TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS	iii
ENGLISH ABSTRACT	iv
THAI ABSTRACT	vi
TABLE OF CONTENTS	viii
LIST OF TABLES	ix
LIST OF ILLUSTRATIONS	xiii
ABBREVIATIONS	χV
CHAPTER I INTRODUCTION	1
II LITERATURE REVIEW	3
III MATERIALS AND METHODS	18
IV RESULTS AND DISCUSSION	28
V CONCLUSIONS	60
REFERENCES	62
APPENDIX	66
VITA	86

LIST OF TABLES

Table		Page
1	Classification and description of gels	5
2	Formulation of gel bases	20
3	Formulations of KP gels	22
4	Estimated linear regression line and correlation coefficient of KP in	
	methanol and deionized water	23
5	Solubility of KP in various vehicles	28
6	Actual amount of KP in gels	29
7	Average pH and viscosity of KP gels	30
8	Effects of gelling agents on KP permeation flux and Q _{180min}	32
9	Effects of CBP2020 concentration on KP permeation flux and Q _{180min}	34
10	Effects of CBP980 concentrations on KP permeation flux and Q _{180min}	36
11	Effects of HP concentrations on KP permeation flux and Q _{180min}	38
12	Effects of ethanol concentrations on KP permeation flux and Q _{180min}	41
13	Effects of pH on KP permeation flux and Q _{180min}	43
14	Effects of mono-additives on KP Permeation flux and Q _{180min}	46
15	Effects of combined additives on KP Permeation flux and Q _{180min}	48
16	Comparison of skin permeation between prepared and commercial	
	KP gels	50
17	Effects of temperature on KP released parameters	52
18	Effects of storage conditions on KP content (%w/w)	54
19	Effects of storage under stress conditions on pH of gels	55
20	Effects of storage under stress conditions on viscosity of gels	56

LIST OF TABLES (Continued)

Ta	ble		Page
2	21	Effects of aging under stress conditions (H&C) of Com1 on KP	
		permeation flux and Q _{180min}	58
2	22	Effects of aging under stress conditions (H&C) of F-19 on KP	
		permeation flux and Q _{180min}	59
2	23	Precision of UV spectrophotometry analysis of KP in methanol	67
:	24	Area under the peak of KP for calibration curve of KP in PBS by	
		HPLC Method	71
	25	Area under the peak of KP for intraday and interday determenation	
		with HPLC method	72
	26	Area under the peak of KP used in calibration curve construction	72
	27	Cumulative amount of KP permeated from gels prepared with	
		3%w/w of CBP2020 (Formulation 1)	73
	28	Cumulative amount of KP permeated from gels prepared with	
		2%w/w of CBP2020 (Formulation 2)	73
	29	Cumulative amount of KP permeated from gels prepared with	
		1.5%w/w of CBP2020 (Formulation 3)	74
	30	Cumulative amount of KP permeated from gels prepared with	
		3%w/w of CBP980 (Formulation 4)	74
	31	Cumulative amount of KP permeated from gels prepared with	
		2%w/w of CBP980 (Formulation 5)	75
	32	Cumulative amount of KP permeated from gels containing 1.5% of	
		CBP980 (Formulation 6)	75
	33	Cumulative amount of KP permeated from gels prepared with	
		3%w/w of HPMC (Formulation 7)	- 76

LIST OF TABLES (Continued)

Гаblе		Page
0.4	Cumulative amount of KP permeated from gels prepared with 2%w/w of	
34		76
0.5	HPMC and containing ETOH 35.5% (Formulation 8) Cumulative amount of KP permeated from gels containing ETOH 30%	
35		77
	(Formulation 9)	• •
36	Cumulative amount of KP permeated from gels containing ETOH 40%	77
	(Formulation 10)	78
37	Cumulative amount of KP permeated from gels pH 3.4 (Formulation 11)	
38	Cumulative amount of KP permeated from gels pH 5.7 (Formulation 12)	78
39	Cumulative amount of KP permeated from gels pH 7.0 (Formulation 13)	79
40	Cumulative amount of KP permeated from gels without additive	79
	(Formulation 14)	
41	Cumulative amount of KP permeated from gels containing 5%w/w PG	
	(Formulation 15)	80
42	Cumulative amount of KP permeated from gels containing 0.5%w/w	
	TW80 (Formulation 16)	80
43	Cumulative amount of KP permeated from gels containing 1%w/w L-LA	
	(Formulation 17)	81
44	Cumulative amount of KP permeated from gels containing PG-TW80	
	(Formulation 18)	81
45	Cumulative amount of KP permeated from gels containing PG-L-LA	
	(Formulation 19)	82
46	Cumulative amount of KP permeated from gels containing PG-TW80-	
	L-LA (Formulation 20)	82
47	Cumulative amount of KP permeated from commercial KP gel 1	83
-r r	Section and the section of the secti	

