

TABLE OF CONTENTS

	Page
Acknowledgment	iii
Abstract (Thai)	v
Abstract (English)	vii
Table of contents	x
List of Tables	xv
List of Figures	xx
Abbreviations	xxxvii
Chapter 1 Introduction	1
1.1 Significance of the study	1
1.2 Literature review	4
1.2.1 Cyclodextrin inclusion complexes	4
1.2.2 Applications of cyclodextrin inclusion complexes	10
1.2.3 Application of molecular modeling for cyclodextrin inclusion complexes	13
1.3 Theories and principles	14
1.3.1 Introduction to cyclodextrins	14
1.3.2 Inclusion complex formation	21
1.3.3 Introduction to piroxicam	36

	Page
1.3.4 Introduction to meloxicam	37
1.3.5 Molecular modeling	39
1.4 Objectives of the study	42
1.5 Scope of the study	42
 Chapter 2 Materials and Methods	 44
2.1 Materials	44
2.2 Instruments	45
2.3 Methods	46
2.3.1 Thermodynamic studies	46
2.3.1.1 Phase solubility studies of piroxicam-CDs	46
inclusion complexes	
2.3.1.2 Phase solubility studies of meloxicam-CDs	47
inclusion complexes	
2.3.1.3 Calculation of the stability constants	48
2.3.1.4 Determination of thermodynamic parameters	49
2.3.2 Solid complex preparation	49
2.3.2.1 Piroxicam-CDs inclusion complexes	49
2.3.2.2 Meloxicam-CDs inclusion complexes	51
2.3.3 Characterization of solid complexes	51
2.3.4 Storage-stability studies	54
2.3.5 Molecular modeling	54

	Page
Chapter 3 Results and discussion	56
3.1 Thermodynamic studies of piroxicam-CDs complexes	56
3.1.1 Intrinsic solubility of piroxicam	56
3.1.2 Phase solubility diagrams of piroxicam-CDs complexes	58
3.1.3 Thermodynamic parameters of piroxicam-CDs complexes	70
3.1.4 Effect of pH on piroxicam-CDs complex formation	72
3.2 Thermodynamic studies of meloxicam-CDs complexes	82
3.2.1 Intrinsic solubility of meloxicam	82
3.2.2 Phase solubility diagrams of meloxicam-CDs complexes	
in solution pH 3.0	85
3.2.3 Phase solubility diagrams of meloxicam-CDs complexes	
in solution pH 6.0	94
3.2.4 Thermodynamic parameters of meloxicam-CDs	
complexes	105
3.3 Preparation of solid complexes	109
3.4 Characterization of solid complexes	111
3.4.1 Dissolution studies	112
3.4.1.1 Dissolution studies of piroxicam-CDs complexes	112
3.4.1.2 Dissolution studies of meloxicam-CDs complexes	146
3.4.2 Differential scanning calorimetry	159
3.4.2.1 DSC of piroxicam-CDs complexes	159

	Page
3.4.2.2 DSC of meloxicam-CDs complexes	169
3.4.3 X-ray diffractometry	173
3.4.3.1 XPD of piroxicam-CDs complexes	174
3.4.3.2 XPD of meloxicam-CDs complexes	189
3.4.4 Fourier transform infrared spectroscopy	194
3.4.4.1 FTIR of piroxicam-CDs complexes	194
3.4.4.2 FTIR of meloxicam-CDs complexes	208
3.4.5 Near infrared spectroscopy	219
3.4.5.1 NIR of piroxicam-CDs complexes	219
3.4.5.2 NIR of meloxicam-CDs complexes	232
3.5 Storage stability studies	241
3.5.1 Dissolution studies	241
3.5.2 DSC studies of stored complexes	245
3.5.3 XPD studies of stored complexes	248
3.6 Molecular modeling	251
3.6.1 Quantitative Structure Property Relationship model	251
3.6.2 Conformational studies of the complexes	261
Chapter 4 Conclusion	271
References	274

