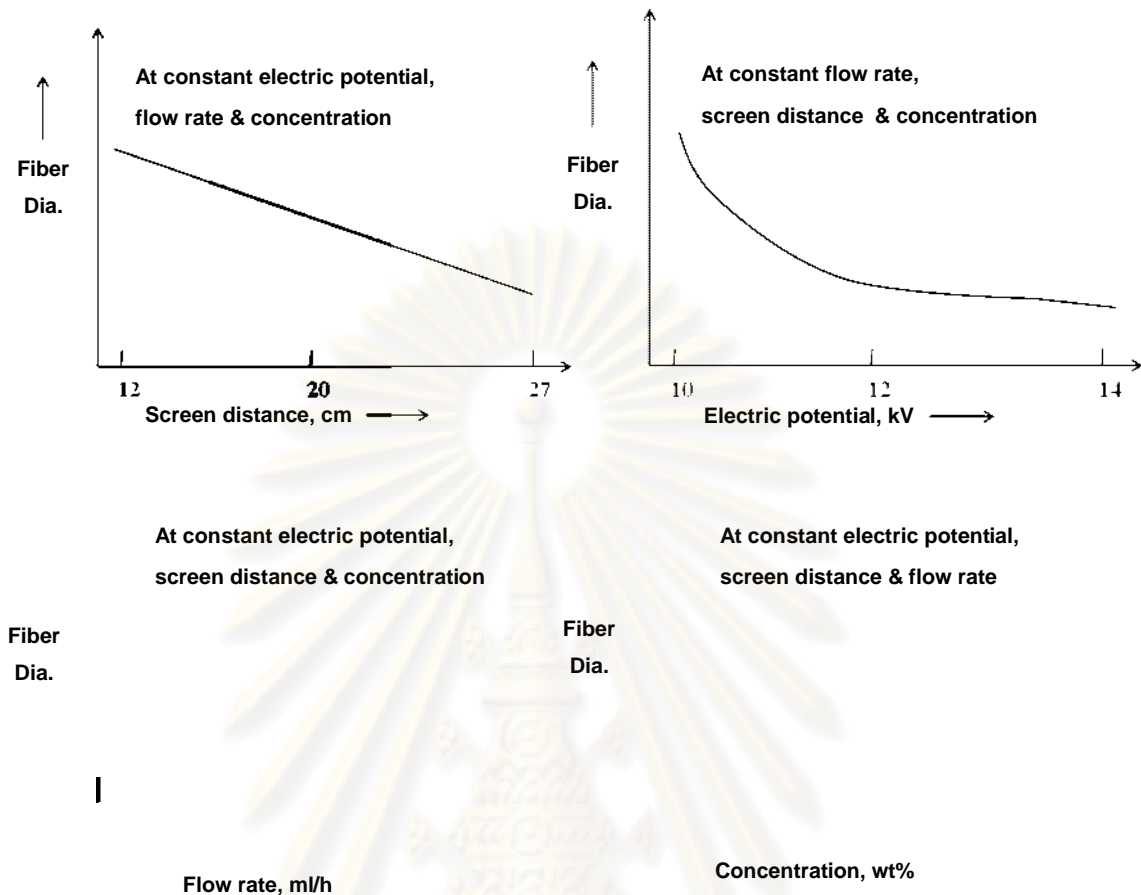
no branching or splitting from the primary jet. However the capacity of presented model does not fully take into account the kinetics of drying of the nanofiber and the changing consequence in rheology that affects the finer dimensions and deposit patterns.

### **2.3.2 Factors Affecting Morphology of Electrospun Fibers**

There are several parameters affecting the electrospinning process [67-69] that include:

- (1) system parameters such as the type of polymer, the conformation of polymer chain, viscosity (or concentration), elasticity, electrical conductivity and the polarity and surface tension of the solvent
- (2) process parameters such as electrical potential, the distance between spinneret and collector and the feeding rate
- (3) ambient parameters such as humidity, temperature and air velocity of the surrounding.

For instance, the polymer solution must have concentration high enough to cause polymer entanglements but not so high that the viscosity prevents motion of polymer induced by the electric field. The solution must also have viscosity and surface tension high enough to maintain a stable drop at the end of the spinneret. The power supply should be adequate to overcome the viscosity and surface tension of the polymer solution to form and sustain the jet from the spinneret. In addition, the gap between the spinneret and collector should not be too small to create sparks between the electrodes but should be large enough for the solvent to evaporate in time for the fiber to form. The morphology and diameter of electrospun fibers changes can occur upon a several parameters. Figure 2.9 shows an example of the effect of process parameters on fiber diameter.



**Figure 2.9** The effect of process parameters on fiber diameters [70].

### 2.3.3 Crosslinked Nanofibers

Crosslinked polymer nanofibers can be accomplished during electrospinning by an *in-situ* photo-induced polymerization technique or post-spin treatments by heat or UV radiation-induced crosslinking technique [71].

**An *in-situ* photo-induced polymerization technique.** This method is viable for the production of continuous hydrogel nanofibers with one-step of procedure. In this process, the photo-induced polymerization and crosslinking of polymer jet take place simultaneously during the electrospinning process. The jet consists of monomer, crosslinker and photoinitiator which polymerizes and crosslinks in flight [27, 72].

However, this process uses a chemical reaction during the electrospinning process hence it need the term reactive-mode electrospinning.

**Heat or UV radiation-induced crosslinking techniques.** They are crosslinking in a separate processing step after the polymer nanofibers are fabricated [73-75]. In this process, the random crosslinking is conveniently carried out by either heating or exposing UV radiation with a polymer that contains a small amount of crosslinking agent. The crosslinking agent can be electrospun along with the polymer and subsequently activated by heat or UV-visible radiation.

In conclusion, a heat-induced crosslinking is the most interesting special treatment technique being used to fabricate the electrospun nanofibers because it is an inexpensive and simple method. For example, under conditions of 140 °C and over 5-8 min, it was used to prepare bicomponent poly(vinyl alcohol)/poly(acrylic acid) water-insoluble hydrogel nanofibrous membranes [25, 76].

## 2.4 Literature Review

In recent years, there are many and continuous reports on preparation of hydrogels and nanofibers:

Tang *et al.* (2007) [28] generated poly(styrene-co-maleic anhydride) (SMA) hydrogel nanofibers responsive to ionic strength. An alternating SMA and a random SMA with respectively MAh content of 48 and 32% were synthesized. They were electrospun in the presence of crosslinker diethylene glycol, followed by heat-induced crosslinking at 145 °C and subsequent hydrolysis in NaOH/EtOH to turn SMA in to crosslinked sodium form SMA (SMA-Na) hydrogel nanofiber. These hydrogel nanofibers were able to retain fiber form after immersing in water for 24 hours. Their water absorption ratio was up to 37.6 and 8.2 g g<sup>-1</sup> in distilled water and 0.25 N NaCl aqueous solution, respectively.

Liu *et al.* (2007) [29] prepared poly[acrylamide-*co*-(maleic acid)] [poly(AM-MA)] hydrogel nanofibrous membrane by electrospinning an aqueous poly(AM-MA) solution with diethylene glycol as crosslinker, followed by a heat-induced esterification crosslinking reaction at 145 °C. This hydrogel nanofibers were sensitive to external stimuli ionic strength and pH. The maximum water-swelling ratios of the poly(AM-MA) hydrogel nanofibers were 18.1 and 22.5 g g<sup>-1</sup> in a solution of 0.05 mol dm<sup>-3</sup> ionic strength and in an aqueous solution of pH 11, respectively.

Song *et al.* (2008) [77] fabricated poly(*N*-isopropylacrylamide)-*co*-polystyrene (PNIPA-*co*-PS) nanofibers by electrospinning and explored the possibility to utilize the PNIPA-*co*-PS nanofibers as a sensitive and efficient way to enhance the permeation and uptake of the anticancer drug. It was found that PNIPA-*co*-PS nanofiber could play an important role in facilitating the cell track and drug delivery to the cancer cell. Moreover, they [78] also fabricated poly(*N*-isopropylacrylamide)-*co*-polystyrene (PNIPA-*co*-PS) and the blends of PNIPA-*co*-PS nanofibers with titanium dioxide (TiO<sub>2</sub>) nanoparticles as the new nanocomposites to enhance the relevant detection sensitivity of biomolecular recognition of an anti cancer drug daunorubicin.

Rockwood *et al.* (2008) [79] prepared fibrous mats of poly(NIPA) by electrospinning. When spun from water, poly(NIPA) formed small diameter fibers; however, these were of short length suggesting that the electrospinning jet was not able to withstand the whipping motion. In contrast, fibers spun from acetone or THF had diameters in the range of 5-17 μm. These were able to withstand the electrospinning process and were, therefore, able to produce non-woven, fibrous mats. Additionally, characterization with polarized Raman and FT-IR showed that electrospun mats of all types had identical chain structure when compared to the bulk polymer indicating that the electrospinning process did not a change in conformational structure.

Many researchers report the possibility of esterification reaction between maleic acid moiety and hydroxyl group by heating:

Kesim *et al.* (2003) [16] studied macromolecular reactions of synthesized poly(*N*-isopropylacrylamide-co-maleic anhydride) [poly(NIPA-co-MAh)] with polyethyleneglycol (PEG with a methoxy chain end and molecular weight of 2000 g mol<sup>-1</sup>) and polyethyleneimine (PEI with molecular weight of 2000 g mol<sup>-1</sup>) as a way to obtain new reactive amphiphilic water soluble polymers potentially useful as carriers for gene delivery. It was shown that synthesized copolymer with given composition have low critical solution temperature (LCST) in the range of 30.2-46.4 °C at pH values of 4.0-7.4, which suggest the possibility of their biomedical application.

Jin *et al.* (2005) [25] prepared fibrous membranes and monolithic films from aqueous mixture of poly(vinyl alcohol) and poly(acrylic acid) at 3.5 COOH/OH molar composition *via* electrospinning and solution casting, respectively. The samples were rendered water insoluble by heat-induced esterification, and their dimensional (planar and thickness) and mass-swelling behavior were measured in buffers ranging from pH 2-10. Lower extents of swelling at higher temperature and longer heating time (5 or 8 min between 135 and 144 °C) indicated higher esterification. The extent of cross-linking were similarly affected by the length and temperature of heating. Both forms of hydrogels exhibited increasing swelling with increasing pH. The fibrous membranes distinguished themselves as being far stronger and faster in re-absorption in the swollen state than the cast-films.

Riyajan *et al.* (2009) [80] synthesized and characterized a new semi-interpenetrating polymer network (semi-IPN) based on epoxidised natural rubber and polyvinyl alcohol containing maleic acid as a crosslinking reagent. It was found that an IR spectroscopic study indicated the presence of an ester linkage at 1730 cm<sup>-1</sup> in maleic acid crosslinked with PVA in semi-IPN films. In addition, the semi-IPNs exhibit good mechanical properties, thermal stability, characteristics of a polyvinyl alcohol-maleic acid polymer network.

As above researches, the electrospinning can produce hydrogel nanofibers by preparing polymer solution which contains maleic acid moieties in its structure in order to be sites for the crosslinking with crosslinking agent diethylene glycol and then crosslinking by heat-induced esterification reaction, finally obtaining hydrogel nanofibers. This work aims to prepare poly[*N*-isopropylacrylamide-*co*-(maleic acid)] by electrospinning and, followed by heat-induced esterification crosslinking reaction.



