CONTENTS

	Page
CONTENTS	viii
LIST OF TABLES	xii
LIST OF FIGURES	xiv
CHAPTER	
1 INTRODUCTION	1
1.1 General Introduction	1
1.2 Literature Review	2
1.2.1 Molecular recognition	2
1.2.2 Molecular imprinted polymer (MIP)	2
1.2.2.1 Introduction of MIP	2
1.2.2.2 Chemical for MIP	3
1.2.2.3 Overview of assembly of MIP	5
1.2.3 Polymerization for synthesis of MIP and general characterization	5
1.2.4 Incorporation MIP and membrane base (MIP membrane)	7
1.2.4.1 Introduction of MIP membrane	7
1.2.4.2 The membrane base	10
1.2.4.3 Preparation of composite MIP membranes	12
1.2.4.3.1In situ polymerization	12
1.2.4.3.2 Phase inversion	12
1.2.4.3.3 Grafting	13
1.2.4.4 Drug delivery by composite MIP membrane	14
1.2.4.4.1 Introduction	14
1.2.4.4.2 Facilitate and retard mechanism	15
1.2.5 Confocal laser scanning microscope (CLSM)	16
1.2.5.1 Principle and operation	16
1.2.5.2 Application	17

CONTENTS (Continued)

	Page
1.3 The rationale and aims of this project	17
1.3.1 The template	17
1.3.2 The transdermal drug delivery application	18
1.3.3 Research study	20
2 THE PREPARATION AND EVALUATION OF THE MIP COMPOSITE CELLULOSE	
MEMBRANE	22
2.1 Chemicals and reagents	22
2.1.1 Standard chemicals	22
2.1.2 Reagents and materials	23
2.2 Preparation of the composite MIP membranes by phase inversion	
and grafted method	24
2.2.1 Preparation of the MIP microparticles	24
2.2.2 Synthesis of the MIP and NIP microparticles	27
2.2.3 Evaluation of the recognition properties of the MIP particles	28
2.2.4 Preparation of the composite MIP particle membrane by	
phase inversion technique	28
2.2.5 Preparation of the composite MIP membrane by grafting method	29
2.2.6 Characterization methods	30
2.2.6.1 Surface morphology	30
2.2.6.2 Electrical resistance measurements	31
2.2.6.3 Pore size measurements	31
2.2.6.4 Mechanical properties measurements	31
2.2.6.5 Degree of swelling of the composite MIP	
cellulose membrane	32
2.2.7 Results and discussion	32
2.2.7.1 The MIP particle composite cellulose membrane	32

CONTENTS (Continued)

	Page
2.2.7.2 The MIP grafted cellulose membrane and its	
Characteristics	34
2.3 Optimization of some parameter in composite MIP membrane synthesis	
and experiment condition	41
2.3.1 In vitro release evaluation of composite MIP membrane	41
2.3.2 Diffusion determination	42
2.3.3 Stereospecific HPLC method	43
2.3.4 Statistical analysis	43
2.3.5 Results and discussion	43
2.3.5.1 In vitro release study	43
2.3.5.2 Enantiomeric release of the MIP composite membrane	46
2.4 In vitro evaluation of transdermal delivery	48
2.4.1 In vitro percutaneous penetration study	49
2.4.2 Results and discussion	50
2.4.2.1 In vitro percutaneous penetration study	50
3 CONFOCAL LASER SCANNING MICROSCOPY STUDY	53
3.1 The rationale	53
3.2 Experimental	53
3.2.1 Synthesis of the fluorescent probe	53
3.2.2 The composite MIP membrane embedded with the	
pyrenebutyryl propranolol ester enantiomer	54
3.2.3 CLSM measurement	54
3.3 Results and Discussion	55
3.3.1 Identification of the fluorescent probes	55
3.3.2 The CLSM study	61
4 DISCUSSION	76

Х

CONTENTS (Continued)

	Page
5 CONCLUSIONS	78
REFERENCES	79
VITAE	85

LIST OF TABLES

Table	Page
2.1 Different formulations of MIP grafted membrane	29
2.2 Characteristics of composite MIP cellulose membrane prepared by phase	
inversion method (mean±SD, n=3)	35
2.3 Characteristic of composite MIP cellulose membrane prepared by grafted method	
(mean±SD, n=3)	36
2.4 In vitro release and diffusion measurement data of propranolol from the composite	
MIP particle membrane when prepared at different ratio of drug to polymer after	
application of pH 7.4 phosphate buffer in donor phase at 37±1°C (mean±SD, n=3,	
* $P \leq 0.05$ of diffusion coefficient between <i>S</i> - and <i>R</i> -isomer)	46
2.5 In vitro release and diffusion measurement data of propranolol from the composite	
MIP particle membrane when prepared at different polymer content after application	
of pH 7.4 phosphate buffer in donor phase at $37\pm1^{\circ}$ C (mean \pm SD, n=3, *P \leq 0.05	
of diffusion coefficient between S- and R-isomer)	47
2.6 In vitro release and diffusion measurement data of propranolol from the MIP	
grafted cellulose membrane when prepared at different formular after application	
of pH 7.4 phosphate buffer in donor phase at $37\pm1^{\circ}$ C (mean±SD, n=3, *P \leq 0.05	
of diffusion coefficient between S- and R-isomer)	48
2.7 In vitro rat skin permeation data of propranolol from composite MIP membrane after	
application of pH 7.4 phosphate buffer at $37\pm1^{\circ}$ C (mean \pm SD, n=3, *P \leq 0.05 of Flux	
between S- and R-isomer)	52
3.1 The concentration of R - and S -propranolol probe and 1-pyrene-butyric acid detected in	
donor and receiver phases after application of solvent to a composite MIP microsphere	
membrane in the pyrene of propranolol probe placed on isolated rat epidermal sections.	
The composite MIP membrane of this type was prepared by integration of S-propranolol	
imprinted polymer (mean \pm S.D., n = 3).	63