	Page
Appendix	290
Appendix A Thermodynamic studies of piroxicam	290
Appendix B Thermodynamic studies of meloxicam	297
Appendix C Dissolution studies of piroxicam	325
Appendix D Dissolution studies of meloxicam	353
Appendix E Molecular modeling	357
Curriculum vitae	360

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
 Copyright © by Chiang Mai University
 All rights reserved

LIST OF TABLES

Table	Title	Page
1	Characteristics of cyclodextrins	15
2	Classification of cyclodextrin derivatives	17
3	Toxicological data of some cyclodextrins	20
4	Intrinsic solubility of piroxicam in distilled water at various temperatures	57
5	Stability constants of piroxicam-BCD inclusion complexes	60
6	Stability constants of piroxicam-GCD inclusion complexes	61
7	Stability constants of piroxicam-HPBCD inclusion complexes	63
8	Stability constants of piroxicam-MeBCD inclusion complexes	64
9	Comparison of the stability constants of piroxicam-CDs inclusion complexes at various temperatures	67
10	Thermodynamic parameters of piroxicam-CDs inclusion complexes	71
11	Solubility of piroxicam in BCD and GCD inclusion complexes	73
12	Solubility of piroxicam in HPBCD and MeBCD inclusion complexes in solution of varying pH values at 37°C	74
13	Stability constants of piroxicam-CDs inclusion complexes in solutions of varying pH values at 37°C	79
14	Comparison of the stability constants of piroxicam-CDs inclusion complexes in solutions of varying pH values at 37°C	81

Table	Title	Page
15	Intrinsic solubility of meloxicam in solution pH 3.0 and 6.0 at various temperatures	83
16	Enthalpy of solution of meloxicam in solution pH 3.0 and 6.0	85
17	Stability constants of meloxicam-BCD inclusion complexes in solution pH 3.0	87
18	Stability constants of meloxicam-GCD inclusion complexes in solution pH 3.0	89
19	Stability constants of meloxicam-HPBCD inclusion complexes in solution pH 3.0	90
20	Stability constants of meloxicam-HPGCD inclusion complexes in solution pH 3.0	92
21	Comparison of the stability constants of meloxicam-CDs complexes in solution pH 3.0 at various temperatures	93
22	Stability constants of meloxicam-BCD inclusion complexes in solution pH 6.0	96
23	Stability constants of meloxicam-GCD inclusion complexes in solution pH 6.0	97
24	Stability constants of meloxicam-HPBCD inclusion complexes in solution pH 6.0	99
25	Stability constants of meloxicam-HPGCD inclusion complexes in solution pH 6.0	100

Table	Title	Page
26	Statistical comparison of the stability constants of meloxicam-CDs complexes in solution pH 6.0 at various temperatures	102
27	Thermodynamic parameters of meloxicam-CDs inclusion complexes in solution pH 3.0 and 6.0	107
28	Percentage of yield of solid complexes	111
29	Dissolution parameters of piroxicam-BCD inclusion complexes prepared by different methods	115
30	Dissolution parameters of piroxicam-GCD inclusion complexes prepared by different method	119
31	Dissolution parameters of piroxicam-HPBCD inclusion complexes prepared by different method	122
32	Dissolution parameters of piroxicam-MeBCD inclusion complexes prepared by different method	125
33	Regression models of %DE30 values and the method of piroxicam-CDs inclusion complex preparations	127
34	Dissolution parameters of piroxicam-CDs physical mixtures prepared from different CD types	130
35	Dissolution parameters of piroxicam-CD inclusion complex of different CD types initially by kneading method	134
36	Dissolution parameters of piroxicam-CD inclusion complex of different CD types initially by co-evaporation method	138

