TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENT	iii
ENGLISH ABSTRACT	iv
THAI ABSTRACT	vi
LIST OF TABLES	x
LIST OF ILLUSTRATIONS	xii
LIST OF ABBREVIATIONS	xiv
INTRODUCTION	1
LITERATURE REVIEW	
1. Pharmacokinetic parameter	5
2. Chemical structure	8
3. Indication	8
4. Mechanism of action	10
5. Clinical Pharmacokinetics	11
6. Therapeutic range and Efficacy	14
7. Adverse reaction	16
8. Precaution and Contraindication	18
9. Drug administration	19
10. Blood sampling	21
11. Assay consideration	21
OBJECTIVES	23
MATERIAL AND METHODS	
1. Subject	24
2. Study Design	24
3. Drug and Method of Administration	25

	Page
4. Blood sampling	25
5. Determination of serum gentamicin concentrations	26
6. Efficacy and Safety criteria	26
7. Calculation	27
8. Statistic analysis	29
RESULTS	30
DISCUSSION	56
CONCLUSION	62
REFERENCES	63
APPENDIX	68
VITA	70

LIST OF TABLES

Table	Page
1. Some factors affecting drug distribution and disposition.	6
2. Pharmacokinetic parameters in preterm infants, children and adults.	14
3. Relationship between peak and trough concentration of gentamicin and treatment.	15
4. In vitro activity of gentamicin against common gram negative organism.	16
5. Risk factors for nephrotoxicity in patients receiving gentamicin.	17
6. Risk factor for gentamicin induced ototoxicity.	18
7. Dosage regimen of gentamicin in Neofax guideline.	21
8. Coefficient of variation of 3 control concentrations of gentamicin.	26
9. Demographic data of neonatal patients.	32
10. Diagnosis of neonatal patients at study entry.	33
11. Dose and duration of gentamicin administration in each group of neonatal patients.	33
12. Concurrent drug administration with gentamicin in each group of neonatal patients.	34
13. Time to sampling in all patients.	35
14. The number of neonates receiving the 1st, the 3rd and the 6th doses of gentamicin in each group of neonatal patients.	35
15. Average gentamicin peak concentration after the 1st, the 3rd and the 6th doses of gentamicin in each group of neonatal patients.	39
16. The numbers of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 1st dose.	40
17. The numbers of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 3rd dose.	40
18. The numbers of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 6th dose.	40

Table	Page
19. Average gentamicin trough concentrations before the 3rd and the 6th doses of gentamicin in each group of neonatal patients.	42
20. The number of neonatal patients whose gentamicin concentration were less than and higher than safety concentration of <2 ug/ml before the 3rd dose.	42
21. The number of neonatal patients whose gentamicin concentration were less than and higher than safety concentration of <2 ug/ml before the 6th dose.	43
22. Gentamicin pharmacokinetic parameters of neonates in each gestational age group.	45
23. Serum creatinine and BUN concentration at the first, third and sixth dose in each gestational age group.	53

LIST OF ILLUSTRATIONS

Figure	Page
1. Relationship between gestational age (weeks) and creatinine clearance (ml/min).	7
2. Chemical structure of gentamicin.	8
3. Two compartment model.	11
4. A drug administered into Vi follows a biphasic decay pattern. The initial decay half-life ($\alpha\ t_{1/2}$) is usually due to drug distribution into Vt. The second decay half-life ($\beta\ t_{1/2}$) is usually due to drug elimination from the body.	12
5. The plot of individual initial peak concentrations of gentamicin (n=48).	36
6. The plot of individual peak gentamicin concentrations after the 3rd dose (n=40).	36
7. The plot of individual peak gentamicin concentrations after the 6th dose (n=15).	37
8. The plot of individual trough gentamicin concentrations before the 3rd dose (n=40).	38
9. The plot of individual peak gentamicin concentrations before the 6th dose (n=15).	38
10. Mean K_e in each gestational age group.	46
11. Mean CL in each gestational age group.	47
12. Mean V_d in each gestational age group.	48
13. Mean $t_{1/2}$ in each gestational age group.	49
14. Correlation between GA and K_e.	50
15. Correlation between GA and CL.	50
16. Correlation between GA and V_d.	50
17. Correlation between GA and t ½.	50
18. Correlation between Birth weight age and K_e.	51
19. Correlation between Birth weight and CL.	51
20. Correlation between Birth weight and V_d.	51
21. Correlation between Birth weight and $t_{1/2}$.	51

Figure	Page
22. Correlation between BSA and K_e.	52
23. Correlation between BSA and CL.	52
24. Correlation between BSA and V_d.	52
25. Correlation between BSA age and $t_{1/2}$.	52
26. Mean serum creatinine level in each gestational age group.	54
27. Mean BUN level in each gestational age group.	55

LIST OF ABBREVIATIONS

BSA	=	body surface area
BUN	=	blood urea nitrogen
BW	=	birth weight
CBC	=	complete blood count
CL	=	clearance
Cr	=	serum creatinine
dl	=	decilitre
ECF	=	extracellular fluid
GFR	=	glomerular filtration rate
GA	=	gestational age
gm	=	gram
hr	=	hour
ICF	=	intracellular fluid
K_e	=	elimination rate constant
kg	=	kilogram
L	=	litre
MIC	=	minimum inhibitory concentration
MIC_{90}	=	minimum concentration that inhibitory 90% of isolates bacteria
mg	=	milligram
ml	=	millilitre
mRNA	=	messenger ribonucleic acid
NICU	=	neonatal intensive care unit
nm	=	nanometre
NSAID	=	nonsteroidal antiinflammatory drug

^{o}C	=	degree celcius
PAE	=	post antibiotic effect
PCA	=	postconceptional age
PDA	=	patent ductus arteriosus
pH	=	a measure of the acidity or alkalinity of a solution
R^2	=	coefficient of correlation square
rpm	=	round per minute
SD	=	standard deviation
TBW	=	total body water
$t_{1/2}$	=	half-life
ug	=	microgram
ul	=	microlitre
V_d	=	volume of distribution