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## CHAPTER III

### EXPERIMENTAL SECTIONS

#### 3.1 Chemicals

All chemicals were analytical reagent grade. The chemicals used in this study were listed in Table 3.1.

**Table 3.1** Chemicals list

<i>Chemical</i>	<i>Suppliers</i>
Acetone	Carlo Erba
Ammonium peroxodisulfate (APS)	Fluka
Diethylene glycol 99% (DEG)	Aldrich
Diethylether	Merck
<i>N,N</i> -Dimethylformamide (DMF)	Fluka
Dimethylsulfoxide (DMSO- $d_6$ )	Merck
Ethyl alcohol absolute (EtOH)	Carlo Erba
<i>N</i> -isopropylacrylamide 97% (NIPA)	Aldrich
Maleic acid 99% (MA)	Aldrich
Nitrogen gas 99.99%	Praxair
Phenolphthalein	May & Baker
Potassium bromide (KBr)	Merck
Potassium hydrogen phthalate (KHP)	May & Baker
Sodium hydroxide anhydrous pellets	Carlo Erba
<i>N,N,N',N'</i> -Tetramethylethylenediamine 99% (TEMED)	Aldrich

### 3.2 Apparatuses

The apparatuses used in this study were listed in Table 3.2.

**Table 3.2** Apparatuses list

<i>Apparatus</i>	<i>Model (company)</i>
Analytical Balance	AT200 (Mettler)
Cover Glasses	22×22 mm (Menzel-Glaser)
Fourier Transforms Infrared Spectrometer (FT-IR)	Spectrum RX-I (Perkin Elmer)
High Voltage Power Supply	230 series (Bertan High Voltage Research)
Nuclear Magnetic Resonance Spectrometer (NMR)	Mercury Plus 400 (Varian)
Oven	UM500 (Mettler)
Scanning Electron Microscope (SEM)	JSM 5410 LV (Jeol)
Shaker	Zx <sup>3</sup> (VELP scientifica)
Syringe Pump	NE-1000 (Prosense)
Water bath	THERMAL TMD/1 (Bosstech)

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### 3.3 Synthesis of Poly[*N*-isopropylacrylamide-*co*-(maleic acid)]

Poly[*N*-isopropylacrylamide-*co*-(maleic acid)] was synthesized by free radical polymerization in aqueous solution. The method was adapted from Vaidya *et al.* [54]. The preparation conditions with varying the monomer feed ratios were shown in Table 3.3.

**Table 3.3** Synthesis conditions of copolymers

<i>Chemical substance</i>	<i>Function</i>	<i>Conditions</i>
<i>N</i> -isopropylacrylamide (NIPA)	Monomer	0.33 mol/L
Maleic acid (MA)	Comonomer	10-50 % mol/mol of the total monomer
<i>N,N,N',N'</i> -tetramethylethylenediamine (TEMED)	Accelerator	1 % v/v of the monomer solution
Ammonium peroxodisulfate (APS)	Initiator	10% wt/wt of the total monomer

*N*-isopropylacrylamide (NIPA) (M.W. 113.16) (1.1 g, 0.0098 mol) and maleic acid (MA) (M.W. 116.07) (0.13, 0.28, 0.49, 0.62, 0.75 and 1.1 g) were added to a two-necked round bottom flask containing 30 mL of Milli Q water and stirred for 20 min. Then, nitrogen gas was purged in the solution for 1 hour. Ammonium peroxodisulfate (APS) (0.12, 0.14, 0.16, 0.17, 0.19, 0.22 g) was added followed by *N,N,N',N'*-tetramethylethylenediamine (TEMED) solution (300  $\mu$ L) drop wise. The polymerization proceeded at 37 °C for 8 hours under continuous nitrogen stream. The solution became very viscous that represented the progress of polymerization reaction. The polymer was precipitated out of the solution by heating the solution about 80 °C for 20 min. Redissolved the polymer in Milli Q water, and then re-precipitated and washed several times with diethylether in order to remove any unreacted monomers and impurities. Copolymer was dried in an oven at 80 °C for 12 hours and stored in a desiccator.

### 3.4 Investigation of Monomer Feed Ratios of Copolymer on Crosslinking Reaction with Diethylene Glycol

Poly[*N*-isopropylacrylamide-*co*-(maleic acid)] containing diethylene glycol (DEG) films were prepared by hand-casting. The parameters of mixture solutions used in this study were shown in Table 3.4. The multicomponent films were activated by esterification crosslinking reaction by means of heat following the method described by Tang *et al.* [28-29]. The suitable monomer feed ratios of copolymer for crosslinking reactions were evaluated by solubility test.

**Table 3.4** Parameters of mixture solutions

<i>Parameter</i>	<i>Condition</i>
Molar feed ratio of maleic acid	10-50 % mol/mol of the total monomer
Concentration of polymer solution	10-20 % wt/v of solvent
Crosslinking agent diethylene glycol (DEG)	5-20 %wt/wt of copolymer

The mixture solutions were prepared by adding poly(*N*-isopropylacrylamide-*co*-(maleic acid)] (0.05 g) and either *N,N'*-dimethylformamide (DMF) or ethanol (EtOH) (500  $\mu$ L, 333  $\mu$ L, 250  $\mu$ L) in a vial. They were completely dissolved after the mixture was vigorously shaken for 30 min. Then, diethylene glycol (DEG) (2.24  $\mu$ L, 4.47  $\mu$ L, 6.71  $\mu$ L and 8.94  $\mu$ L) was added to the solution and shaken again for 30 min. 30  $\mu$ L of this homogeneous solutions was pipetted onto a cover glass and then cast. The cast film on the glass slide was put in an oven at 145 °C for 10 min to allow the crosslinking reaction to proceed completely, and at 60 °C for 12 hours to remove residual solvent. Film was peeled off and analyzed for solubility characteristics.

The solubility characteristics of the film were determined by immersing the obtained films into distilled water at room temperature for 24 hours. The visual characteristic of the films were observed.

### 3.5 Characterization of Copolymer

The suitable monomer feed ratios of synthesized copolymers were characterized by Fourier Transforms Infrared Spectrometer (FT-IR), Nuclear Magnetic Resonance Spectrometer (NMR) and Acid-base Titration.

#### 3.5.1 Fourier Transforms Infrared Spectrometer (FT-IR)

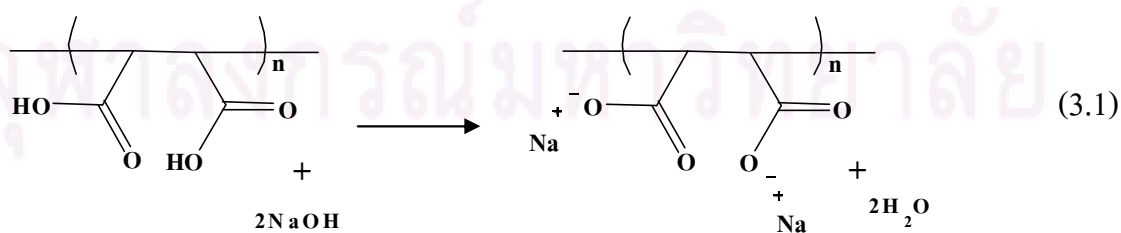
FT-IR was used to identify the characteristic functional groups of the copolymer. Infrared spectra were recorded in the wavenumber range of 400-4,000  $\text{cm}^{-1}$  using the transmittance mode with 4 scans with the wavenumber resolution of  $\pm 4 \text{ cm}^{-1}$  by KBr pellet technique.

#### 3.5.2 Nuclear Magnetic Resonance Spectrometer (NMR)

NMR was used to confirm the structure of the copolymers.  $^1\text{H}$ -NMR spectra were recorded in the chemical shift 0-14 ppm with repetitions of 8 by using  $\text{DMSO-}d_6$  as solvent.

#### 3.5.3 Acid-base Titration

Acid-base titration was used to determine the composition of synthesized copolymers, thereby affording directly the mole fraction of maleic acid-containing copolymer. Titrations of 10 mL of 1 %wt/v copolymer were manually performed in triplicate. Titrations used standardized 0.1 M sodium hydroxide (NaOH) solution as the titrant with phenolphthalein as the indicator, by the following reaction:



**Copolymer**

All solutions were prepared by using deionized (DI) water as follows:

- 1 %wt/v of copolymer was prepared by dissolving 0.5 g of synthesized copolymer in 50 mL DI water.
- 0.1 M sodium hydroxide (NaOH) solution was prepared by dissolving 2.0 g of sodium hydroxide anhydrous pellets in 500 mL DI water.
- 0.1 M potassium hydrogen phthalate solution (KHP) was prepared by dissolving 1.0 g of KHP in 500 mL DI water.

The determination of acid content was done by using different materials obtained from three batches of copolymerization. The titration of each synthesis batch was performed in triplicate.

### **3.6 Electrospinning and Esterification Crosslinking of Copolymer**

Poly[*N*-isopropylacrylamide-*co*-(maleic acid)] hydrogel membrane was prepared by electrospinning and heat-induced esterification crosslinking reaction at 145 °C followed the method described by Tang *et al.* [28-29].

#### **3.6.1 Preparation of Copolymer Solution in the Presence of Diethylene Glycol**

The preparation of suitable proportion of mixture solutions were similar to the methodology described in Section 3.4.

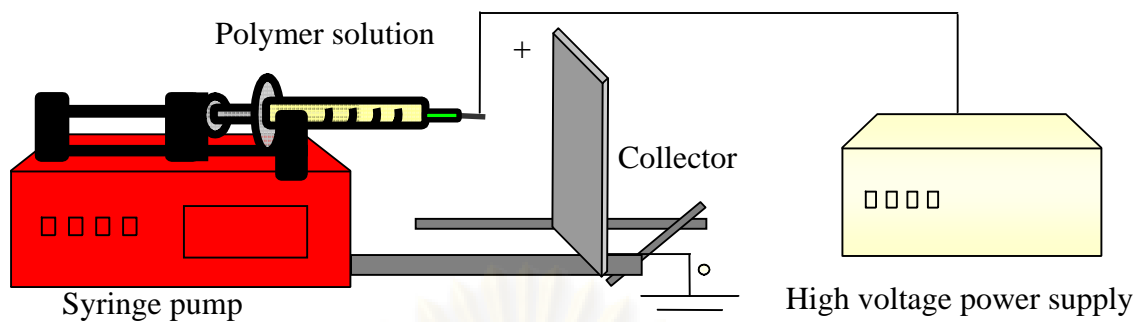
Poly[*N*-isopropylacrylamide-*co*-(maleic acid)] (1.0 g) was dissolved in 10 mL of ethanol (EtOH). The solution was vigorously stirred for 1 hour at room temperature. Then, 44.7  $\mu$ L diethylene glycol (DEG) was added to the solution and stirred for 30 min to obtain homogeneous mixture solutions.

### 3.6.2 Electrospinning Process and Esterification Crosslinking Reaction

The mixture solution was placed in a 5 mL disposable syringe with a 0.80 mm diameter needle which was mounted onto a syringe pump. A positive potential was applied to the polymer solution, by connecting to the high voltage power supply directly to the outside of the needle. The collector was covered with aluminum foil and connected to the grounding electrode. The feeding rate was 1 mL hour<sup>-1</sup> controlled by the syringe pump. When the electric field reaches a critical value, the charged polymer solution overcomes the surface tension and the jet emerges from the needle toward the collection screen. The fibers are collected in membrane form on the aluminum foil. The electrospinning apparatus was shown in Figure 3.1. After that the membrane was put in an oven at 145 °C for 10 min to allow the crosslinking reaction to proceed completely, and at 60 °C for 12 hours again to remove residual water. The crosslink copolymer membrane was obtained.