Table	Title	Page
37	Dissolution parameters of piroxicam-CD inclusion complex of different CD types initially by co-lyophilization method	140
38	Comparison of %DE30 values of piroxicam-CDs inclusion complexes prepared from different CD types	142
39	Regression models of %DE30 values of piroxicam-CDs inclusion complexes and the molar ratios	145
40	Dissolution parameters of meloxicam-CDs inclusion complexes prepared by different methods	151
41	Comparison of %DE30 values of meloxicam-CDs inclusion complexes prepared by different methods	152
42	Dissolution parameters of meloxicam-CDs inclusion complexes prepared from different CD types	156
43	Comparison of %DE30 values of meloxicam-CDs inclusion complexes prepared from different CD types	157
44	DSC parameters of piroxicam intact, piroxicam lyophilized and piroxicam-BCD inclusion complexes	163
45	DSC parameters of piroxicam intact, piroxicam lyophilized and piroxicam-GCD inclusion complexes	166
46	DSC parameters of piroxicam intact, piroxicam lyophilized and piroxicam-HPBCD inclusion complexes	167
47	DSC parameters of piroxicam intact, piroxicam lyophilized and piroxicam-MeBCD inclusion complexes	168

Table	Title	Page
48	DSC parameters of meloxicam intact and meloxicam-CDs physical mixture and inclusion complexes prepared by different methods	173
49	Dissolution parameters of piroxicam in distilled water from intact drug (Prx) and 1:1 and 1:2 KN, COE and COL Prx:BCD inclusion initially prepared and after stored at 30°C for year.(Mean±SD)	243
50	Dissolution parameters of meloxicam in simulated gastric fluid from intact drug (Mlx) and binary mixtures of 1:1 Mlx:BCD; PM, KN, COE, COL. (Mean±SD)	245
51	DSC parameters of piroxicam intact, piroxicam lyophilization and piroxicam-BCD inclusion complexes of various molar ratios initially prepared and after stored at 30°C for 1 year	246
52	DSC parameters of meloxicam intact and meloxicam-CDs inclusion complexes prepared by different methods initially prepared and after stored at 45°C for 4 months	247
53	Training set for Model A	252
54	Training set for Model B	253
55	Test set using Model A	257
56	Test set using Model B	258
57	Optimization of piroxicam structure using PM3, AM1 and B3LYP/6-31G** method	266
58	Optimization of piroxicam-BCD complexes by PM3 method	269

LIST OF FIGURES

Figure	Title	Page
1	Structure of β -cyclodextrin	15
2	Mechanism of clodextrin complex formation	21
3	Typical phase solubility diagrams	32
4	Complexation efficiency	35
5	Structure of piroxicam	37
6	Structure of meloxicam	38
7	Solubility profiles of piroxicam in distilled water at various temperatures	57
8	Phase solubility diagrams of piroxicam-BCD inclusion complexes at various temperatures	59
9	Phase solubility diagrams of piroxicam-GCD inclusion complexes at various temperatures	59
10	Phase solubility diagrams of piroxicam-HPBCD inclusion complexes at various temperatures	62
11	Phase solubility diagrams of piroxicam-MeBCD inclusion complexes at various temperatures	62
12	Phase solubility diagrams of piroxicam-MeBCD inclusion complexes at higher MeBCD concentrations at various temperatures	65

Figure	Title	Page
13	Stability constants of piroxicam-CD inclusion complexes at various temperatures	66
14	Van't Hof plot of piroxicam-CDs inclusion complexes	70
15	Phase solubility diagrams of piroxicam-BCD inclusion complexes in solutions of varying pH values at 37°C	73
16	Phase solubility diagrams of piroxicam-GCD inclusion complexes in solutions of varying pH values at 37°C	74
17	Phase solubility diagrams of piroxicam-HPBCD inclusion complexes in solutions of varying pH values at 37°C	75
18	Phase solubility diagrams of piroxicam-MeBCD inclusion complexes in solutions of varying pH values at 37°C	75
19	Stability constants of piroxicam-CDs inclusion complexes in solutions of varying pH values at 37°C	80
20	Solubility plot of meloxicam in solution pH 3.0 and 6.0 at various temperatures	84
21	Phase solubility diagrams of meloxicam-BCD inclusion complexes in solution pH 3.0 at various temperatures	86
22	Phase solubility diagrams of meloxicam-GCD inclusion complexes in solution pH 3.0 at various temperatures	88
23	Phase solubility diagrams of meloxicam-HPBCD inclusion complexes in solution pH 3.0 at various temperatures	88

