

APPENDIX-I

List of Tables

Chapter-1

Table 1.1 Formulation and API stability testing conditions	9
Table 1.2 SST Parameter and limits for parameters	12
Table 1.3 Impurity thresholds in new drug product	15

Chapter-3

Table 3.1 Drug Profile of Terizidone	31
Table: 3.2. IR spectrum inferences for TRZ	32
Table: 3.3. Gradient flow scheme for stability indicating method of TRZ	35
Table: 3.4. Optimization of analytical method of TRZ	40
Table: 3.5 Summary of stress degradation of TRZ (bulk drug and Formulation)	42
Table 3.6 Peak purity result for chromatogram B, C, E and F	46
Table 3.7 mean peak area and respective concentration of TRZ bulk drug	52
Table 3.8 Intermediate precision and repeatability study of TRZ	53
Table 3.9 Recovery result of TRZ bulk drug and formulation	54
Table 3.10 Robustness study of stability-indicating method of TRZ	55
Table 3.11 Regression equations and r^2 value for acid degradation kinetic	59
Table 3.12 Arrhenius Plot and activation parameters of TRZ in different pH solutions	63
Table 3.13 Arrhenius Plot and activation parameters of TRZ in different pH solutions	64
Table 3.14 Regression equations and correlation coefficients for alkali degradation kinetics of TRZ	65
Table 3.15 Degradation kinetic parameters for TRZ in alkaline medium	69
Table 3.16 Arrhenius plot and activation parameters for TRZ in alkaline medium	70

Appendix-I

Table 3.17 Regression equations and correlation coefficients for neutral degradation kinetics of TRZ	71
Table 3.18 Degradation kinetic parameters for TRZ	73
Table 3.19 Arrhenius plot and activation parameters of TRZ neutral degradation	74
Table 3.20 correlation coefficients and correlation equations for oxidative degradation of TRZ	75
Table 3.21 Degradation kinetic parameters for TRZ oxidative degradation	78
Table 3.22 activation parameters for TRZ oxidative degradation	79
Table 3.23 Proton NMR spectrum analysis of TRZ bulk drug	84
Table 3.24 Proton NMR assignment for TRZ bulk drug and DP-A4	89
Table 3.25 IR Spectrum analysis for DP-A4 of TRZ	92
Table 3.26 NMR analysis of neutral DP	98
Table 3.27 IR Spectrum analysis for DP-N3 of neutral degradation of TRZ	100
Table 3.28 NMR assignment for DP-2 of oxide degradation of TRZ	105
Table 3.29 IR Spectrum analysis for DP-O7 of TRZ in oxidative media	108
Table 3.30 Analysis of HPLC chromatogram of TRZ bulk drug	112
Table 3.31 acid degradation product behavior	114
Table 3.32 ESI/MS spectrum data analysis for TRZ in acid medium	120
Table 3.33 TRZ neutral degraded sample chromatogram behavior	124
Table 3.34 ESI/MS data analysis of TRZ neutral degraded sample	127
Table 3.35 TRZ behavior in oxidative media	131
Chapter-4	
Table 4.1 Drug Profile of Bedaquiline	139
Table 4.2: Inferences of IR Graph for BDQ.	142
Table.4.3. Scheme for Gradient elution	145
Table: 4.4. The laboratory mixture of BDQ	147

