

CONTENTS

Chapter No.	Name of Topic	Page No.
Chapter 1	Introduction	1 - 4
Chapter 2	General Literature Survey	5 - 15
2.1	Development and validation of stability indicating analytical method	5
2.1.1	Introduction	5
2.1.2	Development of stability indicating methods	7
2.1.2.1	Forced Degradation Studies	7
2.1.2.2	Identification of degradants	11
2.1.2	Validation of stability indicating methods	11 - 15
Chapter 3	Research Envisaged	16
Chapter 4	Simultaneous determination of related substances of Telmisartan and Hydrochlorothiazide in tablet dosage form by using reverse phase high performance liquid chromatography	17 – 84
4.0	Introduction	17
4.1	Drug Profile	17
4.1.1	Telmisartan	17
4.1.2	Hydrochlorothiazide	21
4.2	Literature Survey	24
4.3	Present Work and Discussion	29
4.3.1	Selection of Chromatographic Method	29
4.3.2	Selection of Stationary Phase	29
4.3.3	Selection of Wavelength for Analysis	29
4.3.4	Selection and Optimization of Mobile Phase	30
4.4	Forced Degradation Studies	33
4.4.1	Telmisartan Degradation	33
4.4.1.1	Hydrolytic conditions: acid-, base-induced degradation	33
4.4.1.2	Oxidative condition: hydrogen peroxide-induced degradation	33
4.4.1.3	Thermal degradation	34
4.4.1.4	Photolytic degradation	34
4.4.2	Hydrochlorothiazide Degradation	35
4.4.2.1	Hydrolytic conditions: acid-, base-induced degradation	35
4.4.2.2	Oxidative condition: hydrogen peroxide-induced degradation	35
4.4.2.3	Thermal degradation	35
4.4.2.4	Photolytic degradation	36
4.4.3	Observations in forced degradation studies	36
4.5	Experimental Work	46
4.5.1	Instrumentation	46

CONTENTS

4.5.2	Chemical and Reagents	46
4.5.3	Working Standard	47
4.5.4	Solution Preparation	47
4.6	Validation of the Developed Method	52
4.6.1	Validation Parameters and Acceptance Criteria	52
4.6.2	System Suitability	57
4.6.3	Specificity	58
4.6.4	Determination of Limit of Detection (LOD) and Limit of Quantitation (LOQ)	63
4.6.5	Linearity and Range	65
4.6.6	Accuracy	68
4.6.7	Precision	74
4.6.7.1	System Precision	74
4.6.7.2	Method Precision	75
4.6.7.3	Intermediate Precision (Ruggedness)	77
4.6.8	Stability in Analytical Solution	82
4.6.9	Filter Compatibility	83
4.6.10	Robustness	83
4.6.11	Conclusions	84
Chapter 5	Simultaneous determination of Telmisartan and Hydrochlorothiazide in tablet dosage form using reverse phase high performance liquid chromatography	85 - 121
5.0	Introduction	85
5.1	Literature Survey	85
5.2	Present Work and Discussion	90
5.2.1	Selection of Chromatographic Method	90
5.2.2	Selection of Stationary Phase	90
5.2.3	Selection of Wavelength for Analysis	90
5.2.4	Selection and Optimization of Mobile Phase	91
5.3	Forced Degradation Studies	93
5.3.1	Hydrolytic conditions: acid-, base-induced degradation	93
5.3.2	Oxidative condition: hydrogen peroxide-induced degradation	94
5.3.3	Thermal degradation	94
5.3.4	Photolytic degradation	95
5.3.5	Observations in forced degradation studies	95
5.4	Experimental Work	96
5.4.1	Instrumentation	96
5.4.2	Chemical and Reagents	97
5.4.3	Working Standard	97
5.4.4	Solution Preparation	98
5.5	Validation of the Developed Method	100
5.5.1	Validation Parameters and Acceptance Criteria	100

CONTENTS

5.5.2	System Suitability	104
5.5.3	Specificity	104
5.5.4	Linearity and Range	108
5.5.5	Accuracy	111
5.5.6	Precision	113
5.5.6.1	System Precision	113
5.5.6.2	Method Precision	113
5.5.6.3	Intermediate Precision (Ruggedness)	115
5.5.7	Stability in Analytical Solution	118
5.5.8	Filter Compatibility	119
5.5.9	Robustness	120
5.5.10	Conclusions	121
Chapter 6	Simultaneous determination of drug release during dissolution of Telmisartan and Hydrochlorothiazide in tablet dosage form using reverse phase high performance liquid chromatography	122 - 155
6.0	Introduction	122
6.1	Literature Survey	122
6.2	Present Work and Discussion	125
6.2.1	Selection of Chromatographic Method	125
6.2.2	Selection of Stationary Phase	125
6.2.3	Selection of Wavelength for Analysis	125
6.2.4	Selection and Optimization of Mobile Phase	126
6.3	Experimental Work	128
6.3.1	Instrumentation	128
6.3.2	Chemical and Reagents	128
6.3.3	Working Standard	129
6.3.4	Solution Preparation	129
6.4	Validation of the Developed Method	132
6.4.1	Validation Parameters and Acceptance Criteria	132
6.4.2	System Suitability	136
6.4.3	Specificity	136
6.4.4	Linearity and Range	140
6.4.5	Accuracy	144
6.4.6	Precision	147
6.4.6.1	System Precision	147
6.4.6.2	Method Precision	148
6.4.6.3	Intermediate Precision (Ruggedness)	149
6.4.7	Stability in Analytical Solution	152
6.4.8	Filter Compatibility	153
6.4.9	Robustness	154
6.4.10	Conclusions	155

