

Table of Contents

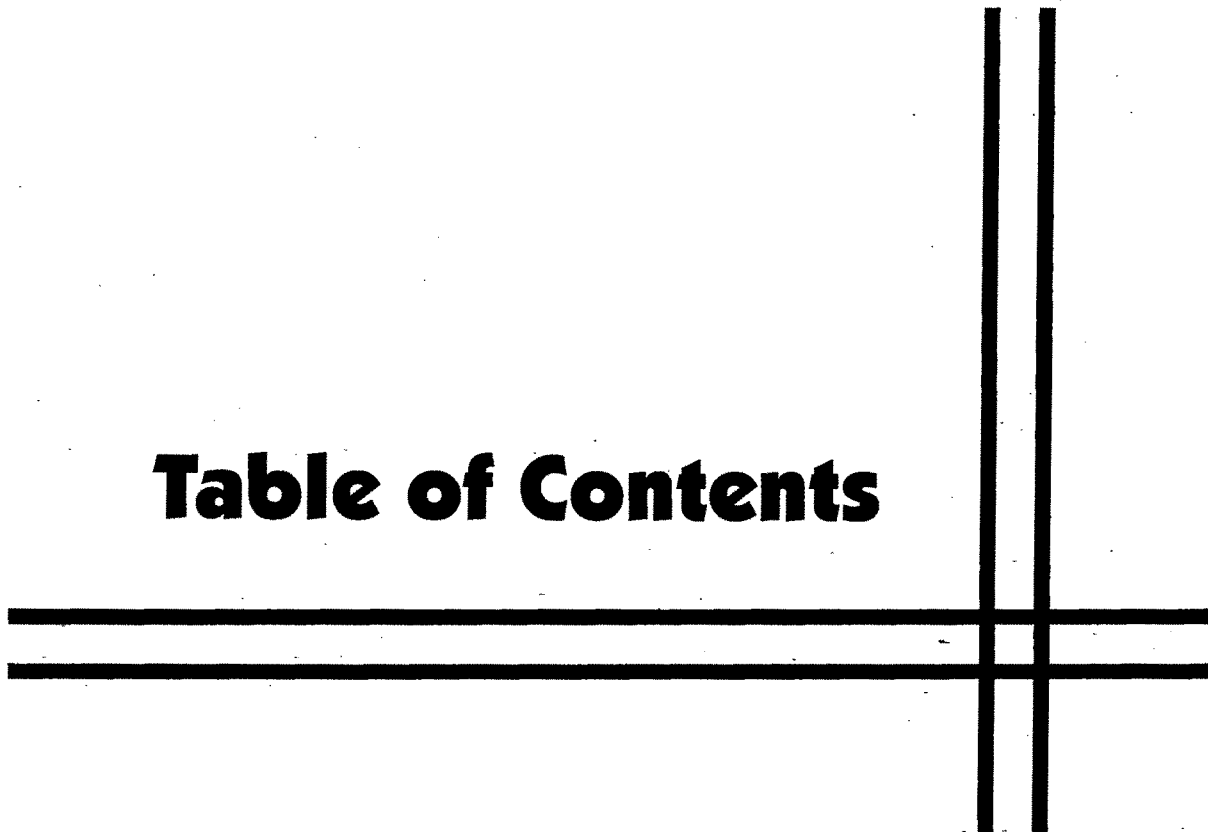


Table of Contents

Chapter 1

1.	Introduction.....	2
1.1.	Self-emulsification (SEDDS).....	5
1.1.1.	Formulation design of SEDDS	7
1.1.2.	Evaluation of SEDDS	8
1.1.2.1.	Literature cited for SEDDS as dissolution enhancer.....	8
1.2.	Liquisolds.....	10
1.2.1.	Theoretical considerations in liquid or powdered solution formulations	11
1.2.2.	Principle Hypothesis for the Mechanism of Powdered Solutions	13
1.2.2.1.	Principle of Sufficient Coating.....	13
1.2.3.	Literature cited for liquid systems as dissolution enhancer	15
1.3.	Solid Dispersions.....	18
1.3.1.	Challenges	20
1.3.2.	The solid state structure.	20
1.3.3.	The mechanism by which dissolution enhancement occurs.....	21
1.3.3.1.	Drug release from solid dispersions.....	21
1.3.3.2.	Particle size reduction and reduced agglomeration	21
1.3.3.3.	Increased solubility or dissolution rate of the drug	21
1.3.4.	Poor understanding of the <i>in vitro in vivo</i> correlation.	22
1.3.5.	Method of preparation	24
1.3.5.1.	Reproducibility of physicochemical properties	24
1.3.5.2.	Dosage form development.....	24
1.3.5.3.	Scale-up of manufacturing processes	25
1.3.6.	Stability	25
1.3.6.1.	Literature cited for solid dispersions as dissolution enhancer.....	25
1.4.	Solubilization and surfactants.....	44
1.5.	pH adjustment.....	44
1.6.	Co-solvent.....	45

1.7.	Microemulsion	45
1.8.	Modification of polymorphs	45
1.9.	Reduction in particle size.....	46
1.10.	Microcrystals/Nanocrystals/ Nanomorphs®	46
1.10.1.	Literature cited for microcrystals/nanocrystals as dissolution enhancer	47
1.11.	Some other vital techniques from future perspective.....	49
1.11.1.	Pearl milling.....	49
1.11.2.	High pressure homogenization.....	50
1.11.3.	Rapid expansion from supercritical to aqueous solution (RESAS).....	51
1.11.4.	Spray freezing into liquid (SFL).....	51
1.11.5.	Evaporative precipitation into aqueous solution (EPAS).....	51
1.11.6.	Complexation.....	52
1.12.	References	53
	OBJECTIVES OF THE WORK.....	62
1.13.	Drug Profiles.....	63

Chapter 2.

2.1. Self Emulsifying Drug Delivery Systems	65