The characterization of morphology and the diameter of fibers was done by Scanning Electron Microscope (SEM). The electrospinning was conducted at a flow rate of 1 mL hour<sup>-1</sup>, on electric potential of 15-30 kV and a distance between the needle and the collection screen of 10-25 cm. The total time of electrospinning was around 2 hours.

The characterization of functional groups of fibers was done by Fourier Transforms Infrared Spectrometer (FT-IR). The swelling of fibers was also investigated by water absorption measurement. The electrospinning was conducted at a flow rate of 1 mL hour<sup>-1</sup>, on the suitable electric potential and distance between the needle and collection screen chosen from previous experiment. The total time of electrospinning was around 5 hours.



**Figure 3.1.** Schematic of the electrospinning process.

### 3.7 Characterization of Electrospun Copolymer Hydrogel Membrane

The electrospun copolymer hydrogel membrane was characterized by Scanning Electron Microscope (SEM) and Fourier Transforms Infrared Spectrometer (FT-IR).

#### 3.7.1 Scanning Electron Microscope (SEM)

SEM was used to investigate the morphology and the fiber diameter of the electrospun copolymer hydrogel membrane. Samples for SEM were carefully cut into small pieces and exposed to gold vapor deposition to prepare photogenic sample, and put in an electron probe analyzer to give the SEM photographs. The accelerated voltage was 15 kV. The magnification at 20,000 was used for the measurement the diameter of the fiber and at 3,500 for the measurement of the node fiber. The diameter of fibers was reported as the average values with standard deviation ( $n=30$ ) by Sem Afore program.

#### 3.7.2 Fourier Transforms Infrared Spectrometer (FT-IR)

FT-IR was used to identify the characteristic functional groups of the electrospun copolymer hydrogel membrane. Infrared spectra were recorded by using the procedure previously used in the 3.5.1

### 3.8 Water Absorption Measurement

Water absorption measurement was used to investigate the swelling characteristics of the electrospun copolymer hydrogel membrane at temperatures of water ranging from 10 to 50 °C. The membrane strips with size of 2×2 cm<sup>2</sup> were immersed in deionized (DI) water for 1 hour. Then the membrane was taken out, the free water at the surface was removed by filter paper and brought to weigh ( $W_w$ ). Later on, they were dried in an oven at 80 °C until the weight of the dry membrane was constant and brought to weigh ( $W_d$ ). The water absorption ratio was calculated according to the following Equation 3.2.

$$\text{Water absorption ratio} = \left[ \frac{W_w - W_d}{W_d} \right] \quad (3.2)$$

Where:  $W_w$  = the weight of wet membrane (g)

$W_d$  = the weight of dried membrane (g)

The weight loss of electrospun copolymer hydrogel membrane was calculated according to the following Equation 3.3.

$$\text{Weight loss (\%)} = \left[ \frac{W_i - W_p}{W_i} \right] \times 100 \quad (3.3)$$

Where:  $W_i$  = the weight of the initial dried membrane (g)

$W_p$  = the weight of the post-water treated and dried membrane (g)

## CHAPTER IV

### RESULTS AND DISCUSSION

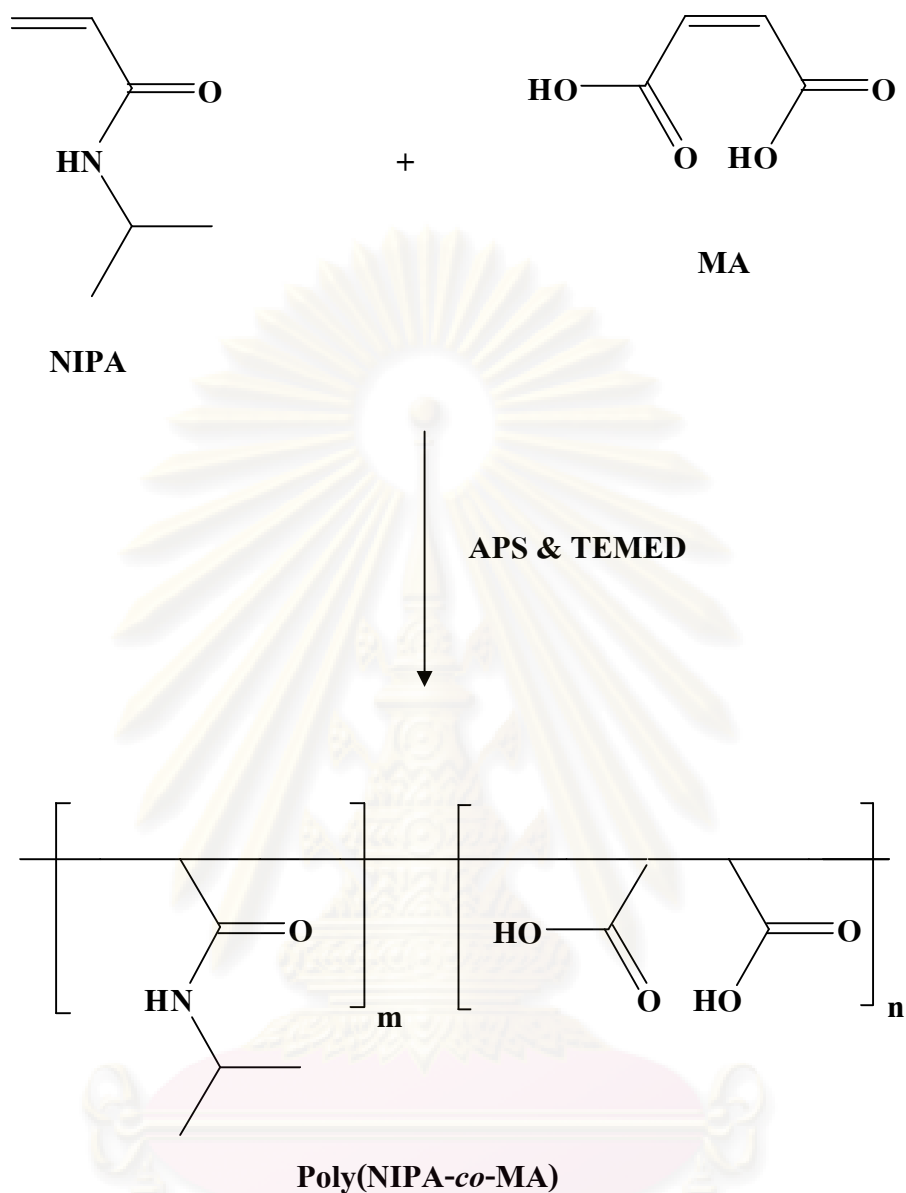
Poly[*N*-isopropylacrylamide-*co*-(maleic acid)] hydrogel membrane was prepared by electrospinning and crosslinking by heat-induced esterification reaction. This work consists of four parts including (1) synthesis of the copolymer, (2) characterization of the copolymer, (3) preparation and characterization of electrospun copolymer hydrogel membranes and (4) water absorbing behavior of copolymer hydrogel membranes at different temperature (10-50 °C).

#### 4.1 Synthesis of Copolymer

In this section, the copolymer consisting of *N*-isopropylacrylamide (NIPA) and maleic acid (MA) or poly(NIPA-*co*-MA) was synthesized by free radical copolymerization. The reaction is shown in Scheme 4.1. The synthesis procedure was adapted from the published literature [54]. In order to introduce the sites for the crosslinking reaction on the backbone of copolymer, various monomer feed ratios were investigated in the copolymerization process.

A crosslinking of poly(NIPA-*co*-MA) *via* heat-induced esterification reaction between maleic acid (MA) units and diethylene glycol (DEG) as a crosslinking agent with the elimination of water [28-29] was applied. This mechanism is presented in Scheme 4.2.





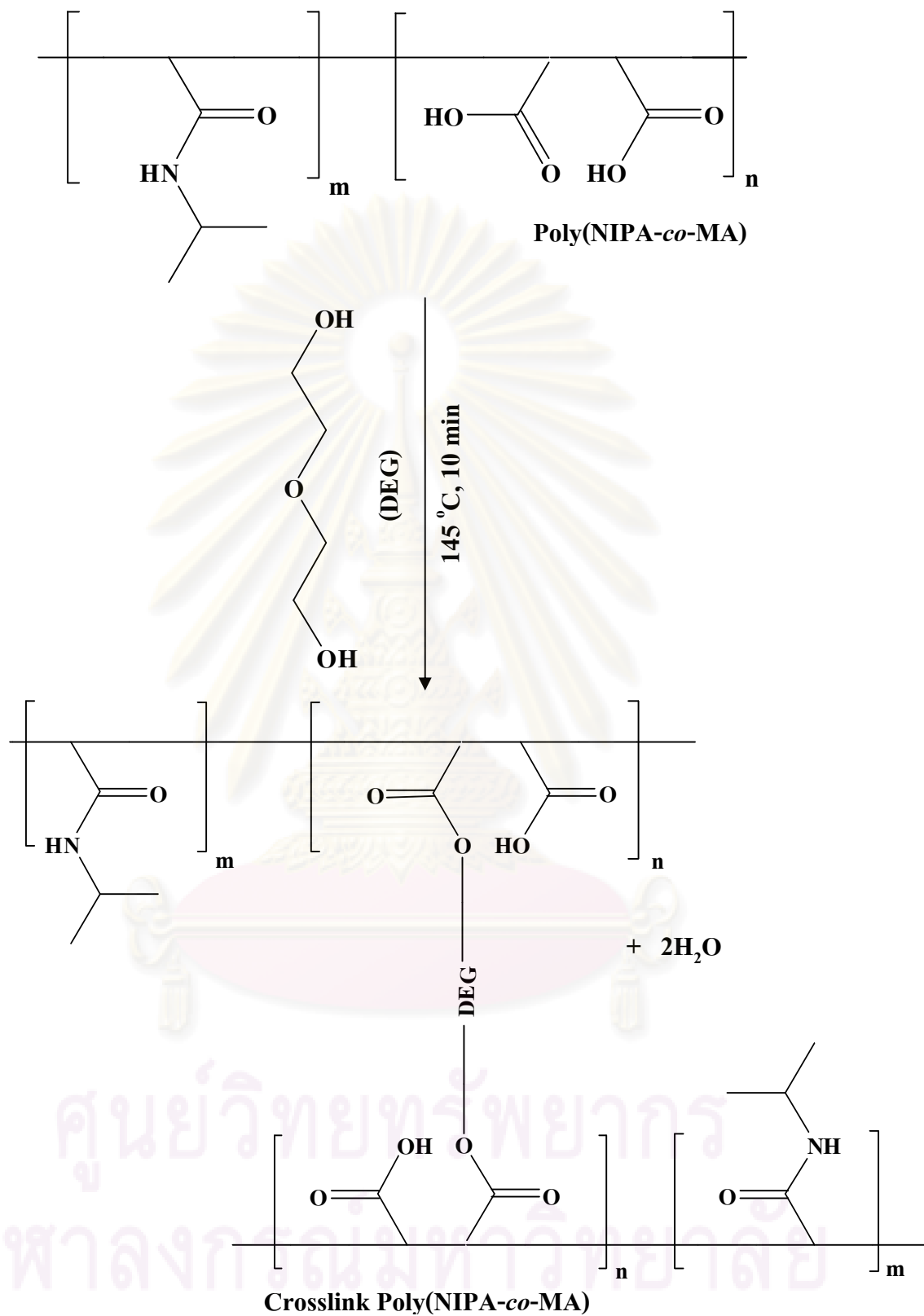
NIPA = *N*-isopropylacrylamide,

MA = maleic acid,

APS = ammonium peroxodisulfate,

TEMED = *N,N,N',N'*-tetramethylethylenediamine

**Scheme 4.1** Synthesis of poly(NIPA-co-MA).



**Scheme 4.2** Crosslinking of poly(NIPA-*co*-MA) with DEG.

The parameters in preparation of crosslinked poly(NIPA-*co*-MA) including the feed molar ratio of MA in copolymerization, the amount of crosslinking agent, diethylene glycol (DEG), and concentration of polymer solution, were varied. Thus, multicomponent films were prepared in DMF by hand-casting, followed by a heat-induced esterification crosslinking reaction at 145°C. After that the films were immersed in water at room temperature for 24 hours. The solubility of the film was summarized in Table 4.1.