Appendix-I

Table: 4.5. Optimization of HPLC method for BDQ	150
Table: 4.6 Summary of stress degradation study of BDQ bulk drug and synthetic mixture.	151
Table: 4.7 Peak purity test for BDQ bulk drug and degraded (acid and oxidative medium) sample chromatogram	155
Table 4.8 Mean peak area versus concentration table for linearity of BDQ	160
Table: 4.9. Result of intermediate precision and Repeatability	160
Table: 4.10 Result of accuracy study for BDQ bulk drug and laboratory mixture	161
Table: 4.11 Results of robustness study for BDQ	162
Table: 4.12 gradient sequences for degradation kinetic study of BDQ	164
Table: 4.13 Regression equations and r^2 value for acid degradation kinetic	166
Table 4.14 Arrhenius Plot and activation parameters of bedaquiline in acid solutions	170
Table: 4.15 Acid degradation kinetic parameters for BDQ	171
Table: 4.16 Regression equations and r^2 value for alkali degradation kinetics	172
Table 4.17 Arrhenius plot and activation parameters for BDQ in alkaline medium	176
Table 4.18 Degradation kinetic parameters for BDQ in alkaline medium	176
Table 4.19 correlation coefficient and regression equations for oxidative degradation kinetics of BDQ	177
Table 4.20 Activation parameters for oxidation of BDQ	181
Table 4.21 Degradation kinetic parameters for oxidation of BDQ	182
Table 4.22 Multi factorial design parameters	184
Table 4.23 Degradation kinetic parameters by conventional and multi factorial method	191
Table 4.24 Multi factorial design criteria for alkali degradation kinetics of BDQ	192
Table 4.25 Degradation kinetic parameters by conventional and multi factorial method	198

Appendix-I

Table 4.26 Degradation kinetic parameters by conventional and multi factorial method	205
Table 4.27 Proton NMR spectrum analysis for BDQ API	212
Table 4.28 NMR assignment for acid DP of BDQ (DP-A8)	218
Table 4.29 IR spectrum analysis of DP-8	220
Table 4.30 NMR assignment for DP-3	225
Table 4.31 IR spectrum analysis of DP-8	227
Table 4.32 Chromatographic parameters for BDQ and impurity-1	231
Table 4.33 chromatographic behavior of acid degradation impurity of BDQ	233
Table 4.34 LC/ESI-MS data for bedaquiline and its acid DPs	241
Table 4.35 BDQ and its oxidative degradation products in chromatogram	245
Table 4.36 LC/ESI-MS data for oxidative degradation products of BDQ	250
Chapter-5	
Table 5.1 Physicochemical properties of rifabutin	257
Table 5.2 IR spectrum analysis of rifabutin sample	258
Table 5.3 Method development trials and optimization for rifabutin	265
Table 5.4 summary of stress degradation study of rifabutin bulk drug and formulation	266
Table 5.5 Peak purity results for chromatogram B, C, D and F	271
Table 5.6 Range and mean peak area of rifabutin linearity study	275
Table 5.7 The result of precision study of rifabutin	276
Table 5.8 Accuracy study and result	276
Table 5.9 Result of robustness study	277
Table 5.10 correlation coefficient and regression equations for order of reaction	280
Table 5.11 Degradation kinetic parameters for rifabutin	284
Table 5.12 Activation parameters for degradation kinetics of rifabutin	285

Appendix-I

Table 5.13 correlation coefficient and regression equation for alkali degradation kinetic of rifabutin	286
Table 5.14 Degradation kinetic parameters for rifabutin	288
Table 5.15 correlation coefficient and regression equation for order of reaction	289
Table 5.16 Degradation kinetics parameters for rifabutin	292
Table 5.17 Activation parameters for rifabutin	293
Table 5.18 Factors and limits for design of experiment	294
Table 5.19 Degradation kinetic parameters by conventional and multi factorial method	301
Table 5.20 Multi factorial design criteria for alkali degradation kinetics	301
Table 5.21 Responses for alkaline degradation kinetics of rifabutin	302
Table 5.22 comparison of degradation kinetic parameters value obtained by multi-factorial tool and conventional study	307
Table 5.23 factors and levels for oxidative degradation kinetics	307
Table 5.24 Response for the design of oxidative degradation kinetics	307
Table 5.25 Degradation kinetic parameters value by multi-factorial tool and conventional study	314
Table 5.26 Assignment for ^1H , ^{13}C and APT NMR spectrum for rifabutin and DP-AL 6	325
Table 5.27 IR spectrum analysis for alkaline DP	326
Table 5.28 IR spectrum analysis of for isolated acid DP A5 of rifabutin	333
Table 5.29 Proton NMR analysis of rifabutin bulk drug	339
Table 5.30 Rifabutin degradation behavior in alkaline medium	338
Table 5.31 LC/ESI-MS data for alkaline degradation products of rifabutin	343
Table 5.32 Rifabutin degradation behavior in acidic medium	346
Table 5.33 LC/ESI-MS data for acidic degradation products of rifabutin	353
Table 5.34 Rifabutin behavior in oxidative medium	355