Figure	Title	Page
24	Phase solubility diagrams of meloxicam-HPGCD inclusion complexes in solution pH 3.0 at various temperatures	91
25	Comparison of the stability constants of meloxicam-CDs complexes in solution pH 3.0 at various temperatures	91
26	Phase solubility diagrams of meloxicam-BCD inclusion complexes in solution pH 6.0 at various temperatures	95
27	Phase solubility diagrams of meloxicam-GCD inclusion complexes in solution pH 6.00 at various temperatures	95
28	Phase solubility diagrams of meloxicam-HPBCD inclusion complexes in solution pH 6.00 at various temperatures	98
29	Phase solubility diagrams of meloxicam-HPGCD inclusion complexes in solution pH 6.00 at various temperatures	98
30	Stability constants of meloxicam-CDs complexes in solution pH 6.0 at various temperatures	101
31	Stability constants (K) of meloxicam-CDs complexes in solution pH 3.0 and 6.0 at various temperatures	103
32	Van't Hof plot of meloxicam-CDs inclusion complexes in solution pH 3.0	105
33	Van't Hof plot of meloxicam-CDs inclusion complexes in solution pH 6.0	106
34	Dissolution profiles of 1:1 piroxicam-BCD inclusion complexes in distilled water prepared by different methods	113

Figure	Title	Page
35	Dissolution profiles of 1:2 piroxicam-BCD inclusion complexes in distilled water prepared by different methods	114
36	Dissolution profiles of 2:1 piroxicam-BCD inclusion complexes in distilled water prepared by different methods	114
37	Dissolution profiles of 1:1 piroxicam-GCD inclusion complexes in distilled water prepared by different methods	117
38	Dissolution profiles of 1:2 piroxicam-GCD inclusion complexes in distilled water prepared by different methods	118
39	Dissolution profiles of 2:1 piroxicam-GCD inclusion complexes in distilled water prepared by different methods	118
40	Dissolution profiles of 1:1 piroxicam-HPBCD inclusion complexes in distilled water prepared by different methods	120
41	Dissolution profiles of 1:2 piroxicam-HPBCD inclusion complexes in distilled water prepared by different methods	121
42	Dissolution profiles of 2:1 piroxicam-HPBCD inclusion complexes in distilled water prepared by different methods	121
43	Dissolution profiles of 1:1 piroxicam-MeBCD inclusion complexes in distilled water prepared by different methods	123
44	Dissolution profiles of 1:2 piroxicam-MeBCD inclusion complexes in distilled water prepared by different methods	124
45	Dissolution profiles of 2:1 piroxicam-MeBCD inclusion complexes in distilled water prepared by different methods	124

Figure	Title	Page
46	Dissolution profiles of 1:1 piroxicam-CDs physical mixtures in distilled water prepared from different types of cyclodextrins	128
47	Dissolution profiles of 1:2 piroxicam-CDs physical mixtures in distilled water prepared from different types of cyclodextrins	129
48	Dissolution profiles of 2:1 piroxicam-CDs physical mixtures in distilled water prepared from different types of cyclodextrins	129
49	Dissolution profiles of 1:1 piroxicam-CDs inclusion complexes of different CD types prepared by kneading method	132
50	Dissolution profiles of 1:2 piroxicam-CDs inclusion complexes of different CD types prepared by kneading method	133
51	Dissolution profiles of 2:1 piroxicam-CDs inclusion complexes of different CD types prepared by kneading method	133
52	Dissolution profiles of 1:1 piroxicam-CDs inclusion complexes of different CD types prepared by co-evaporation method	135
53	Dissolution profiles of 1:2 piroxicam-CDs inclusion complexes of different CD types initially prepared by co-evaporation method	136
54	Dissolution profiles of 2:1 piroxicam-CDs inclusion complexes of different CD types prepared by co-evaporation method	136
55	Dissolution profiles of 1:1 piroxicam-CDs inclusion complexes of different CD types prepared by co-lyophilization method	138
56	Dissolution profiles of 1:2 piroxicam-CDs inclusion complexes of different CD types prepared by co-lyophilization method	139