**Table 4.1** Solubility of crosslinked poly(NIPA-*co*-MA) film with varying the proportion of mixture solutions after water immersion at room temperature for 24 hours

<i>MA amount in feed</i> (%mol/mol)	<i>Concentration of</i> <i>copolymer solution</i> (%wt/v)	<i>DEG amount</i> (%wt/wt of copolymer)	<i>Solubility</i> <sup>a</sup>
<i>In N,N-Dimethylformamide</i>			
10	10	5, 10, 15, 20	soluble
	15	5, 10, 15, 20	soluble
	20	5, 10, 15, 20	soluble
20	10	5, 10, 15, 20	soluble
	15	5, 10, 15, 20	soluble
	20	5, 10, 15, 20	soluble
30	10	5, 10, 15, 20	soluble
	15	5, 10, 15, 20	soluble
	20	5, 10, 15, 20	soluble

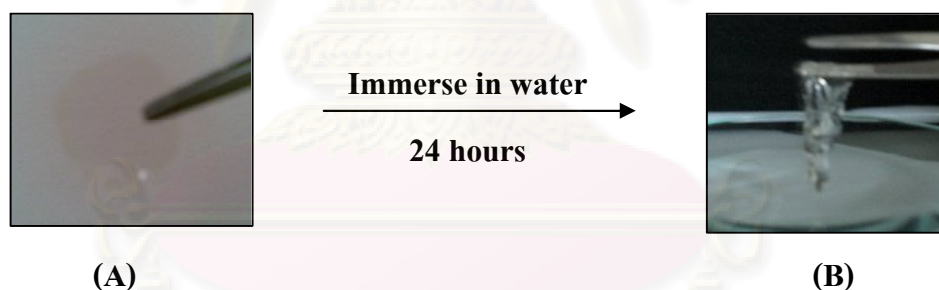
<sup>a</sup>observed in triplicate

**Table 4.1** (continued) Solubility of crosslinked poly(NIPA-co-MA) film with varying the proportion of mixture solutions after water immersion at room temperature for 24 hours

<i>MA amount in feed (%mol/mol)</i>	<i>Concentration of copolymer solution (%wt/v)</i>	<i>DEG amount (%wt/wt of copolymer)</i>	<i>Solubility<sup>a</sup></i>
<i>In N,N-Dimethylformamide</i>			
35	10	5, 10, 15, 20	insoluble
	15	5, 10, 15, 20	insoluble
	20	5, 10, 15, 20	insoluble
40	10	5, 10, 15, 20	insoluble
	15	5, 10, 15, 20	insoluble
	20	5, 10, 15, 20	insoluble
50	10	5, 10, 15, 20	insoluble
	15	5, 10, 15, 20	insoluble
	20	5, 10, 15, 20	insoluble
<i>In Ethanol</i>			
35	10	5, 10, 15, 20	insoluble
	15	5, 10, 15, 20	insoluble
	20	5, 10, 15, 20	insoluble

<sup>a</sup>observed in triplicate

Hydrogels or water-containing gels are polymeric materials characterized by both hydrophilicity and insolubility in water [81]. From Table 4.1, as MA amount in feed increased from 35 to 50 %mol/mol (keeping other parameters constant), films were insoluble in water and able to retain film form as shown in Figure 4.1. Conversely, below 35%mol/mol MA in feed (keeping other parameters constant), films were readily soluble and lost in water. As generally known, a poly(NIPA) is quickly soluble in water, but it becomes water-insoluble when there is three dimensional network form in the crosslink-poly(NIPA) or c-poly(NIPA) [82-83]. The principal purpose of the introduction of MA moieties into the backbone of poly(NIPA) was to make the copolymer possessing crosslink sites with maintaining the properties of the poly(NIPA) hydrogel. Consequently, 35%mol/mol MA in feed of copolymerization was selected for further experiments.



**Figure 4.1** Images of crosslinked poly(NIPA-co-MA) film cast from mixture solution at 35%mol/mol MA in feed, 5%wt/wt DEG and 10%wt/v of copolymer

(A) before, (B) after immersing in water at room temperature for 24 hours.

The effect of the solvent used in film casting was also investigated. As mentioned above, The crosslinked copolymer films prepared from 35%mol/mol MA in feed with DMF as a solvent were water insoluble in any DEG concentrations,

the solvent using in film casting was change to ethanol. The results of solubility test were also presented in Table 4.1. The property of the film prepared in ethanol was similar to those cast in DMF. It can be assumed that solvent work as only intimate connecting media between copolymer chains and the crosslinker. Thus, ethanol was selected for next experiments since it is commonly used organic solvent, has low toxicity and is not expensive.

The synthesis of poly(NIPA-*co*-MA) with 35%mol/mol MA in feed was easy and simple by radical polymerization in aqueous solution. The progress of copolymerization could be observed visually by the rise of the viscosity of the solution. The product was obtained as white to pale-yellow precipitate. The yield of poly(NIPA-*co*-MA) was  $55 \pm 2$  % ( $n = 3$ ) as shown in Table 4.2. The yield represents the conversion from monomer to polymer [84]. The percentage yield was calculated according to the following Equation 4.1.

$$\text{Yield (\%)} = \left[ \frac{\text{weight of the copolymer (g)}}{\text{weight of total monomers (g)}} \right] \times 100 \quad (4.1)$$

**Table 4.2** Yield of synthesized poly(NIPA-*co*-MA) with 35%mol/mol MA in feed

No.	Monomer		Synthesized copolymer (g)	Yield (%)
	NIPA (g)	MA (g)		
1	1.1093	0.6129	0.9196	53
2	1.1092	0.6131	0.9471	55
3	1.1095	0.6133	0.9761	57
Mean $\pm$ S.D.				$55 \pm 2$

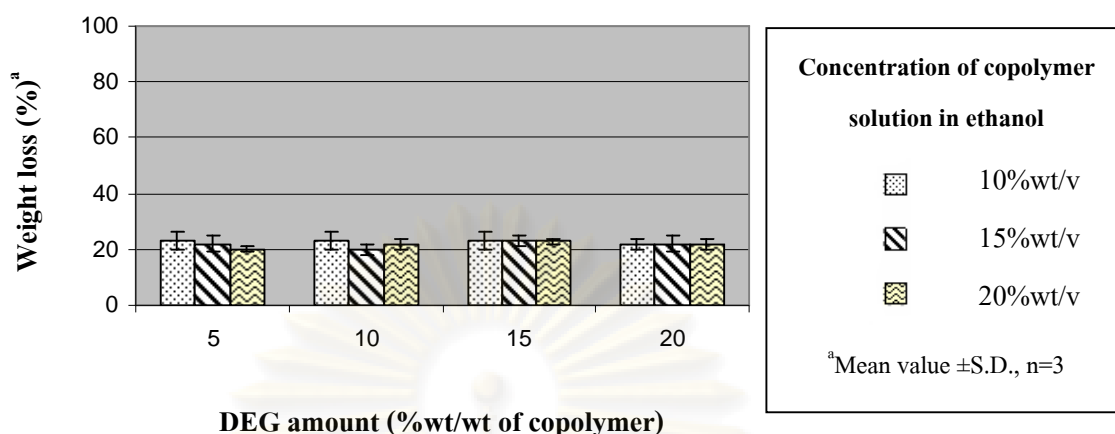
In order to study the effect of amount of crosslinking agent diethylene glycol (DEG) and concentration of polymer solution, the weight loss in water of crosslinked copolymer was considered. The weight loss of crosslinked poly(NIPA-*co*-MA) film was calculated according to the following Equation 4.2.

$$\text{Weight loss (\%)} = \left[ \frac{W_i - W_p}{W_i} \right] \times 100 \quad (4.2)$$

Where:  $W_i$  = the weight of the initial dried film (g)

$W_p$  = the weight of the post-water treated and dried film (g)

The weight loss represents the dissolution and diffusion of polymers that were not crosslinked in the material and uncompletion of crosslinking [85]. From Figure 4.2, changing the amount of crosslinking agent diethylene glycol (DEG) from 5 to 20 %wt/wt did not significantly affect the weight loss of crosslinked poly(NIPA-*co*-MA) films. Thus the minimum amount of DEG (5%wt/wt) was chosen. In addition, considering the effect of concentration of copolymer, the % weight loss was no significant difference. Thus, the minimum concentration of copolymer was chosen for further experiments since it is easy to preparation of solution which spends less time. Moreover, it has low viscosity that is easy to obtain nanofibers by electrospinning. Solutions with high solids content (high viscosity) may not only impede the fiber-extension process, yielding relatively thicker nanofibers, but may also make it difficult to pump the polymer solution because of its high viscosity [86].



**Figure 4.2** The weight loss of crosslinked poly(NIPA-*co*-MA) film prepared from 35%mol/mol MA in feed solution with varying amount of DEG and concentration of copolymer in EtOH after water immersion at room temperature for 24 hours

In conclusion, the effect of molar feed ratios of MA influenced the crosslinking reaction while the effect of the amount of crosslinking agent diethylene glycol (DEG), concentration of copolymer solutions and type of solvent were not significant. Therefore, the optimum preparation conditions of the crosslinked-poly(NIPA-*co*-MA) could be achieved with molar feed ratio of MA comonomer 35%mol/mol in copolymerization process from 10%wt/v solution of synthesized polymer in ethanol with crosslinking agent DEG amount 5%wt/wt of copolymer addition, followed by an activated via heating at 145 °C for 10 min.