List of Figures

Chapter-1

Fig.1.1 Microscopic image of <i>Mycobacterium tuberculosis</i>	1
Fig.1.2 Sources of impurities in synthetic reaction	6
Fig.1.3 Drug substance and drug product stability study flow chart	10
Fig.1.4 Flow chart for impurity profiling	11

Chapter-3

Figure: 3.1 IR spectrum of TRZ	31
Figure: 3.2 DSC thermogram of TRZ	32
Figure: 3.3 UV Spectrophotometric curve for TRZ	33
Figure: 3.4 UV spectra of TRZ bulk drug (10.00-70.00µg/ml)	39
Fig.: 3.5 Chromatograms of A) chromatogram for blank sample B) Chromatogram showing selectivity of method C) Acid degradation D) Alkali Degradation E) Neutral Degradation F) Oxidative Degradation	45
Fig. 3.6 Peak purity for A) Process related impurity and B) TRZ bulk drug chromatogram	47
Fig. 3.7 Peak purity for acid degraded sample A) Peak-1 B) Peak-2 C) Peak-3 and D) API	48
Fig. 3.8 Peak purity for alkali degraded sample chromatogram of TRZ A) API Peak B) Peak-1 C) Peak-2 D) Peak-3	49
Fig. 3.9 peak purity for neutral degradation chromatogram of TRZ A) Peak-1 B) Peak-2 C) Peak-3 D) API Peak E) Peak-4 F) Peak-5	50
Fig.3.10 Peak purity for oxide degraded sample chromatogram of TRZ A) Peak-1, B) Peak-2 C) API Peak	51
Fig. 3.11 Overlay chromatogram and linearity plot for TRZ bulk drug (0.05- 0.3mg/ml)	52
Fig. 3.12 First order of reaction showing (A) effect of temperatures (B) effect of stressor concentration	61
Fig.3.13 Effect of temperature and stressor concentration on A) Half life B) shelf life C) Rate constant, and D) Activation energy of TRZ acid degradation kinetics	62
Fig. 3.14 Arrhenius plot for degradation kinetics of TRZ	64
Fig. 3.15 Effect of (A) temperatures (B) alkali concentration on TRZ	67

