TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENT	iii
ABSTRACT (ENGLISH)	iv
ABSTRACT (THAI)	vi
LIST OF TABLES	x
LIST OF ILLUSTRATIONS	хi
ABBREVIATIONS	xii
CHAPTER 1 Introduction	1
CHAPTER 2 Literature review	3
2.1 Carbamazepine in clinical practice	3 .
2.2 Pharmacology of carbamazepine	4
2.2.1 Mechanisms of action	4
2.2.2 Pharmacokinetics	6
2.3 Drug interactions	10
2.4 Side effects	11
2.5 Therapeutic drug monitoring of anticonvulsants	11
2.6 Salivary therapeutic drug monitoring for anticonvulsants	12
2.6.1 Physiology of the saliva glands	14
2.6.2 Pharmacokinetic principles of drug distribution in saliva	15
2.6.3 Diseases and drugs influencing salivary secretion	17
2.7 Relationship between plasma-saliva concentration of	
carbamazepine and clinical effect	18
2.8 Methodology	22

	Page
CHAPTER 3 Materials and Methods	23
3.1 Materials and instruments	23
3.2 Apparatus	24
3.3 HPLC system	24
3.4 Method	25
3.4.1 Subject	25
3.4.2 Sample collection techniques	25
3.4.3 Extraction and assay procedure	25
3.4.4 Standard curve	26
3.4.5 Accuracy and precision of the assay procedure	26
3.4.6 Stability of carbamazepine in frozen plasma and saliva	26
3.4.7 Data analysis	26
3.4.8 Application to the patients	27
CHAPTER 4 Results	28
4.1 Precision of assay procedure	29
4.2 Accuracy of assay procedure	34
4.3 Stability of carbamazepine in frozen plasma and saliva	35
4.4 The correlation between plasma and saliva	
carbamazepine concentration	36
4.5 Application to the patients	38
CHAPTER 5 Conclusion and Discussion	41
REFERENCES	43
APPENDIX A	
CURRICULUM VITAE	

LIST OF TABLES

Cable		Page
1	Advantages and disadvantages of using samples for therapeutic	
	drug monitoring	13
2	Studies of saliva and blood concentration of CBZ	20
3	Intraday variation of analysis method for carbamazepine in plasma	30
4	Intraday variation of analysis method for carbamazepine in saliva	31
5	Interday variation of analysis method for carbamazepine in plasma	32
6	Interday variation of analysis method for carbamazepine in saliva	33
7	Percent recoveries of analysis method for carbamazepine in plasma	34
8	Percent recoveries of analysis method for carbamazepine in saliva	34
9	Stability of carbamazepine in fiozen plasma	35
10	Stability of carbamazepine in frozen saliva	35
11	The individual data of application to patient	39

LIST OF ILLUSTRATIONS

Figure		Page
1	Structural formula of carbamazepine	3
2	Major pathways of metabolism of carbamazepine in man	8
3	Plasma clearance carbamazepine (CBZ)-D ₄ when given as	
	a single oral dose at different times before and during maintenance	
	CBZ treatment in three patients with recently discovered epilepsy.	
	Multiple dosing was started on day 5.	9
4	Plasma concentration of CBZ (o) and CBZ- D ₄ (o) in 2 alcoholic	
	patients, who were treated with CBZ during the withdrawal period.	9
5	Time course of salivary CBZ levels in a patient receiving 200 mg	
	of the drug twice daily	19
6	Chromatogram of A) plasma carbamazepine and B) saliva carbamazepine	
	(RT \approx 3.2 min) and propylparaben (RT \approx 4.0 min) as internal standard	28
7	Intraday variation of analysis method for carbamazepine in plasma	30
8	Intraday variation of analysis method for carbamazepine in saliva	31
9.0	Interday variation of analysis method for carbamazepine in plasma	32
10	Interday variation of analysis method for carbamazepine in saliva	33
11	The correlation between saliva and plasma CBZ concentration	
	of all 50 volunteers	37

ABBREVIATIONS

°C degree celcius

CBZ carbamazepine

CBZ-E carbamazepine-10,11-epoxide

CBZ-H tran-10,11-dihydroxy-10,11-dihydro-carbamazepine

EIA enzyme immunoassay

FIA fluorescence immunoassay

FPIA fluorescence polarization immunoassay

GLC gas-liquid chromatography

HPLC high-performance liquid chromatography

L/kg liter per kilogram

mcl microliter

mcmole micromole

mg milligram

ml milliliter

ng nanogram

nm nanometer

[PCBZ] plasma carbamazepine concentration

PP propylparaben

rpm round per minute

[SCBZ] saliva carbamazepine concentration

t ½ elimination half-life

UV ultraviolet