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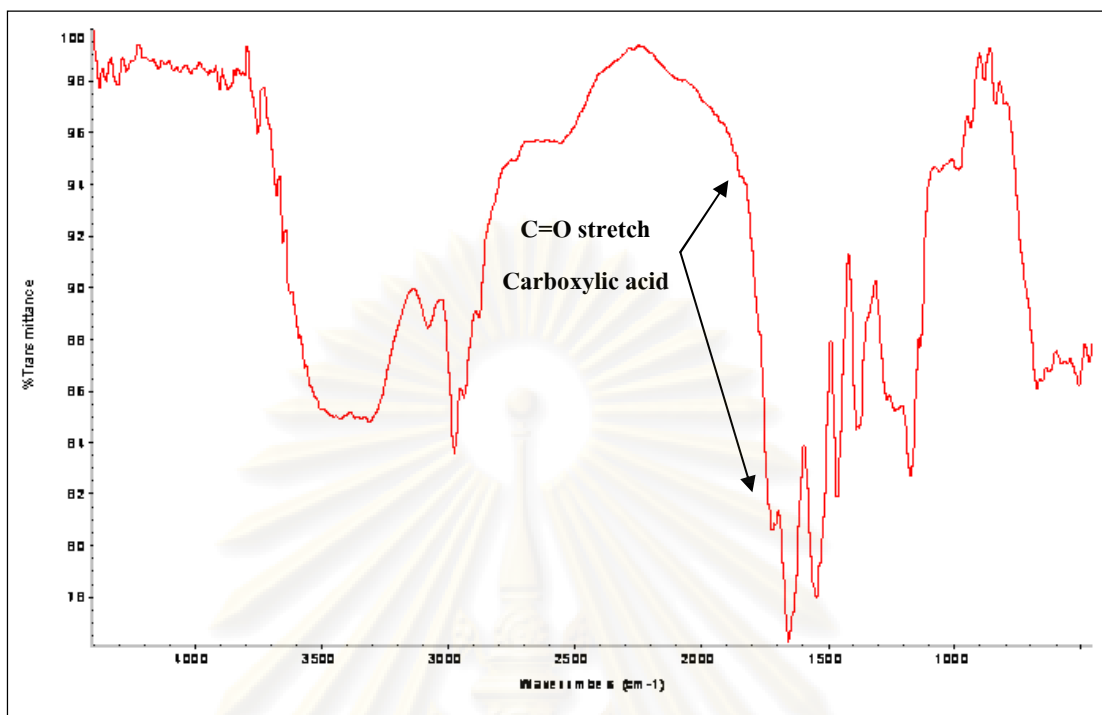
## 4.2 Characterization of Copolymer

The suitable monomer feed ratios of synthesized poly(NIPA-*co*-MA) copolymers were characterized by Fourier Transforms Infrared Spectroscopy (FT-IR), Nuclear Magnetic Resonance Spectroscopy (NMR) and Acid-base Titration. The results were illustrated and discussed as the following.

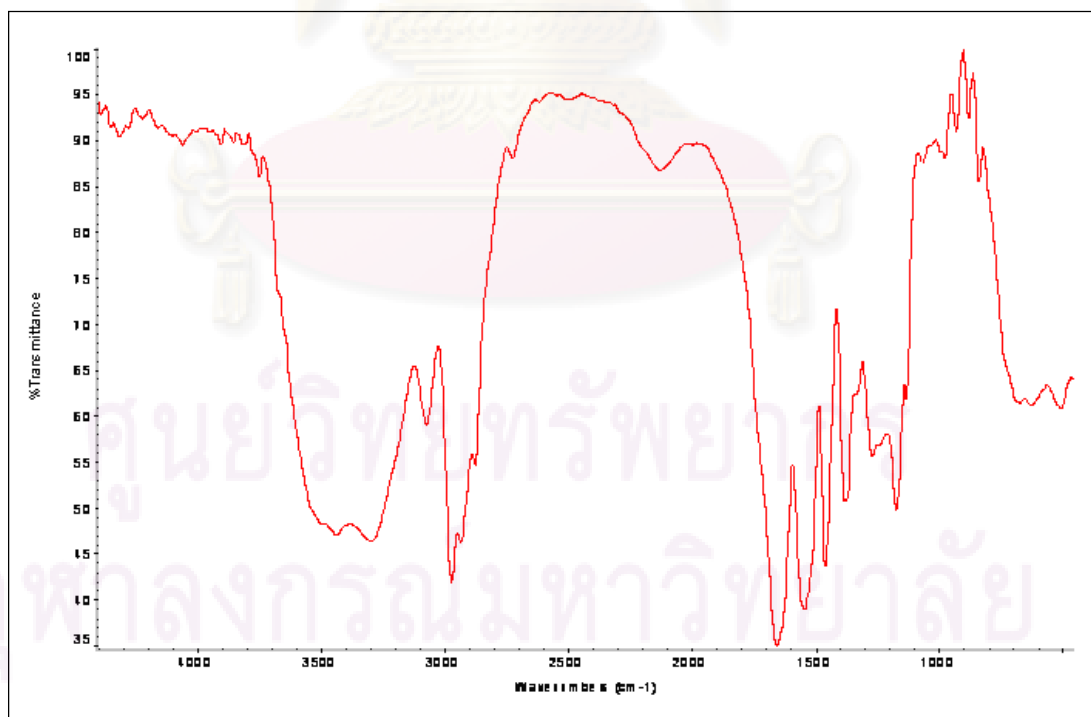
### 4.2.1 Fourier Transforms Infrared Spectroscopy (FT-IR)

The poly(NIPA-*co*-MA) was characterized by FT-IR. The IR spectrum of synthesized poly(NIPA-*co*-MA) was shown in Figure 4.3. The absorption bands of NIPA and MA unit was found. For NIPA units, the characteristic bands of copolymer were observed at 3301 (m, broad) and 3075 (w)  $\text{cm}^{-1}$  assigned to N-H stretching band of secondary amide, at 2976 (s) 2929 (w) and 2874 (w)  $\text{cm}^{-1}$  assigned to C-H stretching band, at 1657 (s)  $\text{cm}^{-1}$  assigned to C=O stretching of amide I band, at 1545 (m-s)  $\text{cm}^{-1}$  assigned to N-H bending of amide II band, at 1461 (s)  $\text{cm}^{-1}$  assigned to C-N stretching of amide III band and at 1381 (s) and 1271 (m)  $\text{cm}^{-1}$  assigned to band for  $\text{CH}_3$  deformation in isopropyl group. For MA units, the characteristic bands of copolymer were observed at 3680-3200 (s, broad)  $\text{cm}^{-1}$  assigned to O-H stretching band of carboxylic group and at 1778 (w) and 1719 (m)  $\text{cm}^{-1}$  assigned to C=O stretching band of carboxylic group. When compared FT-IR spectrum of poly(NIPA-*co*-MA) and poly(NIPA), FT-IR spectrum of poly(NIPA-*co*-MA) show a new peak of carboxylic group at 1778 and 1719  $\text{cm}^{-1}$  which was significantly different from FT-IR spectrum of poly(NIPA) as shown in Figure 4.4.

Therefore, FT-IR characterization was entirely clear to confirm the copolymerization of MA comonomer onto the NIPA polymer.



**Figure 4.3** FT-IR spectrum of poly(NIPA-co-MA).

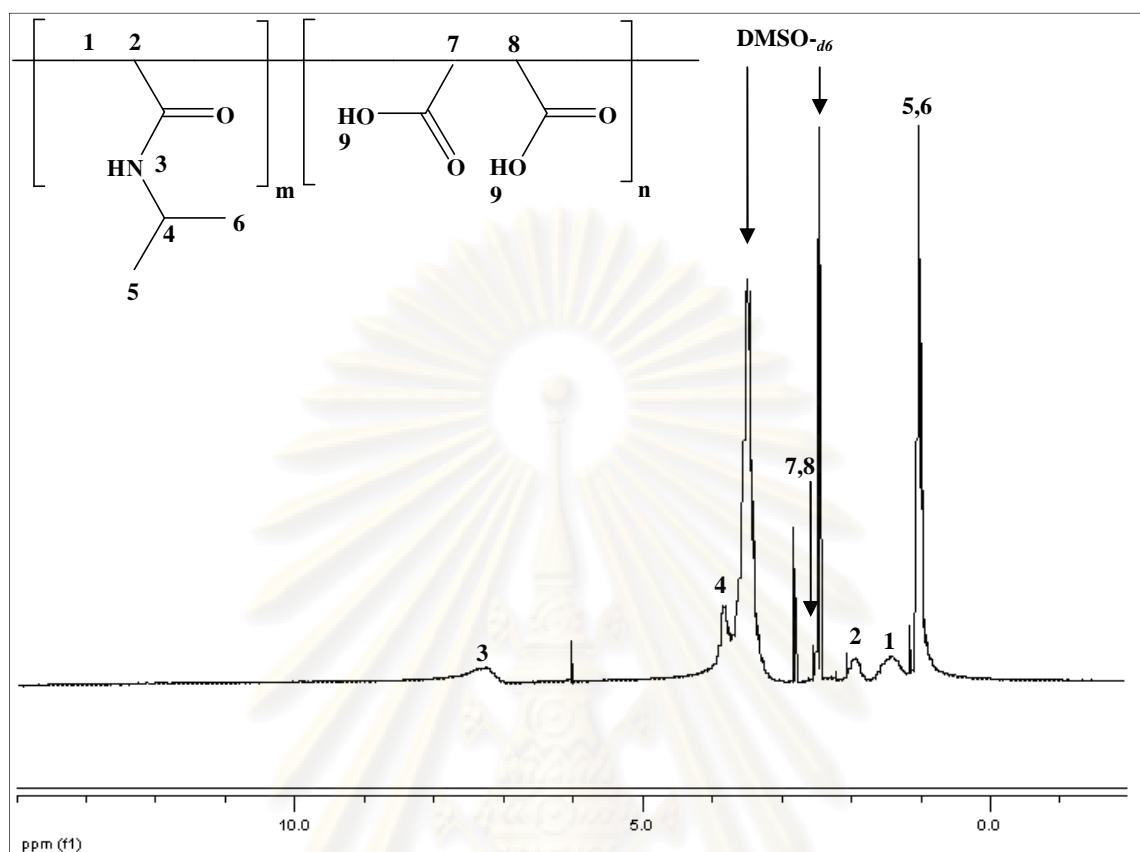


**Figure 4.4** FT-IR spectrum of poly(NIPA).

#### 4.2.2 Nuclear Magnetic Resonance Spectroscopy (NMR)

The poly(NIPA-*co*-MA) was characterized by  $^1\text{H-NMR}$ . The NMR spectrum of synthesized poly(NIPA-*co*-MA) was shown in Figure 4.5. The proton signals of NIPA and MA units were found. For NIPA units,  $^1\text{H-NMR}$  signals of copolymer were observed at 1.40 ppm (broad, 2H) of  $\text{CH}_2$  (backbone), 1.92 ppm (q,  $J = 1.5$  Hz, 1H) of CH (backbone), 7.04 - 7.56 ppm (broad, 1H) of NH, 3.82 ppm (m, 1H) of CH (isopropyl) and 1.02 ppm (d,  $J = 6.4$  Hz, 6H) of  $\text{CH}_3$  (isopropyl). For MA units,  $^1\text{H-NMR}$  signal of copolymer was observed at 2.48 ppm (t,  $J = 2.0$ , 2H) of CH (backbone). But the proton of carboxylic group could not be found at the chemical shifts from 0 to 14 ppm since it was a de-shielding by the influence of electron-withdrawing effect that causes paramagnetic shift. Thus the chemical shifts is above 14 ppm which is agreed with  $^1\text{H-NMR}$  spectra of poly[*N*-isopropylacrylamide-*co*-(maleic anhydride)] and poly[*N*-isopropylacrylamide-*co*-(maleic acid)]-*graf*-polyethyleneglycol that were reported by Kesim *et al.* [16]. They reported that the proton of carboxylic group appeared at the chemical shift of 16.98 ppm.

Therefore, from  $\text{H}^1$ -NMR spectra, it can be implied that the incorporation of MA comonomer into the backbone polymer chain was successful.



