
TABLE OF CONTENTS

CERTIFICATES

ACKNOWLEDGEMENT

LIST OF ABBREVIATIONS AND SYMBOLS

LIST OF FIGURES

LIST OF TABLES

	PAGE NO.
CHAPTER 1	1
INTRODUCTION.....	1
CHAPTER 2	8
LITERATURE REVIEW	8
2.1. BRAIN CANCER AND TREATMENT	8
2.2. RESVERATROL	9
2.3. PHYSICO CHEMICAL PROPERTIES OF RSV.....	10
2.4. THERAPEUTIC POTENTIAL OF RSV	10
2.4.1. RSV against myocardial infarction and cardioprotection	10
2.4.2. RSV against platelet aggregation	11
2.4.3. RSV against stroke and brain damage.....	12
2.4.4. RSV against oxidative stress and inflammation.....	12
2.4.5. RSV against obesity and diabetes	13
2.4.6. RSV in vasodilation.....	14
2.4.7. RSV against cholesterol and triglycerides deposition	14
2.4.8. RSV against cancer prevention and glioma	14
2.5. PROBLEM WITH RSV FOR THERAPEUTIC APPLICATIONS.....	16
2.6. NANOFORMULATIONS OF RSV	16
2.7. TPGS	19
2.8. TPGS BASED FORMULATIONS IN CANCER DIAGNOSIS AND THERAPY.....	20
2.8.1. TPGS emulsified PLGA nanoparticles	20
2.8.2. Drug conjugated TPGS prodrug in cancer therapy.....	23
2.8.3. TPGS coated liposomes in cancer diagnosis and therapy	24
2.8.4. TPGS in micelles for cancer diagnosis and therapy.....	27
2.9. TPGS COPOLYMER BASED NANOMEDICINE IN CANCER DIAGNOSIS AND THERAPY	30
2.10. DSPE PEG 2000 AND PEGYLATED NANOPARTICLES	38

CHAPTER 3	44
OBJECTIVES AND PLAN OF WORK	44
3.1. OBJECTIVES	44
3.2. PLAN OF WORK.....	45
CHAPTER 4	46
MATERIALS AND METHODS.....	46
4.1. MATERIALS.....	46
4.2. HPLC ANALYTICAL METHOD	47
4.3. PREPARATION METHODS.....	48
4.3.1. <i>Solid lipid nanoparticles</i>	48
4.3.2. <i>Blend nanoparticles</i>	51
4.3.3. <i>Core-shell polymer-lipid hybrid nanoparticles</i>	54
4.3.4. <i>Liposomes</i>	57
4.4. PARTICLE SIZE, POLYDISPERSITY INDEX AND ZETA POTENTIAL.....	60
4.5. ENTRAPMENT EFFICIENCY.....	61
4.6. SHAPE OF NANOFORMULATIONS	61
4.7. <i>IN VITRO</i> DRUG RELEASE	61
4.8. DRUG EXCIPIENT INTERACTION ANALYSIS.....	62
4.9. DIFFERENTIAL SCANNING CALORIMETRIC (DSC) ANALYSIS.....	62
4.10. X-RAY DIFFRACTION ANALYSIS.....	63
4.11. CYTOTOXICITY AGAINST C6 GLIOMA CELLS.....	63
4.12. CELLULAR UPTAKE OF COUMARIN-6 LOADED NANOFORMULATIONS	64
4.13. EVALUATION OF HAEMOLYSIS.....	65
4.14. EVALUATION OF ERYTHROCYTE MEMBRANE INTEGRITY	66
4.15. PLATELET AGGREGATION	67
4.16. PHARMACOKINETIC STUDIES	68
4.17. TISSUE DISTRIBUTION STUDIES.....	70
4.18. STATISTICAL ANALYSIS.....	70
CHAPTER 5	72
RESULTS AND DISCUSSION	72
5.1. HPLC ANALYTICAL METHOD	72
5.2. SOLID LIPID NANOPARTICLES	74
5.2.1. <i>Particle size, polydispersity index and zeta potential</i>	74
5.2.2. <i>Entrapment efficiency</i>	76
5.2.3. <i>Selection of best formulation</i>	78
5.2.4. <i>Shape of SLN formulations</i>	78
5.2.5. <i>In vitro drug release</i>	79
5.2.6. <i>Drug excipient compatibility studies</i>	81