Figure	Title	Page
57	Dissolution profiles of 2:1 piroxicam-CDs inclusion complexes by co-lyophilization method	139
58	Dissolution profiles of 1:1 meloxicam-BCD inclusion complexes in simulated gastric fluid prepared by different methods	147
59	Dissolution profiles of 1:1 meloxicam-GCD inclusion complexes in simulated gastric fluid prepared by different methods	147
60	Dissolution profiles of 1:1 meloxicam-HPBCD inclusion complexes in simulated gastric fluid prepared by different methods	148
61	Dissolution profiles of 1:1 meloxicam- HPGCD inclusion complexes in simulated gastric fluid prepared by different method	148
62	Dissolution profiles of 1:1 meloxicam-CDs physical mixtures of different CD types initially prepared	154
63	Dissolution profiles of 1:1 meloxicam-CDs inclusion complexes of different CD types prepared by kneading methods	154
64	Dissolution profiles of 1:1 meloxicam-CDs inclusion complexes of different CD types prepared by co-evaporation methods	155
65	Dissolution profiles of 1:1 meloxicam-CDs inclusion complexes of different CD types prepared by co-evaporation methods	155
66	DSC thermograms of piroxicam , piroxicam-BCD physical mixtures of various molar ratios initially prepared and BCD	161
67	DSC thermograms of piroxicam , piroxicam-BCD inclusion complexes of various molar ratios prepared by kneading method	161

Figure	Title	Page
68	DSC thermograms of piroxicam , piroxicam-BCD inclusion complexes of various molar ratios prepared by co-evaporation method	162
69	DSC thermograms of piroxicam , piroxicam-BCD inclusion complexes of various molar ratios prepared by co-lyophilization method	162
70	DSC thermograms of piroxicam , piroxicam-GCD physical mixtures of various molar ratios prepared	164
71	DSC thermograms of piroxicam , piroxicam-GCD inclusion complexes of various molar ratios prepared by kneading method	164
72	DSC thermograms of piroxicam , piroxicam-GCD inclusion complexes of various molar ratios prepared by co-evaporation method	165
73	DSC thermograms of piroxicam , piroxicam-GCD inclusion complexes of prepared by co-lyophilization method	165
74	DSC thermograms of piroxicam , piroxicam-MeBCD physical mixtures of various molar ratios prepared	169
75	DSC thermograms of meloxicam, BCD, 1:1 physical mixture and the inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	171

Figure	Title	Page
76	DSC thermograms of meloxicam, GCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	171
77	DSC thermograms of meloxicam, HPBCD, 1:1 physical mixture and the inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	172
78	DSC thermograms of meloxicam, HPGCD, 1:1 physical mixture and the inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	172
79	X-ray diffractograms of BCD, piroxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	176
80	X-ray diffractograms of BCD, piroxicam, 1:2 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	177
81	X-ray diffractograms of BCD, piroxicam, 2:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	178
82	X-ray diffractograms of GCD, piroxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	180

Figure	Title	Page
83	X-ray diffractograms of GCD, piroxicam, 1:2 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	181
84	X-ray diffractograms of GCD, piroxicam, 2:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	182
85	X-ray diffractograms of HPBCD, piroxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	183
86	X-ray diffractograms of HPBCD, piroxicam, 1:2 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	184
87	X-ray diffractograms of HPBCD, piroxicam, 2:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	185
88	X-ray diffractograms of MeBCD, piroxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	186
89	X-ray diffractograms of MeBCD, piroxicam, 1:2 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	187

