

TABLE OF CONTENTS

S. No.	Title	Page No.
	Declaration	ii
	Abstract	iii-iv
	Acknowledgement	v-vii
	Table of Contents	viii-xiii
	List of Figures	xiv-xvii
	List of Tables	xviii-xx
	List of Publications	xxi
	List of Abbreviations	xxii-xxiii
Chapter 1	INTRODUCTION	1-27
1.1	Skin drug delivery	2
1.2	Psoriasis	4
1.2.1	Pathogenesis of Psoriasis	4
1.3	Available Treatment Strategies for Psoriasis	7
1.4	Resveratrol as a potent antioxidant and anti-psoriatic molecule	8
1.5	Need of topical Nanotechnological based Drug Delivery System	10
1.6	Polymeric micelles	14
1.7	Nanoemulsion	17
1.7.1.	Components in the topical nanoemulsion formulations for antipsoriatic drugs	17
1.7.1.1	Oil Phase	17
1.7.1.2	Surfactant	19
1.7.1.3	Co-surfactant	19
1.7.1.4	Other Excipients	19
1.7.2	Stability of nanoemulsion	19
1.8	Quality by Design (QbD) and Design of Experiments (DoE) based Optimization and development of nanocarriers systems	20
1.9	Research Envisaged	22

1.10	Research Aim and Objectives	25
1.11	Plan of Work	26
Chapter 2	LITERATURE REVIEW	28-35
Chapter 3	BIOACTIVE AND EXCIPIENTS PROFILE	36-45
3.1	Profile of Bioactive Resveratrol	36
3.1.1	Mechanism of action	38
3.2	Excipient Profile	39
3.2.1	Co-surfactant (Transcutol-P)	39
3.2.2	Surfactant (Tween 80)	40
3.2.3	Pluronic F-127	41
3.2.4	Pluronic P-123	42
3.2.5	TPGS	43
3.2.6	Ethyl Oleate	44
3.2.7	Carbopol	45
Chapter 4	EXPERIMENTAL (MATERIALS AND METHODS)	46-77
4.1	Materials and Equipment	46
4.1.1	Chemicals and Excipients	46
4.1.2	Equipment	48
4.2	Preformulation studies of Bioactive (Resveratrol)	51
4.2.1	Identification of Resveratrol	52
4.2.1.1	Organoleptic properties	52
4.2.1.2	UV Spectroscopy for determining λ_{max}	52
4.2.1.3	FTIR Spectroscopy	53
4.2.1.4	Determination of melting point	53
4.2.2	Development of the analytical methods	54
4.2.2.1	UV-Visible spectroscopy studies	54
4.2.2.2	HPLC method for Resveratrol determination	54
4.2.3	Determination of partition coefficient	56
4.2.4	Determination of solubility	56
4.3	Formulation development	56
4.3.1	Formulation of Resveratrol loaded polymeric micelles: QbD based optimization	58

4.3.1.1	Defining QTPP and Identifying CQAs for applying QbD approach	58
4.3.1.2	Risk assessment	58
4.3.1.3	Preparation of Resveratrol loaded polymeric micelles	59
4.3.1.4	DoE (Central Composite Design) based optimization of Resveratrol loaded polymeric micelles	60
4.3.1.5	Characterization of developed colloidal micellar formulation	63
4.3.1.5.1	Size, polydispersity index, and zeta potential	63
4.3.1.5.2	Morphological evaluation	63
4.3.1.5.3	Micellar Incorporation Efficiency	63
4.3.1.5.4	Skin permeation and skin deposition studies	63
4.3.1.6	Formulation of carbomer based hydrogel embedded with colloidal micelles	64
4.3.2	Formulation of Resveratrol loaded Vitamin E based nanoemulsion	64
4.3.2.1	Pseudo ternary phase diagram	65
4.3.2.2	Formulation of Resveratrol loaded vitamin E based nanoemulsion	65
4.3.2.3	Factorial design and Response surface methodology employed optimization of resveratrol loaded nanoemulsion	66
4.3.2.4	Formulation of carbomer based nanoemulsion hydrogel (Nanoemulgel)	69
4.3.2.5	Characterization of developed Nanoemulsion and nanoemulgel	69
4.3.2.5.1	Globule size, zeta potential, and PDI	69
4.3.2.5.2	Surface morphology via Transmission electron microscopy	69
4.3.2.5.3	Resveratrol content in nanoemulgel	70
4.3.2.5.4	Skin permeation and skin deposition studies	70
4.4	Some other important evaluations of formulated Micellar hydrogel and Nanoemulgel	70
4.4.1	Determination of pH	70
4.4.2	Spreadability studies	70