Appendix-I

degradation	
Fig. 3.16 effect of stressor concentration and temperature on (A) Half life (B) Shelf life (C) Rate constant (D) activation energy	68
Fig. 3.17 Arrhenius plot for alkaline degradation of TRZ	70
Fig. 3.18 stressor and temperatures effects on (A) TRZ degradation (B) half life (C) shelf life and (D) rate constant	72
Fig. 3.19 Arrhenius plot for neutral degradation of TRZ	73
Fig. 3.20 Effect of (A) temperatures (B) stressor concentration on TRZ degradation in oxide medium	76
Fig.3.21 The effect of temperatures and stressor concentrations on (A) Half life (B) Shelf life (C) Rate constant (D) Activation energy	77
Fig.3.22 Arrhenius plot and activation parameters for TRZ degradation in oxidative medium	79
Fig. 3.23 Proton NMR spectrum of TRZ bulk drug	83
Fig.3.24 Confirmation by A) HPLC chromatogram of HCl degraded sample of TRZ B) HPLC chromatogram of isolated DP-A4 C) UPLC chromatogram of DP-A4 D) MS/MS spectra of DP-A4	87
Fig. 3.25 characterization of DP by Proton NMR of DP-A4	88
Fig. 3.26 Chemical structure of A) TRZ API and B) DP-A4	90
Fig.3.27 IR spectrum of DP-A4 of acid degradation for TRZ	91
Fig.3.28 A) HPLC chromatogram of water degraded TRZ bulk sample B) HPLC chromatogram of isolated DP-2 C) UPLC chromatogram of isolated DP-2 D) LC/MS/MS spectrum of DP-2	94
Fig.3.29 Fragmentation pathway for A) Acid degradation impurity and B) Neutral degradation impurity of TRZ	95
Fig.3.30 A) Proton NMR B) APT NMR C) C ¹³ NMR for neutral DP	97
Fig.3.31 Chemical structure elucidated for A) DP-N3 and B) TRZ bulk drug	99
Fig.3.32 IR spectrum for isolated DP-N3 of neutral condition for TRZ	99
Fig.3.33 A) HPLC chromatogram for oxide degraded TRZ sample B) HPLC chromatogram for isolated DP-O7 C) UPLC chromatogram for isolated DP-O7 D) MS/MS spectra of DP-O7	102
Fig. 3.34 Fragmentation pathway for oxide DP of TRZ	103
Fig. 3.35 Proton NMR of oxide DP-O7	104

Appendix-I

Fig. 3.36 suggested chemical structure for DP-O7	106
Fig.3.37 IR spectrum for isolated DP-O7 of oxidizing condition for TRZ	107
Fig.3.38 TRZ bulk drug HPLC identification A) HPLC Chromatogram B) UPLC chromatogram for TRZ and process related impurity C) ESI/MS spectrum for TRZ process related impurity D) ESI/MS spectrum for process related impurity	112
Fig.3.39 Process related impurity of TRZ	113
Fig. 3.40 UPLC chromatogram of acid degraded sample	115
Fig. 3.41 ESI/MS spectra for A) DP-1 B) DP-2 C) DP-3 D) DP-4 E) DP-5 F) DP-6 and G) DP-7	118
Fig. 3.42 Degradation pathway for TRZ in acid medium	123
Fig. 3.43 ESI/MS spectrum analysis for TRZ degraded in neutral media	126
Fig.3.44 proposed degradation pathway for TRZ in neutral media	129
Fig.3.45 A) UPLC chromatogram of oxide degraded sample of TRZ B) ESI/MS spectrum of major DP	132
Fig.3.46 Proposed degradation pathway for TRZ in oxidative medium	133
Chapeter-4	
Fig. 4.1 IR spectrum of BDQ	140
Fig.4.2 DSC thermogram of BDQ	142
Fig. 4.3 UV Spectrophotometric graph for BDQ	143
Fig.4.4 Linearity and range of UV spectra for BDQ bulk drug (0.01-0.07mg/ml)	149
Fig. 4.5 Stress degradation study by RP-HPLC for BDQ A) method specificity B)method selectivity for BDQ C) Acid stress degradation D)Alkali stress degradation E)Neutral stress degradation F)Oxidative stress degradation of BDQ	154
Fig.4.6 peak purity test for BDQ bulk drug chromatogram A) process related impurity B) BDQ bulk drug	156
Fig.4.7 peak purity test for acid degraded sample of BDQ chromatogram A) DP1 and 2 B) DP 6 and 7 C)DP-3 D) DP-4 E) DP-8 F) API G) DP-7	157
Fig. 4.8 Peak purity test for oxide degraded sample of BDQ chromatogram A) DP-1 B) DP-2 C) API D) DP-3	158
Fig. 4.9 Overlay chromatogram for linearity and range of BDQ	159