5.2.7. DSC analysis	84
5.2.8. X-Ray diffraction analysis.....	85
5.2.9. Cytotoxicity against C6 glioma cells.....	86
5.2.10. Cellular uptake of Coumarin-6 loaded SLN	88
5.2.11. Evaluation of haemolysis	90
5.2.12. Evaluation of erythrocyte membrane integrity.....	92
5.2.13. Platelet aggregation	95
5.2.14. Pharmacokinetic studies	99
5.2.15. Tissue distribution studies.....	103
5.2.16. Comparative results of RSV-TPGS-SLN and RSV-PEG-SLN.....	107
5.3. BLEND NANOPARTICLES	108
5.3.1. Particle size, polydispersity index and zeta potential	109
5.3.2. Entrapment efficiency	112
5.3.3. Selection of best formulation	114
5.3.4. Shape of RSV-PLGA-BNPs.....	114
5.3.5. In vitro drug release	115
5.3.6. Drug interaction analysis	116
5.3.7. DSC analysis	118
5.3.8. X-Ray diffraction analysis.....	119
5.3.9. Cytotoxicity against C6 glioma cells.....	119
5.3.10. Cellular uptake	121
5.3.11. Evaluation of haemolysis	122
5.3.12. Evaluation of erythrocyte membrane integrity.....	124
5.3.13. Platelet Aggregation	124
5.3.14. Pharmacokinetic studies	127
5.3.15. Tissue distribution studies.....	130
5.3.16. Concluding results of RSV-PLGA-BNPs	133
5.4. CORE-SHELL POLYMER-LIPID HYBRID NANOPARTICLES.....	134
5.4.1. Particle size, poly dispersity index and zeta potential.....	135
5.4.2. Entrapment efficiency	137
5.4.3. Selection of best formulation	138
5.4.4. Shape of HNPs.....	139
5.4.5. In vitro drug release	139
5.4.6. Drug-excipient interaction analysis.....	141
5.4.7. DSC analysis	144
5.4.8. Analysis of crystallinity.....	145
5.4.9. Cytotoxicity studies	146
5.4.10. Cellular uptake of HNPs	148
5.4.11. Evaluation of haemolysis	150
5.4.12. Evaluation of erythrocyte membrane integrity.....	152
5.4.13. Platelet Aggregation	154

5.4.14. Pharmacokinetic studies	158
5.4.15. Tissue distribution studies.....	162
5.4.16. Comparative results of RSV-TPGS-HNPs and RSV-PEG-HNPs.....	166
5.5. LIPOSOMES.....	167
5.5.1. Vesicular size, polydispersity index and zeta potential.....	168
5.5.2. Encapsulation efficiency.....	171
5.5.3. Selection of optimized formulations	172
5.5.4. Shape of liposomes	173
5.5.5. In vitro drug release	174
5.5.6. Drug-excipient interaction analysis.....	177
5.5.7. DSC analysis	180
5.5.8. Crystallinity analysis.....	181
5.5.9. In vitro cytotoxicity studies	182
5.5.10. Cellular uptake of Coumarin-6 loaded liposomes	183
5.5.11. Evaluation of haemolysis	185
5.5.12. Erythrocyte membrane integrity.....	187
5.5.13. Platelet aggregation	189
5.5.14. Pharmacokinetic studies	193
5.5.15. Tissue distribution studies.....	198
5.5.16. Comparative results of RSV-TPGS-Lipo and RSV-PEG-Lipo.....	202
CHAPTER 6	203
SUMMARY AND CONCLUSION.....	203
6.1. SUMMARY OF RESULTS	203
6.2. CONCLUSION	212
REFERENCES.....	213
LIST OF PUBLICATIONS	251
REPRINTS OF PUBLISHED PAPERS	
PERSONAL PROFILE	