4.4.3	Rheological behavior and viscosity	70
4.4.4	<i>In vitro</i> Resveratrol release	71
4.4.5	Skin permeation and deposition profile	72
4.4.6	Skin targeting studies: Histopathology by CLSM	73
4.4.7	<i>In vitro</i> antioxidant activity using DPPH Assay	74
4.5	<i>In vivo</i> efficacy studies (antipsoriatic activity) using IMQ-induced psoriatic-like plaque model in Swiss Albino Mice	75
4.5.1	Psoriasis Area and Severity Index (PASI) score	76
4.5.2	Cytokines level in serum and spleen dimension & weight	76
4.5.3	Histology of skin	77
4.6	Stability Studies	77
4.7	Statistical analysis	77
Chapter 5	RESULTS AND DISCUSSION	78-164
5.1	Preformulation Studies	78
5.1.1	Identification of Resveratrol	78
5.1.1.1	Physical appearance	78
5.1.1.2	UV spectroscopy for determining λ_{\max}	78
5.1.1.3	Fourier Transform Infra-Red spectroscopy	78
5.1.1.4	Determination of melting point	81
5.1.2	Development of the analytical methods	81
5.1.2.1	UV-visible spectroscopy studies	81
5.1.2.2	HPLC method for Resveratrol determination	82
5.1.3	Determination of partition coefficient	86
5.1.4	Solubility determination	86
5.2	Formulation development	87
5.2.1	Formulation of Resveratrol loaded polymeric micelles: QbD based optimization	87
5.2.1.1	Defining QTPP and Identifying CQAs for applying QbD approach	87
5.2.1.2	Risk assessment analysis	89
5.2.1.3	DoE (Central Composite Design) based optimization of Resveratrol loaded polymeric micelles	90

5.2.1.4	Model generation for optimization in polymeric micelles	94
5.2.1.5	Model analysis and diagnostic for optimization in polymeric micelles	95
5.2.1.6	Response analysis through polynomial equations for polymeric micelles	102
5.2.1.6.1	Effect of CMAs on the MIE of polymeric micelles (Y1)	102
5.2.1.6.2	Effect of CMAs on particle size (Y2)	107
5.2.1.6.3	Effect of CMAs on skin deposition potential (Y3)	108
5.2.1.7	Search for optimum formulation based on desirability approach and checkpoint analysis	109
5.2.1.8	Characterization of developed polymeric Micellar (PM) formulation	112
5.2.1.8.1	Size, polydispersity index, and zeta potential	112
5.2.1.8.2	Morphological evaluation	113
5.2.1.8.3	Encapsulation efficiency	114
5.2.1.9	Formulation and characterization of the corresponding hydrogel	114
5.3.1	Formulation of Resveratrol loaded Vitamin E based nanoemulsion	115
5.3.1.1	Preliminary screening studies: Solubility studies of resveratrol in several excipients	115
5.3.1.2	Construction of pseudo ternary phase diagram	117
5.3.1.3	Formulation and optimization of Resveratrol loaded vitamin E based nanoemulsion using 3^2 factorial design	118
5.3.1.4	Model generation for optimization in nanoemulsion	120
5.3.1.5	Model analysis and diagnostic for optimization in nanoemulsion	122
5.3.1.6	Response surface methodology through polynomial equations for nanoemulsion	129
5.3.1.7	Optimization using desirability approach and checkpoint analysis	136
5.3.1.8	Characterization Studies of Developed Resveratrol Loaded Nanoemulsion and Nanoemulgel	139

5.3.1.8.1	Size, polydispersity index, and zeta potential	139
5.3.1.8.2	Surface morphology via TEM	141
5.3.1.8.3	Resveratrol content in NEG	141
5.4	Some other important evaluations of formulated Micellar hydrogel and Nanoemulgel	142
5.4.1	Determination of pH	142
5.4.2	Spreadability studies	142
5.4.3	Rheological behavior and viscosity	143
5.4.4	<i>In vitro</i> Resveratrol release	143
5.4.5	Skin permeation studies (<i>ex vivo</i>)	147
5.4.6	Skin deposition	148
5.4.7	Histopathological studies – skin distribution by CLSM	151
5.4.8	<i>In vitro</i> antioxidant activity using DPPH Assay	152
5.5	<i>In vivo</i> efficacy studies (antipsoriatic activity) using IMQ-induced psoriatic-like plaque model in Swiss Albino Mice	154
5.5.1	Psoriasis Area and Severity Index (PASI) score	154
5.5.2	Cytokines level in serum and Spleen dimension & weight	156
5.5.3	Histology of skin	160
5.6	Stability Studies	160
Chapter 6	SUMMARY AND CONCLUSION	165-175
6.1	Summary	165
6.2	Conclusion	175
	REFERENCES	176-192
	APPENDIX	193-194