Figure	Title	Page
90	X-ray diffractograms of MeBCD, piroxicam, 2:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	188
91	X-ray diffractograms of BCD, meloxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	190
92	X-ray diffractograms of GCD, meloxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	191
93	X-ray diffractograms of HPBCD, meloxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	192
94	X-ray diffractograms of HPGCD, piroxicam, 1:1 physical mixture and the inclusion complex prepared by kneading, co-evaporation and co-lyophilization method	193
95	FTIR spectra of piroxicam , intact	195
96	FTIR spectra of β -cyclodextrin, intact	195
97	FTIR spectra of gamma-cyclodextrin, intact	196
98	FTIR spectra of hydroxypropyl- β -cyclodextrin, intact	196
99	FTIR spectra of hydroxypropyl-gamma cyclodextrin, intact	197
100	FTIR spectra of methylated - β -cyclodextrin, intact	197
101	FTIR of 1:1 piroxicam-BCD physical mixtur	198

Figure	Title	Page
102	FTIR of 1:1 piroxicam-BCD inclusion complex prepared by kneading method	199
103	FTIR of 1:1 piroxicam-BCD inclusion complex prepared by co-evaporation method	200
104	FTIR of 1:1 piroxicam-BCD inclusion complex prepared by co-lyophilization method	200
105	FTIR spectra of 1:1 piroxicam-GCD physical mixture	201
106	FTIR spectra of 1:1 piroxicam-GCD inclusion complex prepared by kneading method	202
107	FTIR spectra of 1:1 piroxicam-GCD inclusion complex prepared by co-evaporation method	202
108	FTIR spectra of 1:1 piroxicam-GCD inclusion complex prepared by co-lyophilization method	203
109	FTIR spectra of 1:1 piroxicam-HPBCD physical mixture	204
110	FTIR spectra of 1:1 piroxicam-HPBCD inclusion complex prepared by kneading method	204
111	FTIR spectra of 1:1 piroxicam-HPBCD inclusion complex prepared by co-evaporation method	205
112	FTIR spectra of 1:1 piroxicam-HPBCD inclusion complex prepared by co-lyophilization method	205
113	FTIR spectra of 1:1 piroxicam-MeBCD physical mixture	206

Figure	Title	Page
114	FTIR spectra of 1:1 piroxicam-MeBCD inclusion complex prepared by kneading method	207
115	FTIR spectra of 1:1 piroxicam-MeBCD inclusion complex prepared by co-evaporation method	207
116	FTIR spectra of 1:1 piroxicam-MeBCD inclusion complex prepared by co-lyophilization method	208
117	FTIR spectra of meloxicam, intact	209
118	FTIR spectra of 1:1 meloxicam-BCD physical mixture	210
119	FTIR spectra of 1:1 meloxicam-BCD inclusion complex prepared by kneading method	210
120	FTIR spectra of 1:1 meloxicam-BCD inclusion complex prepared by co-evaporation method	211
121	FTIR spectra of 1:1 meloxicam-GCD inclusion complex prepared co-lyophilization method	211
122	FTIR spectra of 1:1 physical mixture	212
123	FTIR spectra of 1:1 meloxicam-GCD inclusion complex prepared by kneading method	213
124	FTIR spectra of 1:1 meloxicam-GCD inclusion complex prepared by co-evaporation method	213
125	FTIR spectra of 1:1 meloxicam-HPBCD inclusion complex prepared by co-lyophilization method	214
126	FTIR spectra of 1:1 meloxicam-HPBCD physical mixture	215