**Figure 4.5**  $^1\text{H}$ -NMR spectrum of poly(NIPA-co-MA).

### 4.2.3 Acid content

The composition of acid content in poly(NIPA-co-MA) was determined by an acid-base titration of the carboxylic groups. The results were displayed in Table 4.3. The maleic acid (MA) composition in feed and in copolymer were calculated by the following Equation 4.3 and 4.4, respectively.

$$\text{MA composition in feed (eq.g}^{-1}\text{ monomers)} = \frac{\text{weight of MA} \times 2}{(\text{weight of MA} + \text{weight of NIPA}) \times 116.07} \quad (4.3)$$

$$\text{MA composition in copolymer (eq.g}^{-1}\text{ copolymer)} = \frac{\text{concentration of NaOH} \times \text{volume of NaOH} \times 5}{\text{weight of copolymer} \times 1000} \quad (4.4)$$

From the Equation 4.3 and 4.4, % MA incorporation could be calculated by the following Equation 4.5.

$$\text{MA incorporation (\%)} = \frac{\text{MA composition in copolymer}}{\text{MA composition in feed}} \times 100 \quad (4.5)$$

From Table 4.3, the incorporation percentage maleic acid (MA) in poly(NIPA-*co*-MA) was  $22.9 \pm 0.3$  % (n=3). The mole ratio of NIPA/MA in poly(NIPA-*co*-MA) was calculated by the following Equation 4.6.

$$\text{Mole ratio} = \frac{\text{mole NIPA (mol)}}{\text{mole MA (mol)}} \quad (4.6)$$

From Equation 4.6, the mole ratio of NIPA/MA in poly(NIPA-*co*-MA) was 2:1.

In this work, MA comonomers were incorporated into the polymer chain and serve as crosslinking sites for the crosslinking reaction with diethylene glycol (DEG) crosslinking agent. The crosslinks were formed by esterification reaction that were activated by heat as shown in Scheme 4.2. Thus, the diethylene glycol (DEG) composition in copolymer was calculated by using the following Equation 4.7.

$$\text{DEG composition in copolymer (eq.g}^{-1}_{\text{copolymer}}) = \frac{\text{DEG amount (\%wt/wt of copolymer)} \times 2}{100 \times 106.12} \quad (4.7)$$

From the Equation 4.4 and 4.7, MA/DEG ratio (in eq/g<sub>copolymer</sub>) could be calculated by the following Equation 4.8.

$$\text{MA/DEG ratio} = \frac{\text{MA composition in copolymer}}{\text{DEG composition in copolymer}} \quad (4.8)$$

The MA/DEG ratio was defined as the ratio of maleic acid to diethylene glycol equivalents in the crosslinked copolymer. This explains its crosslinking reaction. If there is an equilibrium point in its reaction between MA moieties and DEG, the MA/DEG ratio is one. If the relative equivalent of MA in the hydrogel is more than equivalent of DEG, MA/DEG is greater than one. If MA/DEG ratio is less than one, the relative equivalent of MA in the hydrogel is less. At amount of DEG 5%wt/wt of copolymer, MA/DEG ratio is estimated as 1.5 times. This result shows that copolymers have enough MA moieties as crosslink site for the crosslinking reaction with DEG and residue of carboxylic acid groups of hydrogel after crosslinking reaction.



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**Table 4.3** Composition of MA in poly(NIPA-co-MA) by acid-base titration.

No.	Preparation of copolymer solution (50 mL)		Titration		Amount of MA		% MA incorporation
	Weight of copolymer (g)	Concentration (%wt/v)	Volume of sample (mL)	Volume of std. <sup>a</sup> 0.10 M NaOH (mL)	In feed (by calculation) (eq/g <sub>monomer</sub> )	In copolymer (by titration) (eq/g <sub>copolymer</sub> )	
1	0.4956	1.0	10.00	1.40	$6.21 \times 10^{-3}$	$1.41 \times 10^{-3}$	22.7
2	0.5511	1.1	10.00	1.55	$6.21 \times 10^{-3}$	$1.41 \times 10^{-3}$	22.7
3	0.5340	1.1	10.00	1.55	$6.21 \times 10^{-3}$	$1.45 \times 10^{-3}$	23.3
Mean $\pm$ S.D.							22.9 $\pm$ 0.3

<sup>a</sup> Mean value, n = 3

### 4.3 Electrospun Copolymer Hydrogel Membrane

In this section, poly(NIPA-*co*-MA) was fabricated by electrospinning, followed by a heat-induced esterification crosslinking reaction. The morphology of copolymer hydrogel membranes on varying electrical potentials and distances between the needle and the collection screen was investigated by Scanning Electron Microscopy (SEM). The functional groups of electrospun hydrogel fibrous membrane were characterized by Fourier Transforms Infrared Spectroscopy (FT-IR).

From preliminary study, the mixture solution in aqueous system was used for electrospinning process. The membrane from spinning process was formed a film instead of fiber. Therefore, it can be implied that water is not a good solvent agreed with the results published by Rackwood *et al.* [79]. The electrospinning jet of poly(NIPA)/water system could not withstand the whipping motion; the jet broke to form short fibers. Electrospinning of poly(NIPA) was limited but many reports showed that it could be electrospun from different organic solvent [78-79]. Some commonly used organic solvent such as ethanol (EtOH), acetone and *N,N*-dimethylformamide (DMF) were firstly considered. Poly(NIPA-*co*-MA) could dissolve in EtOH and DMF while it could not dissolve in acetone. The homogeneous mixture of poly(NIPA-*co*-MA) and crosslinking agent diethylene glycol (DEG) was obtained by dissolving in EtOH and DMF (at concentration of copolymer solution 10%wt/v of solvent). Afterwards, mixture solutions in EtOH or DMF were electrospun. The continuous spinning and a stable drop at the end of the needle tip was observed which indicated the proper viscosity and surface tension of the solution. However, the solution in DMF exhibited emanation of jet and pungent odor during electrospinning. Therefore, a mixture solution in ethanol was selected for electrospinning process since it is good spinability, low toxicity and not expensive.



Based on a few preliminary studies and experiments [28-29, 78-79], the electrospin process had been fixed initially as following:

The electrospinning solution contained 10%wt/v of poly(NIPA-*co*-MA) copolymer in ethanol (EtOH) and 5%wt/wt crosslinking agent diethylene glycol (DEG). The mixture solution was loaded into a disposable syringe with a 0.80 mm diameter needle which was connected to a high-voltage supply capable of generating electric potential in range 15-30 kV. An aluminum foil was applied as the collector while the distance between the needle and the collection screen was 10-25 cm. The feeding rate was 1 mL hour<sup>-1</sup>. Such-obtained poly(NIPA-*co*-MA) nanofibrous membranes were put in an oven at 145 °C for 10 min to complete the crosslinking reaction, and then dried at 60 °C for 12 hours to remove residual water or solvent.

#### 4.3.1 Morphology of Copolymer Hydrogel Membrane

Electrospinning will occur when electrostatic force overcomes the surface tension of polymer solution. A high potential, in the kilovolt range, used to generate the electrostatic repulsive force on the polymer solution. It changed the droplet of polymer solution at the end of the needle tip to Taylor's cone and then the jets ejected from Taylor's cone. Therefore, applied electric potential and electric field affected morphology and diameter of fibers. Moreover, changing of distance between the needle and the collection screen influenced directly both electric field generated by electric potential and the flight time of jet as reached on the collector [38]. Therefore, the effects of applied electric potential on morphology and diameter of fibers need to be considered together with the distance between the needle and the collection screen.

Figure 4.6 and 4.7 show a series of SEM images (with magnification of 3,500 and 20,000, respectively) at different combinations of distance between the needle and the collection screen and electric potential on electrospinning of poly(NIPA-*co*-MA) containing 5%wt/wt DEG. The quantitative analysis of the results was summarized in

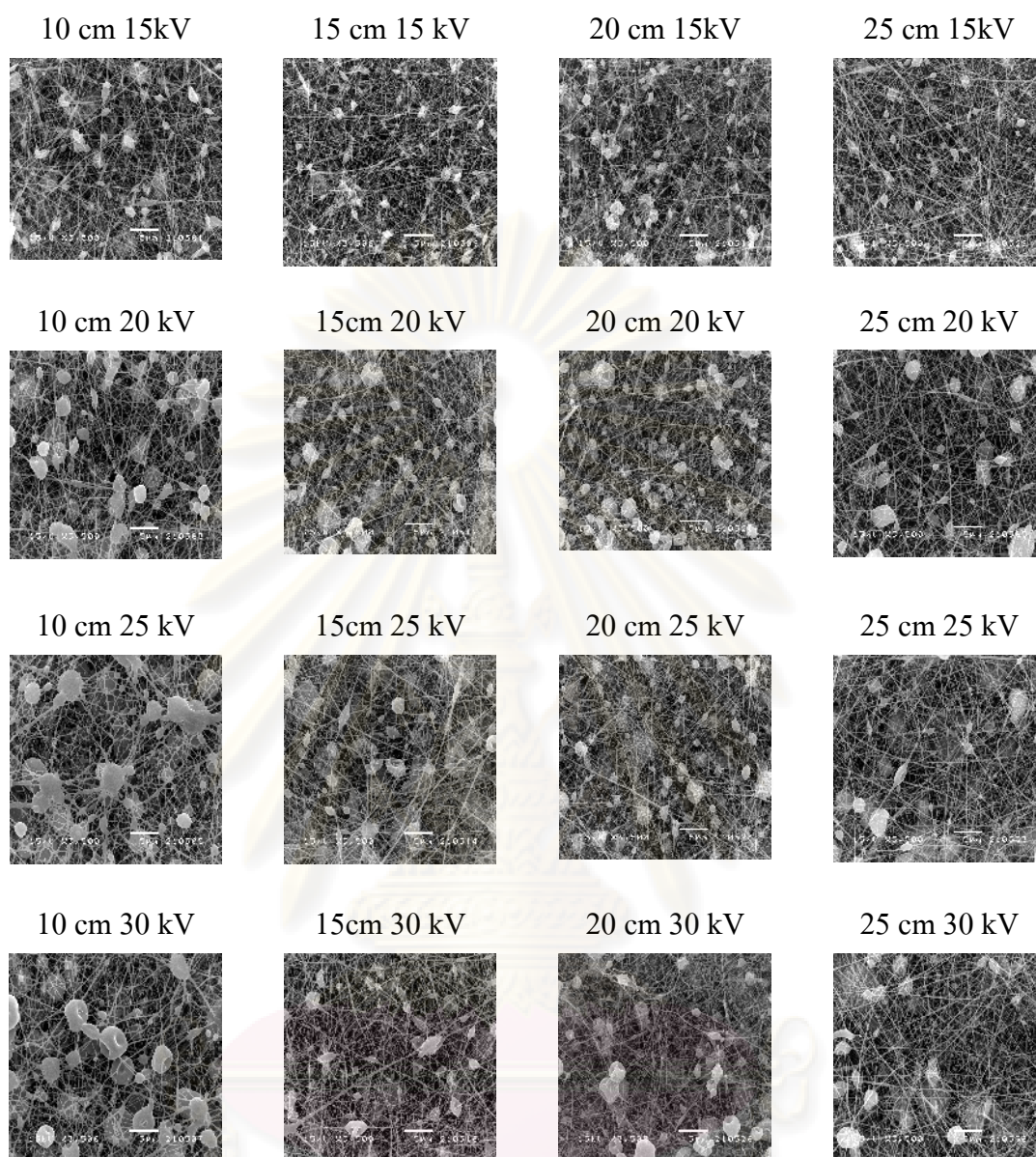
Table 4.4. Normally, increasing electric potential will increase levels of drawing stress of jet that will permit the fiber diameter to decrease [68]. However, in this study, when the electric potential changed from 15 kV to 30 kV (keeping other parameter constant), the average diameter of fibers increased. The diameters of electrospun fibers did not follow as described above when electric potential increased. One possible reason for this event was the evaporation of solvent which happened before drawing stress of jet by highly applied electric potential. Therefore, the diameter of the fibers did not decrease agreed with the report of Uppatham *et al.* [87-88]. However, the node density decreased when electric potential increased. When distances between the needle and the collection screen changed from 10 cm to 25 cm (keeping other parameter constant), the average diameter of fibers decreased because the longer distance means that there was a longer flight time for the solution to be stretched before it reached the collector. Moreover, at the distance of 10 cm, Intra and Inter layer bending fibers features were found when electric potential increased in the range of 25 to 30 kV. It means that the jet would have a very short distance and very high electric field. Decreasing the distance has the same effect as increasing the electric potential supply and this caused an increasing the electric field and also increased the acceleration of the jet to the collector. As a result, the jet may not have enough time for the solvent evaporation before it reached the collector.