LIST OF TABLES (Continued)

Table	Page
3.2 The concentration of R - and S -propranolol probe and 1-pyrene-butyric acid detected in	
donor and receiver phases after application of 48 μ g/ml of propranolol probe to a	
composite microsphere membrane placed on isolated rat epidermal sections. The	
composite MIP membrane of this type was prepared by integration of <i>R</i> -propranolol	
imprinted polymer(mean \pm S.D., n = 3).	67
3.3 The concentration of R - and S -propranolol probe and 1-pyrene-butyric acid detected	
in donor and receiver phases after application of solvent to a MIP grafted cellulose	
membrane placed on isolated rat epidermal sections(mean \pm S.D., n = 3)	72
3.4 The %amount of R-and S-propranolol probe in each compartment from composite	
MIP membrane at different time	75

LIST OF FIGURES

Figure	Page
1.1 Lock and Key Theory of non-covalent bond for MIP	3
1.2 Schematic illustration of preparation of MIP	5
1.3 The application of MIP	8
1.4 Overview of MIP assemblies as MIP membrane	9
1.5 Symmetric macroporous membrane for microfiltration or as base material	
for membrane adsorption	10
1.6 Asymmetric microporous membrane for ultrafiltration	10
1.7 Bacterial cellulose membranes	11
1.8 Confocal laser scanning microscope model	16
1.9 Structure of propranolol	18
2.1 Overview of MIP composite membrane prepared by grafting method	30
2.2 SEM images of molecular imprinted polymer particles	33
2.3The recovery of rebinding of propranolol enantiomers with imprinted and non-	
imprinted polymer of microsphere at various polymer contents in pH 7.4	
phosphate buffer solution and room temperature (mean \pm S.D., n = 3)	34
2.4 The SEM image of the composite MIP cellulose membrane prepared by phase	
inversion method	36
2.5 Cross-section image of the composite MIP cellulose membrane prepared by	
phase inversion method	37
2.6 The surface morphology of the cellulose membrane base	37
2.7 The surface morphology of the composite MIP cellulose membrane prepared by	
grafting method for formulation 1	38
2.8 The surface morphology of the composite MIP cellulose membrane prepared by	
grafting method for formulation 2	38
2.9 The surface morphology of the composite MIP cellulose membrane prepared by	
grafting method for formulation 3	39

LIST OF FIGURES (Continued)

Figure	Page
2.10 Cross-section image of the cellulose membrane base	39
2.11 Cross-section image of the composite MIP cellulose membrane prepared by grafting	
method for formulation 1	40
2.12 Cross-section image of the composite MIP cellulose membrane prepared by	
grafting method for formulation 2	40
2.13 Cross-section image of the composite MIP cellulose membrane prepared by	
grafting method for formulation 3	41
2.14 Time profiles of propranolol enantiomers at different medium (mean±SD, n=3)	45
2.15 The selectivity of composite MIP cellulose membrane when incubate in buffer	
pH 3, 5.5, 7.4 and chloroform (mean±SD, n=3)	45
3.1 IR spectrum of propranolol probe	58
3.2 ¹ H-NMR of propranolol probe	59
3.3 ¹³ C-NMR of propranolol probe	60
3.4 Distribution of the pyrenebutyrate ester of propranolol and pyrenebutyric acid in the	
membrane and rat skin at 1, 12 and 24 hr of the composite MIP microparticles membrane)
in the presence of propranolol probe. The composite MIP membrane of this type was	
prepared by integration of S-propranolol imprinted polymer (mean±SD., n=3)	64
3.5 CLSM image showing distribution of R and S -propranolol fluorescent probe (red) in	
rat skin specimen (cross section) after treatment for 1, 12 and 24 hr overlaid with blank	
(control) rat skin (green) of the composite MIP microparticles membrane; E= epidermal	
side, D= dermal side. The composite MIP membrane of this type was prepared by	
integration of S-propranolol imprinted polymer	65
3.6 Distribution of the pyrenebutyrate ester of propranolol and pyrenebutyric acid in the	
membrane and rat skin at 1, 12 and 24 hr of the composite MIP microparticles membran	e
after application of 48 μ g/ml of propranolol probe to donor phase. The composite MIP	
membrane of this type was prepared by integration of R-propranolol imprinted polymer	68

LIST OF FIGURES (Continued)

Figure	Page
3.7 CLSM image showing distribution of R and S -propranolol fluorescent probe (red) in	
rat skin specimen (cross section) after treatment for 1, 12 and 24 hr overlaid with blank	
(control) rat skin (green) of the composite MIP microparticles membrane; E= epidermal	
side, D= dermal side. The composite MIP membrane of this type was prepared by	
integration of <i>R</i> -propranolol imprinted polymer	69
3.8 Distribution of the pyrenebutyrate ester of propranolol and pyrenebutyric acid	
in the membrane and rat skin at 1, 6, 12 and 24 hr of composite MIP grafted	
membrane (mean±SD., n=3)	73
3.9 CLSM image showing distribution of R and S -propranolol fluorescent probe (red) in	
rat skin specimen (cross section) after treatment for 1, 12 and 24 hr overlaid with blank	
(control) rat skin (green) of composite MIP grafted membrane; E= epidermal side,	
D= dermal side	74