UNIVERSITI TEKNOLOGI MARA

CHARACTERIZATION OF TRANSDERMAL DRUG DELIVERY USING NONDESTRUCTIVE VISIBLE SPECTROPHOTOMETRY AND ARTIFICIAL NEURAL NETWORK

AZNIDA BINTI ALIAS

Thesis submitted in fulfillment of the requirements for the degree of **Master of Science**

Faculty of Electrical Engineering

March 2017

ABSTRACT

Assessment of drug content and matric characteristics, such as state of polymerpolymer and drug-polymer interaction are utmost important with respect the therapeutic effectiveness of transdermal drug delivery system. Conventional methods for analysis result in sample being unrecoverable from test, disposal of a large amount of solvents, reagents and accessories, as well as, restrict the analysis to statistically selected samples. This thesis present a new technique in drug content and drug concentration assessment of nifedipine and hyroxypropylmethyl cellulose films with 25%, 50% and 75% relative humidity using nondestructive testing technique of Visible Spectrophotometry. The crossed study of the polymeric films by Differential Scanning Calorimetry, Fourier Transform Infrared Spectroscopy, Ultraviolet Spectrophotometry and Visible Spectrophotometry indicated physicochemical changes as the drug and polymer varied. The significant wavelength and intensity of visible spectrophotometry associated with different polymeric films and relative humidity were determined. Correlation study of drug concentration from visible spectrophotometry and drug content were done using artificial neural network. This intelligent technique have presented the reliability of Visible Spectrophotometry in detecting drug content and identifying drug concentration at minimum and maximum of 0 to 20mg and 0 to 32.11 %w/w respectively.

ACKNOWLEDGEMENT

Alhamdulillah, all praises belongs to Allah the Almighty, the Mercifulness and Salam to Nabi Muhammad S.A.W.

Immeasurable appreciation and deepest gratitude for the help and support extended to the following persons who in one way or another have contributed in making this study possible.

Prof. Dr. Haji Mohd. Nasir Bin Haji Taib, my supervisor for his guidance and invaluable advice,

Assoc. Prof. Dr. Wong Tin Wui, my co-supervisor for his discussions and helpful in pharmaceutical part,

Members of Advanced Signal Processing Research Group (ASPRG), Particle Design Research Group (PDRG) and Nondestructive Biomedical and Pharmaceutical Research Centre for tremendous helps and being supportive,

Kementerian Sains, Teknologi & Alam Sekitar for giving me a scholarship throughout of my first 2 years study,

Ahmad Riduan Bin Dahron, my lovely and understanding husband that helps me in managing the housework and kids,

Alias Bin Abdul Samad (Abah) and (Mak), my dear parents for their thoughtful as this research take more years than we have expected,

My kids (Danish, Darwisy and Firas), siblings and *best friends* for being with me in the best and worst condition,

And last but not least *people who have directly or indirectly contributed* to the completion of the thesis.

May Allah bless all of you. InsyaAllah, Ameen.

Aznida binti Alias March 2017

TABLE OF CONTENTS

Page

	0
CONFIRMATION BY PANEL OF EXAMINERS	ii
AUTHOR'S DECLARATION	iii
ABSTRACT	iv
ACKNOWLEDGEMENT	v
TABLE OF CONTENTS	vi
LIST OF TABLES	x
LIST OF FIGURES	xii
LIST OF SYMBOLS	XV
LIST OF ABBREVIATIONS	xviii
CHAPTER ONE: INTRODUCTION	1
1.1 Background	1
1.2 Problem Statement	2
1.3 Objectives of the Study	2
1.4 Scope of the Study	3
1.5 Thesis Organization	3
CHAPTER TWO: LITERATURE REVIEW	5
2.1 Introduction	5
2.2 Transdermal Drug Delivery System	5
2.2.1 Basic of the Skin and Advantages of TDDS	5
2.2.2 Current Research and Analytical Instrument for TDDS	7
2.2.2.1 Fourier Transform Infrared Spectroscopy, Ultraviolet	8
Spectrophotometry and Differential Scanning Calorimetry	
2.2.3 Transdermal Drug Delivery Design	11
2.3 Visible Spectrophotometry as a Nondestructive Testing Technique	12
2.4 Artificial Neural network	18
2.4.1 Applications of ANN in Pharmaceutical Sciences and Spectrum	20
Analysis	

2.4.2 Multilayer Feed-forward Neural Network with Backpropagation	22
Algorithm	
2.4.2.1 Data Pre-processing	24
2.5 Summary	26
CHAPTER THREE: THEORETICAL BACKGROUND	27
3.1 Introduction	27
3.2 Analytical Instrument	27
3.2.1 Molecular Spectroscopy	27
3.2.1.1 Ultraviolet and Visible Spectrophotometry	28
3.2.1.2 Fourier Transform Infrared Spectroscopy	33
3.2.2 Thermal Method	36
3.2.2.1 Differential Scanning Calorimetry	36
3.3 Artificial Neural Network	38
3.3.1 The Multilayer Perceptron	39
3.3.1.1 The Levenberg Marquardt Algorithm	40
3.3.2 Data Preparation	41
3.3.2.1 The Boxplot Analysis	41
3.3.2.2 Synthetic Data Generation	42
3.3.2.3 Normalization and Divide Data	42
3.3.5 Performance Measure and Test Fitting	42
CHAPTER FOUR: METHODOLOGY	44
4.1 Introduction	44
4.2 Experimental Approach	44
4.3 Materials	46
4.4 Research Methodology	47
4.4.1 Preparation of Films	47
4.4.2 Characterization of Films	48
4.4.2.1 Ultraviolet Spectrophotometry	48
4.4.2.2 Differential Scanning Calorimetry	49
4.4.2.3 Fourier Transform Infrared Spectroscopy	49
4.4.2.4 Nondestructive Visible Spectrophotometry	50