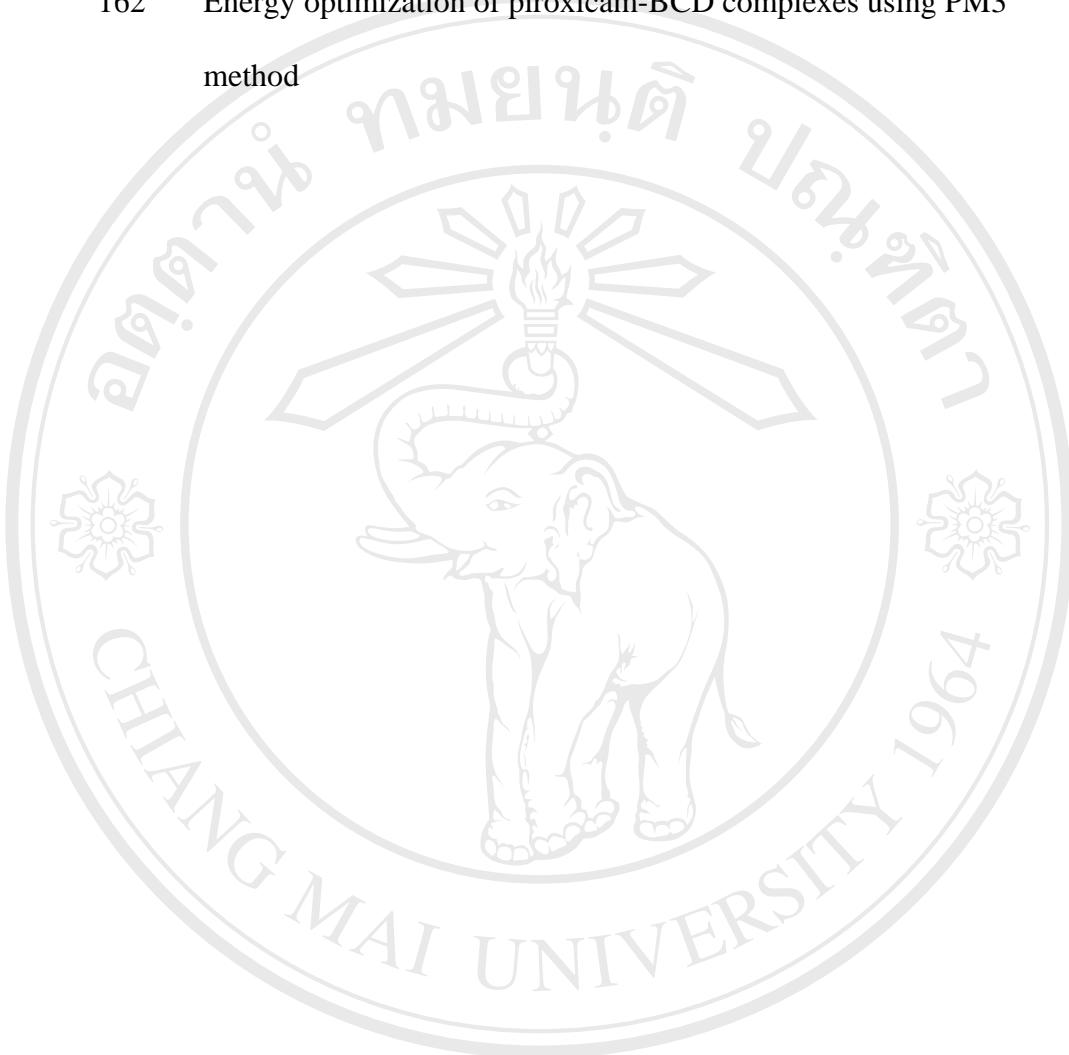
Figure	Title	Page
127	FTIR spectra of 1:1 meloxicam-HPBCD inclusion complex prepared by kneading method	215
128	FTIR spectra of 1:1 meloxicam-HPBCD inclusion complex prepared by co-evaporation method	216
129	FTIR spectra of 1:1 meloxicam-HPBCD inclusion complex prepared by co-lyophilization method	216
130	FTIR spectra of 1:1 meloxicam HPGCD physical mixture	217
131	FTIR spectra of 1:1 meloxicam-HPGCD inclusion complex prepared by kneading method	218
132	FTIR spectra of 1:1 meloxicam-HPGCD inclusion complex prepared by co-evaporation method	218
133	FTIR spectra of 1:1 meloxicam-HPGCD inclusion complex prepared by co-lyophilization method	219
134	NIR spectra of piroxicam, BCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	221
135	NIR spectra of piroxicam, BCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	223
136	NIR spectra of piroxicam, GCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	224