LIST OF TABLES (Continued)

Table		Page
		മാ
48	Cumulative amount of KP permeated from commercial KP gel 2	83
49	Cumulative amount of KP permeated from gel Formulation 19 under	
	stress conditions	784
50	Cumulative amount of KP permeated from commercial KP gel1 under	
	stress conditions	84
51	Cumulative amount of KP released from commercial KP gel1 through	
	cellophane membrane at 25 °C	85
52	Cumulative amount of KP released from Commercial KP gel1 through	
	cellophane membrane at 37 °C	85

LIST OF ILLUSTRATIONS

Figure		Page
1	Cross-sectional view of human skin, showing various skin tissue layers	8
	and appendages	
2	The macro routes for drug permeation through skin; via 1. the sweat	
	gland, 2. across the intact stratum corneum, and 3. the hair follicles	10
3	The micro routes for drug permeation across the intact stratum	
	corneum	10
4	Modified Franz [®] diffusion cells	19
5	Effects of gelling agents on KP permeation through rat skin	32
6	Effects of CBP2020 concentrations on KP permeation through rat skin	34
7	Effects of CBP980 concentrations on KP permeation through rat skin	36
8	Effects of HP concentrations on KP permeation through rat skin	38
9	Effects of ETOH concentrations on KP permeation through rat skin	41
10	Effects of pH on KP permeation through rat skin	43
11	Effects of mono-additives on KP permeation through rat skin	46
12	Effects of combined additives on KP permeation through rat skin	48
13	Comparison of prepared KP gel and commercial products on KP	
	permeation through rat skin	50
14	Effects of temperature on KP released through cellophane membrane	52
15	Effects of aging under stress conditions (H&C) of Com1 on the KP	
. 5	permeation profile	58
16	Effects of aging under stress conditions (H&C) of F-19 on the KP	
	permeation profile	59
	r-	

LIST OF ILLUSTRATIONS (Continued)

igure		Page
17	Chromatogram of KP in methanol KP has maximum absorbance at	
	the wavelength 255 nm	66
18	Calibration curve for determination of KP in methanol by	
	UV spectrophotometry at the wavelength 255 nm	68
19	Chromatogram of KP in PBS analyzed using HPLC, KP retention time	!
	was about 2.075 min	69
20	The calibration curve of KP in PBS assay by HPLC Method	: 70

LIST OF ABBREVIATIONS

% = Percentage

AUC = Area Under the Curve

CBP2020 = Carbopol[®]980 NF

CBP940 = Carbopol®940

CBP980 = Carbopol[®]2020 ETD

cm = centimeter

cm² = square centimeter

Com1 = Commercial ketoprofen gel 1

Com2 = Commercial ketoprofen gel 2

cP = centipoise

DI water = Deionized water

DSC = Differential Scanning Colorimetry

et al. = And others

ETOH = Ethanol

F = Formulation

g = Gram

H&C = Heating and cooling six cycles

HP, HPMC = Hydroxypropylmethylcellulose E4M

HPC = Hydroxypropylcellulose

HPLC = High Performance Liquid Chromatography

hr = Hour

KNa = Ketoprofen sodium

KP = Ketoprofen

LC = Liquid crystal

LIST OF ABBREVIATIONS (Continued)

L-LA = L-Lactic acid

mg = Milligram

min = Minute

ml = Milliliter

mm = Millimeter

nm = Nanometer

NSAID = Nonsteroidal anti-inflammatory drug

°C = Degree Celsius

PBS = Phosphate Buffer Saline

PEG = Polyethylene glycol

PG = Propylene glycol

pH = The negative logarithm of the hydrogen ion concentration

Q_{180min} = The cumulative amount of KP permeated within 180 min

R² = Correlation coefficient

rpm = Revolution per minute

RSD = Relative Standard Deviation

RT = Room temperature for six months

SD = Standard deviation

TEA = Triethanolamine

TW80 = Tween 80

UV = Ultraviolet

v/v = Volume by volume

w/w = Weight by weight

 μg = Microgram

 $\mu m = Micrometer$