Further analysis showed that the node density decreased when electric potential increased (see Table 4.4). The increasing of the applied voltage raise to higher electrostatic repulsion forces which provides higher drawing stress in the jet between the needle and the collector that makes density of nodes lower [89]. Thus the formation of nodes in the fibers had correlation to the spinning voltage. However, the shape of the node changed from spherical to spindle like when the electric field varied from high to low levels since the electric field is high, the stretching of jets is ready to be halted immediately due to its solidification. At the highest electric field (at 10 cm

30 kV), the node features are spherical shape and the collapse skin because of fast evaporation of solvent. Normalization of the observed fiber density by the observed node density resulted in the fiber-to-node ratio. The node density is the average number of nodes per unit area while the fiber density is the average number of fibers per unit area. The high fiber-to-node ratio means the higher fiber density and suppresses the node (lower node density). The high fiber-to-node ratio was found at 25 cm 30 kV and 25 cm 25 kV (i.e. 34.1 and 29.5, respectively) with the spindle like nodes on fiber.

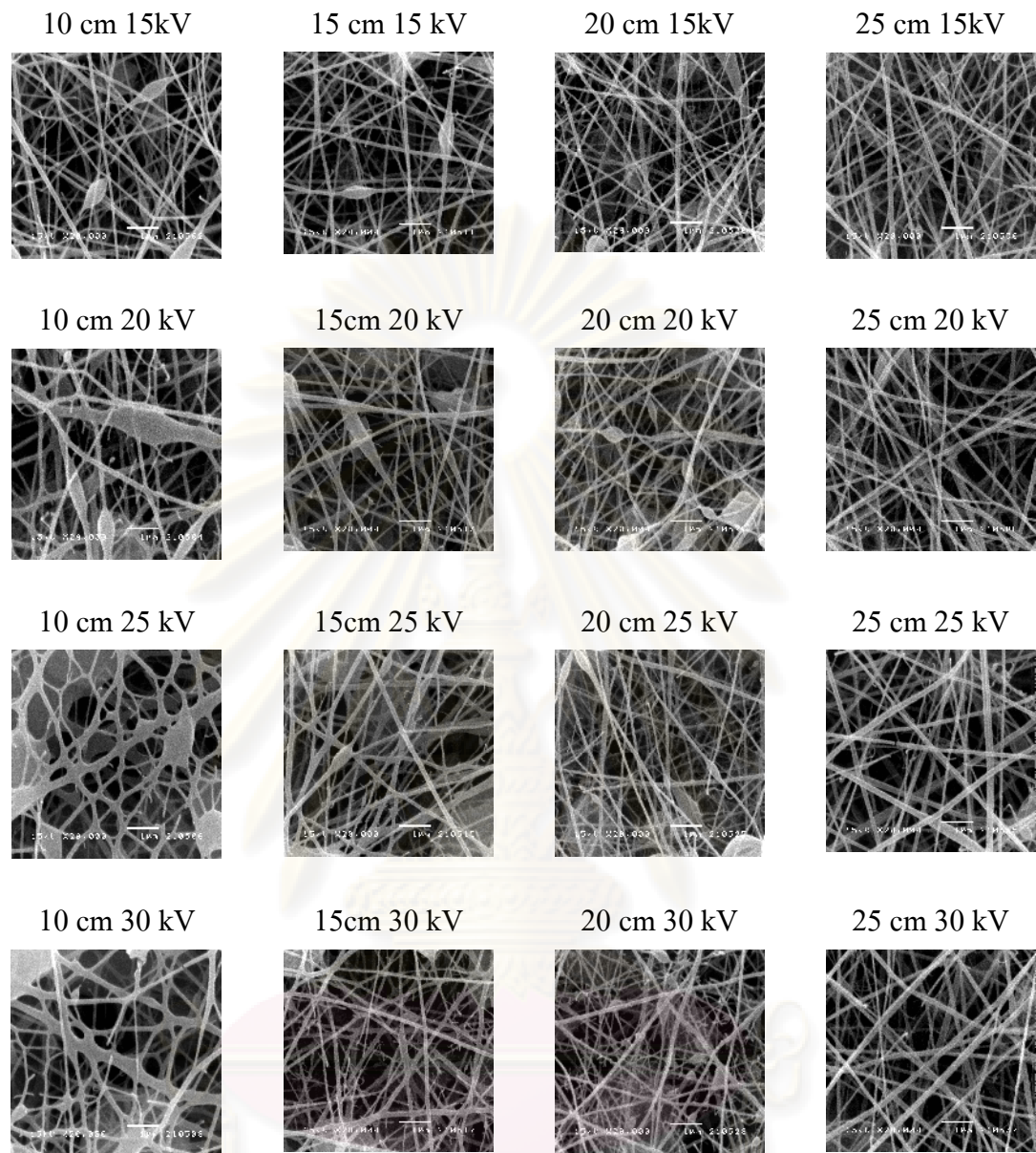
The SEM images of 20 cm 15 kV, 25 cm 15 kV, 25 cm 20 kV, 25 cm 25 kV and 25 cm 30 kV showed satisfactory fiber mats because regular and straight fibers were formed. It was uniform non-woven fabric structure. However, condition at 20 cm 15 kV, 25 cm 15 kV and 25 cm 20 kV, less fibers reacted on the collector which was caused by both a very long distance and very low electric field. Moreover, this condition had more density of nodes than the conditions at 25 cm 25 kV and at 25 cm 30 kV. For the distance of 25 cm at 30 kV, it was found that the spinning produced severe static electricity and spark. Therefore, the optimum electric potential and distance between needle and collector screen were obtained at 25 kV and 25 cm, respectively.

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**Figure 4.6** SEM images of electrospun poly(NIPA-*co*-MA) fibers containing DEG, original magnifications of 3,500.

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**Figure 4.7** SEM images of electrospun poly(NIPA-co-MA) fibers containing DEG, original magnifications of 20,000.

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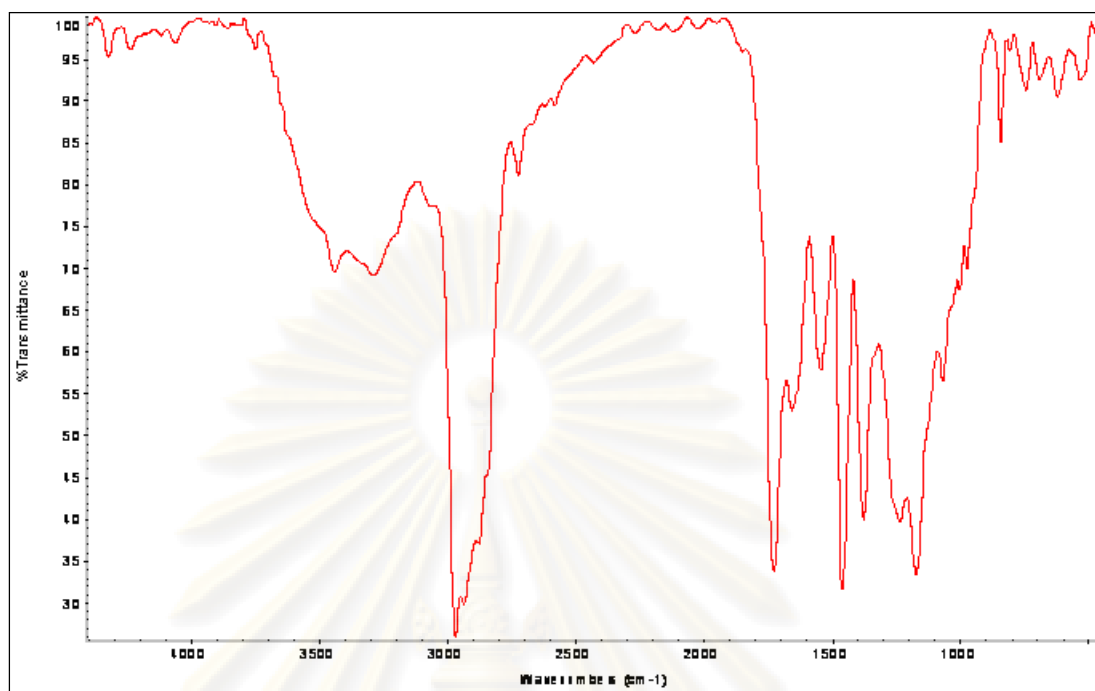
**Table 4.4** Quantitative analysis of electrospun poly(NIPA-co-MA) fibers containing DEG.

<i>Distance (cm)</i>	<i>Potential (kV)</i>	<i>Fiber Diameters (nm)</i>	<i>Node Density [node/ (cm)<sup>2</sup>] × 10<sup>-6</sup></i>	<i>Range of Node Size (nm)</i>	<i>Fiber Density [fiber/ (cm)<sup>2</sup>] × 10<sup>-6</sup></i>	<i>Fiber/ Node Ratio</i>
10	15	110±34	8.28	400-700	102.35	12.4
	20	134±42	8.08	400-1500	62.73	7.8
	25	146±53	7.46	500-900	51.17	6.9
	30	160±58	6.34	300-1000	53.79	8.5
15	15	101±22	12.30	300-600	110.97	9.0
	20	113±35	9.52	300-700	99.30	10.4
	25	126±40	7.22	300-600	61.53	8.5
	30	137±42	6.64	300-800	72.44	10.9
20	15	92±28	12.17	400-700	86.31	7.1
	20	104±35	8.60	500-700	76.29	8.9
	25	120±37	7.53	400-900	87.82	11.7
	30	126±38	7.30	300-600	71.52	9.8
25	15	88±34	7.09	600	97.23	13.7
	20	99±27	5.18	400-800	97.00	18.7
	25	117±33	2.90	500-600	85.60	29.5
	30	121±35	2.40	1300-2000	81.84	34.1

### 4.3.2 FT-IR Spectrum of Copolymer Hydrogel Membrane

The electrospun poly(NIPA-co-MA) fibers containing DEG was characterized by FT-IR. The IR spectrum of fibers was shown in Figure 4.8. The absorption bands of NIPA unit and esterification of MA unit with DEG were found. The new peaks appeared at 1872 (w) and 1847 (w)  $\text{cm}^{-1}$  assigned to C=O stretching of ester group and at 1067 (w, broad) and 1020 (w)  $\text{cm}^{-1}$  assigned to C-O stretching of ester group. These are characteristic absorption peaks of crosslinked poly(NIPA-co-MA) membrane which exhibited significant difference with characteristic absorption of synthesized copolymer as shown in Figure 4.3. In addition, FT-IR spectrum of crosslinked copolymer membrane and film were compared. The IR spectrum of crosslinked copolymer film was shown in Figure 4.9. The result of some important peak assignments from IR spectra of crosslinked spun membrane in comparison with those of cast film was summarized in Table 4.5. It was found that the IR spectra of crosslinked copolymer membrane and film were very similar. It indicated that the process of electrospinning did not alter the functional groups of polymer.