CONTENTS

Chapter 7	Determination of related substances of Nicorandil in tablet dosage form by using reverse phase high performance liquid chromatography	156 - 190
7.0	Introduction	156
7.1	Drug Profile	156
7.2	Literature Survey	157
7.3	Present Work and Discussion	159
7.3.1	Selection of Chromatographic Method	159
7.3.2	Selection of Stationary Phase	159
7.3.3	Selection of Wavelength for Analysis	159
7.3.4	Selection and Optimization of Mobile Phase	160
7.4	Forced Degradation Studies	161
7.4.1	Hydrolytic conditions: acid-, base-induced degradation	161
7.4.2	Oxidative condition: hydrogen peroxide-induced degradation	162
7.4.3	Thermal degradation	162
7.4.4	Photolytic degradation	162
7.4.5	Observations in forced degradation studies	163
7.5	Identification of the Major Degradants by LC-MS	166
7.6	Experimental Work	172
7.6.1	Instrumentation	172
7.6.2	Chemicals and Reagents	172
7.6.3	Working Standard	173
7.6.4	Solution Preparation	173
7.7	Validation of the Developed Method	175
7.7.1	Validation Parameters and Acceptance Criteria	175
7.7.2	System Suitability	179
7.7.3	Specificity	179
7.7.4	Determination of Limit of Detection (LOD) and Limit of Quantitation (LOQ)	182
7.7.5	Linearity and Range	183
7.7.6	Accuracy	185
7.7.7	Precision	186
7.7.7.1	System Precision	186
7.7.7.2	Method Precision	186
7.7.7.3	Intermediate Precision (Ruggedness)	187
7.7.8	Stability in Analytical Solution	188
7.7.9	Filter Compatibility	189
7.7.10	Robustness	189
7.7.11	Conclusions	190

CONTENTS

Chapter 8	Determination of Assay of Nicorandil in tablet dosage form by using reverse phase high performance liquid chromatography	191 - 214
8.0	Introduction	191
8.1	Literature Survey	191
8.2	Present Work and Discussion	193
8.2.1	Selection of Chromatographic Method	193
8.2.2	Selection of Stationary Phase	193
8.2.3	Selection of Wavelength for Analysis	193
8.2.4	Selection and Optimization of Mobile Phase	194
8.3	Forced Degradation Studies	195
8.3.1	Hydrolytic conditions: acid-, base-induced degradation	195
8.3.2	Oxidative condition: hydrogen peroxide-induced degradation	196
8.3.3	Thermal degradation	196
8.3.4	Photolytic degradation	197
8.3.5	Observations in forced degradation studies	197
8.4	Experimental Work	198
8.4.1	Instrumentation	198
8.4.2	Chemical and Reagents	199
8.4.3	Working Standard	199
8.4.4	Solution Preparation	199
8.5	Validation of the Developed Method	201
8.5.1	Validation Parameters and Acceptance Criteria	201
8.5.2	System Suitability	204
8.5.3	Specificity	205
8.5.4	Linearity and Range	208
8.5.5	Accuracy	209
8.5.6	Precision	209
8.5.6.1	System Precision	209
8.5.6.2	Method Precision	209
8.5.6.3	Intermediate Precision (Ruggedness)	211
8.5.7	Stability in Analytical Solution	212
8.5.8	Filter Compatibility	213
8.5.9	Robustness	213
8.5.10	Conclusions	214
Chapter 9	Determination of drug release during dissolution of Nicorandil in tablet dosage form by using reverse phase high performance liquid chromatography	215 - 234
9.0	Introduction	215
9.1	Literature Survey	215
9.2	Present Work and Discussion	216
9.2.1	Selection of Chromatographic Method	216
9.2.2	Selection of Stationary Phase	216
9.2.3	Selection of Wavelength for Analysis	216

CONTENTS

9.2.4	Selection and Optimization of Mobile Phase	217
9.3	Experimental Work	219
9.3.1	Instrumentation	219
9.3.2	Chemical and Reagents	219
9.3.3	Working Standard	220
9.3.4	Solution Preparation	220
9.4	Validation of the Developed Method	222
9.4.1	Validation Parameters and Acceptance Criteria	222
9.4.2	System Suitability	225
9.4.3	Specificity	225
9.4.4	Linearity and Range	228
9.4.5	Accuracy	229
9.4.6	Precision	230
9.4.6.1	System Precision	230
9.4.6.2	Method Precision	230
9.4.6.3	Intermediate Precision (Ruggedness)	230
9.4.7	Stability in Analytical Solution	232
9.4.8	Filter Compatibility	232
9.4.9	Robustness	233
9.4.10	Conclusions	234
Chapter 10	References	235 - 238
	Appendices	
	I – List of Publications & Presentations	239
	I – Certificate of Analysis for APIs	240 - 242
	III – Errata / Notes	243 - 245