Figure	Title	Page
137	NIR spectra of piroxicam, GCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	225
138	NIR spectra of piroxicam, HPBCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	227
139	NIR spectra of piroxicam, HPBCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	228
140	NIR spectra of piroxicam, MeBCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	230
141	NIR spectra of piroxicam, MeBCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	231
142	NIR spectra of meloxicam, BCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	233
143	NIR spectra of meloxicam, BCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	234
144	NIR spectra of meloxicam, GCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	235
145	NIR spectra of meloxicam, GCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	236

Figure	Title	Page
146	NIR spectra of meloxicam, HPBCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	238
147	NIR spectra of meloxicam, HPGCD, 1:1 physical mixture and inclusion complexes prepared by kneading, co-evaporation and co-lyophilization method	239
148	NIR spectra of meloxicam, HPGCD, 1:1 physical mixture and inclusion complexes prepared co-lyophilization method	240
149	Dissolution profiles of piroxicam in distilled water from 1:1 and 2:1 KN piroxicam-BCD inclusion complexes initially prepared and after stored at 30°C for 1 year	241
150	Dissolution profiles of piroxicam in distilled water from 1:1 and 1:2 COE piroxicam-BCD inclusion complexes initially prepared and after stored at 30°C for 1 year	242
151	Dissolution profiles of piroxicam in distilled water from 1:1 and 2:1 COL piroxicam-BCD inclusion complexes initially prepared and after stored at 30°C for 1 year	242
152	Dissolution profiles of meloxicam in simulated gastric fluid from 1:1 KN meloxicam: BCD inclusion complex initially prepared and after stored at 45°C for 4 months	244

Figure	Title	Page
153	Dissolution profiles of meloxicam in simulated gastric fluid from 1:1 COL meloxicam: BCD inclusion complex initially prepared and after stored at 45°C for 4 months	244
154	Dissolution profiles of meloxicam in simulated gastric fluid from 1:1 COE meloxicam: BCD inclusion complex initially prepared and after stored at 45°C for 4 months	245
155	X-ray diffractograms of BCD, piroxicam, 1:1 physical mixture and KN, COE and COL inclusion complexes of piroxicam:BCD after stored at 30°C for 1 year	249
156	X-ray diffractograms of BCD, meloxicam, 1:1 physical mixture and KN, COE and COL inclusion complexes of meloxicam:BCD after stored at 45°C for 4 months	250
157	Correlation plot between log K (observed) and log K (predicted) of the test set using Model A	259
158	Correlation plot between log K (observed) and log K (predicted) of the test set using Model B	259
159	Conformations of piroxicam	262
160	Energy optimization of piroxicam conformation using PM3 and AM1 method	267
161	Energy optimization of piroxicam conformation using B3LYP/6-31G**	267

Figure	Title	Page
162	Energy optimization of piroxicam-BCD complexes using PM3 method	270



ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright © by Chiang Mai University
All rights reserved

ABBREVIATIONS

AM1	Austrin Method 1
ACD	α -Cyclodextrin
BCD	β -Cyclodextrin
CDs	Cyclodextrins
COE	Co-evaporated inclusion complex
COL	Co-lyophilized inclusion complex
%DE30	Percentage dissolution efficiency at 30 minute
DSC	Differential scanning calorimetry
FTIR	Fourier transform infrared spectroscopy
GCD	γ -Cyclodextrin
HPBCD	Hydroxypropyl- β -cyclodextrin
HPGCD	Hydroxypropyl- γ -cyclodextrin
KN	Kneaded inclusion complex
Mlx	Meloxicam
PM	Physical mixture
PM3	Parameterization Method 3
Prx	Piroxicam
mcg	Microgram
MeBCD	Methylated- β -cyclodextrin
NIR	Near infrared spectroscopy
XPD	X-ray powdered diffractometry