Appendix-I

Fig. 4.10 first order reaction: A) Effect of temperature B) Effect of stressor concentration	167
Fig. 4.11 Effect of temperature and stressor concentration on A) Half life B) shelf life C) Rate constant, and D) Activation energy of BDQ acid degradation kinetics	169
Fig. 4.12 Arrhenius plot for degradation kinetics of BDQ	169
Fig. 4.13 A) Effect of temperatures and B) Effect of stressor concentration BDQ degradation	173
Figure: 4.14 Effect of temperature and stressor concentration on A) Half life B) shelf life C) Rate constant D) Activation energy for alkali degradation kinetics of BDQ	175
Fig. 4.15 Arrhenius plot for alkali degradation kinetics of BDQ	175
Fig. 4.16 A) Effect of temperatures and B) effect of stressor concentrations on BDQ degradation	179
Fig. 4.17 effect of temperature and stressor concentrations on (A) Half life (B) shelf life (C) Rate constant, and (D) Activation energy of reaction	180
Fig. 4.18 Arrhenius plot for oxidation of BDQ	181
Fig. 4.19 Pareto chart for analysis of significance of the factors	186
Fig. 4.20 2D contour for A₁) % Drug, B₁) Rate Constant, C₁) Half life, D₁) Shelf life and E₁) Activation energy and 3D plot for A₂) % Drug, B₂) Rate Constant, C₂) Half life, D₂) Shelf life and E₂) Activation energy	189
Fig.4.21 Predication of acid degradation kinetic parameters using Design Expert™ software	190
Fig.4.22 Pareto chart for responses of alkaline degradation kinetics of BDQ	193
Fig. 4.23 2D contour plot for A₁) % Drug, B₁) Rate Constant, C₁) Half life, D₁) Shelf life and E₁) Activation energy and 3D plot for A₂) % Drug, B₂) Rate Constant, C₂) Half life, D₂) Shelf life and E₂) Activation energy	195
Fig.4.24 Predication of alkali degradation kinetic parameters using Design Expert™ software	197
Fig.4.25 Pareto chart for responses of alkaline degradation kinetics of BDQ	199
Fig. 4.26 2D contour plot for A₁) % Drug, B₁) Rate Constant, C₁) Half life, D₁) Shelf life and E₁) Activation energy and 3D plot for A₂) % Drug, B₂) Rate	202

Appendix-I

Constant, C ₂) Half life, D ₂) Shelf life and E ₂) Activation energy	
Fig. 4.27 Predication of oxidative degradation kinetic parameters using Design Expert TM software	204
Fig.4.28 A) UPLC chromatogram and B)ESI-MS spectrum of BDQ API	209
Fig.4.29 Proton NMR spectrum for BDQ API	210
Fig. 4.30 (A) DPs mixture chromatogram of acid degraded sample of BDQ (B) isolated DP-8 chromatogram (C) UPLC chromatogram of isolated DP-8 (D) LC/ESI-MS of isolated DP	214
Fig. 4.31 A) Proton NMR B) Carbon ¹³ NMR and C) APT NMR for isolated acid DP8	216
Fig. 4.32 A) BDQ bulk drug chemical structure B) elucidated structure for DP-8 of BDQ	219
Fig.4.33 IR spectrum of DP-A8	219
Fig. 4.34 (A) Oxidative DPs mixture chromatogram of BDQ (B) isolated DP chromatogram (C) UPLC chromatogram of isolated DP-3 (D) LC/ESI-MS of isolated	222
Fig. 4.35 A) Proton NMR B) Carbon ¹³ NMR and C) APT NMR for DP-O3	224
Fig.4.36 Elucidated structure for DP-O3 by ESI-MS and NMR	226
Fig.4.37 IR spectrum of DP-O3	227
Fig. 4.38 Chromatogram showing BDQ and process related impurity (0.02mg/ml)	230
Fig. 4.39 (A) UPLC chromatogram (B) LC/ESI-MS spectrum for Impurity-1 and BDQ	232
Fig. 4.40 chemical structure for (A) BDQ and (B) Impurity-1	232
Fig. 4.41 UPLC chromatogram of acid degradation products mixture of BDQ	234
Fig. 4.42 LC/ESI-MS spectra of A) Bedaquiline B) DP-1 and DP-2 C) DP-3 D) DP-4 E) DP-5 F) DP-6 G) DP-7 and H) DP-8	237
Scheme.1.Proposed mechanism for degradation pathway of BDQ in acid media	242
Fig. 4.43 A) UPLC chromatogram for oxide DP mixture ,ESI-MS spectrum for B) DP-1 C) DP-2 and D) DP-3 of BDQ	245
Scheme.2.The degradation pathway and DPs of BDQ in oxidative medium	248
Chapter-5	
Fig. 5.1 IR spectrum of rifabutin	257