2.1.1. Materials	65
2.1.2. Methods	65
2.1.2.1. Construction of SEDDS	65
Selection of Excipients	65
2.1.2.2. Evaluation of SEDDS	67
2.1.2.2.1. Particle size evaluation	67
2.1.2.2.2. <i>In vitro</i> drug dissolution	67
2.1.3. Results and Discussion	68
2.1.4. SEDDS of CBZ using Vit. E as oil phase	68
Figure 2.1.1 Contour profile of particle size for the mixture design of CBZ Vit E SEDDS	70
Figure 2.1.2 Contour profile of percent drug dissolved for the mixture design of CBZ Vit E SEDDS	70
2.1.5. SEDDS of CBZ using Labrasol	72
2.1.6. Stability studies for CBZ OCBZ and GPN SEDDS systems	80
2.1.7. Conclusion	84
2.1.8. References	85

2.2. Liquisolds.....	87
2.2.1. Materials.....	87
2.2.2. Methods.....	87
2.2.2.1. Solubility studies CBZ liquisolid systems	89
2.2.2.2. Evaluation of Carbamazepine Liquisolid systems.....	89
2.2.2.2.1. <i>In vitro</i> Dissolution studies	89
2.2.2.2.2. Spectrophotometric analysis and standard curves.....	89
2.2.2.2.3. Assessment and comparison of drug dissolution rates	90
2.2.2.2.4. Measurement of angle of repose of liquisolid systems.....	90
2.2.3. Results and discussion for CBZ Liquisolid systems	93
2.2.3.1. Solubility studies for OCBZ liquisolid systems.....	99
2.2.3.2. Evaluation of Oxcarbamazepine Liquisolid systems	99
2.2.3.2.1. <i>In vitro</i> Dissolution studies	99
2.2.3.2.2. Spectrophotometric analysis and standard curves.....	100
2.2.3.2.3. Assessment and comparison of drug dissolution rates	100
2.2.3.2.4. Measurement of angle of repose of liquisolid systems.....	100
2.2.4. Results and discussion for OCBZ liquisolid systems.....	103
2.2.4.1. Solubility studies for GPN liquisolid systems.....	107
2.2.4.2. Evaluation of Gabapentin Liquisolid systems	108
2.2.4.2.1. <i>In vitro</i> Dissolution studies	108
2.2.4.2.2. Assessment and comparison of drug dissolution rates	109
2.2.4.2.3. Measurement of angle of repose of liquisolid systems.....	109
2.2.5. Results and discussion for GPN liquisolid systems.....	112
2.2.6. Stability studies for CBZ, OCBZ and GPN liquisolid systems.....	116
2.2.7. Conclusion.....	120
2.2.7. References	121