In conclusion, from the electrospun poly(NIPA-co-MA) fibers crosslinked with DEG, it can be confirmed that successful esterification crosslink reaction of the membrane had taken place.



**Figure 4.8** FT-IR spectrum of crosslinked poly(NIPA-co-MA) membrane.



**Figure 4.9** FT-IR spectrum of crosslinked poly(NIPA-co-MA) film.



**Table 4.5** Analysis of FT-IR absorption peaks of the crosslink poly(NIPA-co-MA) membrane in comparison with those of the cast film

<i>Peaks Observed in spun fiber (<math>cm^{-1}</math>)</i>	<i>Peaks Observed in cast film (<math>cm^{-1}</math>)</i>	<i>Functional group</i>
3708 - 3187	3629 - 3200	O-H stretching of carboxylic group
3293 and 3085	3286 and 3074	N-H stretching of secondary amide
2969, 2939 and 2867	2973, 2933 and 2867	C-H stretching in CH CH <sub>2</sub> and CH <sub>3</sub> groups
1872 and 1847	1874 and 1847	C=O stretching of ester group
1741 and 1715	1774 and 1723	C=O stretching of carboxylic group
1654	1647	C=O stretching of amide I
1563	1545	N-H bending of amide II
1450	1461	C-N stretching of amide III
1377 and 1264	1366 and 1246	CH <sub>3</sub> deformation in isopropyl group
1067 and 1020	1067 and 998	C-O stretching of ester group

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#### 4.4 Water Absorbing Behavior of Copolymer Hydrogel Membrane in Different Temperatures

In Table 4.6, temperature-responsive water absorption ratios of poly(NIPA-co-MA) hydrogel membrane were shown. It was found that the hydrogel fibers showed different temperature dependent swelling responses. When the temperatures was raised from 34 to 50 °C, the water absorption ratio of the crosslink-poly(NIPA-co-MA) membrane decreased from 17 to 4 g g<sup>-1</sup>. From the literature, it has been known that poly(NIPA) is a type of thermoresponsive hydrogel whose water absorption mechanism is strongly associated with the chain conformation in aqueous solution. With increasing temperature, the hydrogen bonding weakens, it leads to a reduction in the structuring of water around the hydrophobic groups. As this water structure is released, the interactions between hydrophobic side groups of the polymer increase [90-91]. Moreover, at 34 °C, the hydrogel membrane was translucent and swollen while, at 35 °C and above, the hydrogel membrane became cloudy and shrank. This observation indicates that the hydrogel exhibited Lower Critical Solution Temperature (LCST) behaviors which look like the conventional poly(NIPA) hydrogel at LCST in the vicinity of 34 °C [11]. Figure 4.10 showed that the polymer membrane was transparent at low temperature and became opaque above a critical temperature. Moreover, in this work, when the temperature was increased from 34 to 50 °C, the weight loss of the membrane was decreased from 49 to 21% while, at below 34 °C, the hydrogel membrane dissolved in water. When the hydrogel swelled up and is highly hydrated, therefore it became hydrophilic state. It could not maintain fibrous morphology, on the other hand it became distorted and exploded on the fiber surface and dispersed in water. However, these phenomena might be useful to apply in chemical separation process at high temperature and easy to remove at low temperature. For example, poly(NIPA) has been used for adsorption of heavy metals by temperature-swing solid-phase extraction (TS-SPE) technique [12-13]. First, a

metal ion in an aqueous solution is complex with an extractant. Subsequently, the metal-extractant complexes or micelles are adsorbed onto the poly(NIPA) hydrogel through a hydrophobic interaction above the LCST. Finally, the metal-extractant complexes are desorbed from the poly(NIPA) hydrogel after it is cooled below the LCST.

The cast films were used to compare its ability of temperature-responsive water absorption ratio to the electrospun mats. From Table 4.6, the maximum and minimum water absorption ratio of cast film was  $75 \text{ g g}^{-1}$  at  $10^\circ\text{C}$  and  $8 \text{ g g}^{-1}$  at  $50^\circ\text{C}$ , respectively. The cast films showed temperature sensitive property but there is no precise change at LCST. The reasonable cause for this is due to the membrane has much more surface area than the cast film. The result showed that the LCST point of poly(NIPA-co-MA) electrospun fibrous membrane was sharper than the cast film.



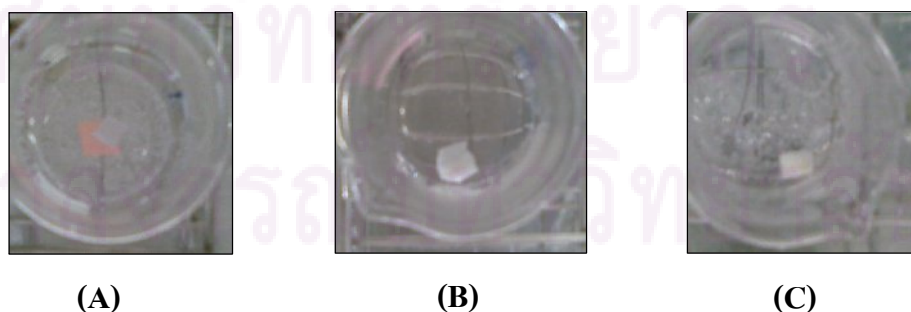
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**Table 4.6** Temperature-responsive water absorption ratio of poly(NIPA-co-MA) hydrogel membrane and film

<i>Temperature</i> (°C)	<i>Membrane</i>		<i>Film</i>	
	<i>Water absorption ratio (g g<sup>-1</sup>)<sup>a</sup></i>	<i>Weight loss (%)<sup>a</sup></i>	<i>Water absorption ratio (g g<sup>-1</sup>)<sup>a</sup></i>	<i>Weight loss (%)<sup>a</sup></i>
10	Not available	Not available	75±5	34±2
20	Not available	Not available	75±12	38±2
30	Not available	Not available	52±1	28±1
33	Not available	Not available	52±7	29±1
34	17±4	49±6	49±2	30±2
35	14±0	49±4	47±5	26±1
40	5±1	31±7	46±5	29±1
45	3±1	21±3	-	-
50	4±0	21±6	8±2	22±3

<sup>a</sup>Mean value ±S.D., n=3

Remarks: Not available due to the dissolution of the membranes in water.



**Figure 4.10** Images of crosslink-poly(NIPA-co-MA) hydrogel membrane containing 5%wt/wt DEG; (A) at 34 °C, (B) at 35 °C and (C) at 50 °C.

## CHAPTER V

### CONCLUSION AND SUGGESTIONS

#### 5.1 Conclusion

The new copolymer poly[*N*-isopropylacrylamide-*co*-(maleic acid)] or poly(NIPA-*co*-MA) nanofiber hydrogel membrane was successfully fabricated by electrospinning using diethylene glycol (DEG) as a crosslinker and a subsequent heat-induced esterification crosslinking reaction at 145 °C for 10 minutes.

A random copolymer poly(NIPA-*co*-MA) consisting of two monomers, *N*-isopropylacrylamide (NIPA) and maleic acid (MA), was synthesized by free radical copolymerization in an aqueous system using APS and TEMED as an initiator and coinitiator, respectively. The MA moieties in the polymer backbone were used as sites for the crosslinking reaction with DEG to obtain water insoluble material. The parameters influencing the crosslinking reaction consisted of the feed molar ratio of MA in copolymerization, the amount of crosslinking agent DEG and the concentration of polymer solution were studied from a polymer solution with DEG *via* film casting and then crosslinked by heat. The optimum crosslinking reaction condition for the crosslinked poly(NIPA-*co*-MA) could be achieved from the synthesized poly(NIPA-*co*-MA) with molar feed ratio of 35%mol MA/mol of the total monomer in copolymerization process solution concentration at 10%wt/v of ethanol with crosslinking agent DEG amount 5%wt/wt of copolymer. These crosslinked poly(NIPA-*co*-MA) film was able to retain film form after immersing in water at room temperature for 24 hours.

The synthetic copolymer was characterized by Fourier Transforms Infrared (FT-IR) and Nuclear Magnetic Resonance (NMR) Spectroscopy and Acid-

base Titration. The results from all characterization techniques could evidently confirm the successful copolymerization of MA comonomer onto the NIPA polymer. Moreover, the incorporation of MA in poly(NIPA-*co*-MA) was estimated to be 23% by acid-base titration. On the basis of these the incorporation of MA in copolymer, the actual mole ratio of NIPA/MA in poly(NIPA-*co*-MA) was 2:1. Furthermore, the analysis result showed that the MA/DEG ratio starting with 5%wt DEG /wt of copolymer was 1.5.

The morphology and diameter of electrospun hydrogel fibrous membranes was investigated by Scanning Electron Microscope (SEM). The morphology and diameter of the obtained fibers were affected by the electric potential and the distance between the needle and the collection screen. The fibers had a diameter ranging from 88 nm to 160 nm. The electrospun hydrogel membrane with regular, straight uniform diameter fibers, low node density and uniform non-woven fabric structure was prepared through optimizing electrospinning parameter: the applied voltage at 25 kV and distance between the needle and the collection screen at 25 cm using a diameter of needle at 0.80 mm and the flow rate at 1 mL hour<sup>-1</sup>. The average diameter of electrospun fibers was 117 nm. The fiber-to-node ratio was evaluated to be 29.5 with the spindle like nodes on fibers. In addition, an IR spectroscopic study which indicated the presence of an ester linkage at 1872 and 1847 cm<sup>-1</sup> confirmed successful crosslinking reaction between DEG hydroxyl group and the copolymer carboxylic group on MA moieties.

The swelling behavior of the electrospun nanofibrous hydrogel membrane in different temperatures (10-50°C) was also investigated. It was found that the electrospun hydrogel membrane which behaved thermosensitive property and had a lower critical solution temperature (LCST) in water in the vicinity of 34 °C. The reduced temperature increased the water absorption ratio but increased the weight loss of electrospun hydrogel membrane. Its maximum and minimum water absorption ratio was 17 g g<sup>-1</sup> at 34 °C and 4.4 g g<sup>-1</sup> at 50 °C, respectively. It had the weight loss ranging from 49% at 34 °C and 21% at 50 °C while at below 34 °C, the hydrogel membrane distorted dissolved in water.

## 5.2 Suggestions for Future Work

The introduction of a rigid chain structure such as phenyl side group into the backbone of poly(NIPA-*co*-MA) may be limited to small extension in order to maintain fiber morphology as much as possible in the water immersion/drying cycles of hydrogel nanofiber. Many factors can influence the morphology of fibers such as molecular weight of polymer, viscosity, surface tension, collector geometry, *etc.* Thus, these important parameters shall be studied during electrospinning process development. Moreover, it is well known that electrospun poly(NIPA-*co*-MA) hydrogel membrane had large surface area, high porosity and light weight. Consequently the electrospun hydrogel membrane shall be applied for many applications such as chemical separation process, sensors, drug delivery devices and tissue engineering scaffold.



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