2.3. Solid Dispersions (SDs).....	94
2.3.1. Materials.....	94
2.3.2. Methods.....	94
2.3.2.1. Preparation of Solid dispersion.....	94
2.3.2.2. Experimental Design	95
2.3.2.3. Solubility Determination	95
2.3.2.4. Differential Scanning Calorimetry (DSC).....	95
2.3.2.5. Scanning Electron Microscopy (SEM)	95
2.3.2.6. <i>In Vitro</i> Dissolution Study for Solid Dispersions	96
2.3.2.7. Wettability Studies.....	96
2.3.2.8. Angle of repose	96
2.3.3. Results and Discussion	98
2.3.4. Solid Dispersions of Carbamazepine	100
2.3.5. Solid dispersions of Oxcarbamazepine	111
2.3.6. Stability studies for CBZ and OCBZ SD systems	123
2.3.7. CONCLUSION.....	125
2.3.8. References	126

2.4. Microcrystals	157
2.4.1. Materials	158
2.4.2. Methods	158
2.4.2.1. Experimental design.....	158
2.4.2.2. Microcrystal preparation (for both CBZ and OCBZ).....	159
2.4.2.3. Characterization and evaluation of microcrystals	159
2.4.2.3.1. Particle size measurements	159
2.4.2.3.2. <i>In vitro</i> Dissolution studies	159
2.4.2.3.3. Angle of repose measurements (Flowability indicator)	160
2.4.2.3.4. Wettability Studies.....	160
2.4.2.3.5. Scanning electron microscopy (SEM)	160
2.4.2.3.6. X – Ray powder diffraction Studies (XRPD)	160
2.4.2.3.7. Differential scanning calorimetry (DSC).....	161
2.4.2.4. Microcrystals of carbamazepine	162
2.4.2.4.1. Effect of formulation independent variables on Particle size and percent drug dissolved.....	171
2.4.2.4.2. Effect of formulation independent variables on Wettability time and Angle of repose	174
2.4.2.4.3. Interaction between the factors	174
2.4.2.4.4. SEM studies	177
2.4.2.5. Microcrystals of Oxcarbamazepine.....	180
2.4.2.5.1. Effect of formulation independent variables on Wettability time and Angle of repose	191
2.4.2.5.2. Interaction between the factors	191
2.4.2.5.3. Thermal Analysis and XRPD Studies.....	192
2.4.2.5.4. SEM studies	194
2.4.2.6. Stability studies for CBZ and OCBZ microcrystals systems	197
2.4.3. Conclusion.....	199
2.4.4. References	200

Chapter 3

3.	Pharmacokinetic Studies.....	202
3.1.	Estimation of drug in plasma	206
3.1.1.	Plasma extraction procedure	206
3.1.1.1.	Extraction efficiency	206
3.1.1.2.	Linearity and range	206
3.1.1.3.	Accuracy and precision.....	206
3.1.2.	HPLC analysis of CBZ	207
3.1.3.	HPLC analysis of OCBZ	208
3.1.4.	HPLC analysis of GPN	209
3.2.	Calculation of doses of the drugs in rabbits	211
3.3.	Pharmacokinetic study of CBZ.....	211
3.3.1.	List of the abbreviations for Variables output obtained by using Wagner-Nelson method for oral administration	217
3.4.	Pharmacokinetic study of OCBZ.....	218
3.5.	Pharmacokinetic study of GPN.....	222
3.6.	Conclusion	226
3.7.	References.....	227

Summary and Conclusions228

Presentations and Publications.....236