Appendix-I

Fig. 5.2 UV spectrophotometric curve for rifabutin (0.09mg/ml)	259
Fig. 5.3 DSC thermogram for melting point analysis of rifabutin	260
Fig. 5.4 The overlay spectrophotometric graph for rifabutin (0.01-0.06mg/ml)	264
Fig. 5.5 Chromatograms of A) Specificity B) Selectivity C) Acid degradation D) Alkali Degradation E) Neutral Degradation F) Oxidative Degradation G) mixture chromatogram	270
Fig. 5.6 Peak purity for rifabutin bulk drug	271
Fig. 5.7 Peak purity test for acid degradation chromatogram of rifabutin A) DP 1 B) DP 2 C) DP 3 and D) API	273
Fig. 5.8 Peak purity plot for chromatogram showing alkali degradation of rifabutin A) DP 1 B) DP 2 and C) API	273
Fig. 5.9 Peak purity plot for oxide degraded sample chromatogram of rifabutin A) Peroxide peak B) API	274
Fig. 5.10 The overlay chromatogram and correlation plot for rifabutin linearity and range	275
Fig. 5.11 The effect of A) different temperatures B) stressor concentrations on rifabutin degradation	282
Fig. 5.12 Effect of stressor concentration and temperature on A) Half life B) Shelf life C) Rate constant D) Activation energy	283
Fig. 5.13 Arrhenius plot for degradation kinetic of rifabutin	285
Fig. 5.14 effect of NaOH concentration on degradation of rifabutin	286
Fig. 5.15 3D plot for effect of stressor concentration on A) half life B) shelf life and C) rate constant	287
Fig. 5.16 Effect of A) temperatures B) stressor concentration on degradation of rifabutin	290
Fig. 5.17 Effect of stressor concentration and temperature on A) Half life B) Shelf life C) Rate constant and D) Activation energy	291
Fig. 5.18 Arrhenius plot for activation parameters of rifabutin degradation	293
Fig. 5.19 Pareto chart for the analysis of significant factors for A) % Drug, B) Rate Constant, C) Half life, D) Shelf life and E) Activation energy	296
Fig. 5.20 2D contour for A₁) % Drug, B₁) Rate Constant, C₁) Half life, D₁) Shelf life and E₁) Activation energy and 3D plot for A₂) % Drug, B₂) Rate Constant, C₂) Half life, D₂) Shelf life and E₂) Activation energy	299

Appendix-I

Fig. 5.21 Prediction of kinetic parameters for degradation sample of 0.1N HCl at 40 ⁰ C for 30minutes	300
Fig.5.22 Pareto chart for A) % Drug, B) Rate Constant, C) Half life, D) Shelf life	303
Fig.5.23 2D contour plot for A ₁) % Drug, B ₁) Rate Constant, C ₁) Half life, D ₁) Shelf life and 3D plot for A ₂) % Drug, B ₂) Rate Constant, C ₂) Half life, D ₂) Shelf life	305
Fig. 5.24 Predication of alkali degradation kinetic parameters using Design Expert TM software A) % drug B) Rate constant C) half life D) shelf life	306
Fig.5.25 Pareto chart for response to evaluate significant factors	309
Fig. 5.26 2D contour plot for A ₁) % Drug, B ₁) Rate Constant, C ₁) Half life, D ₁) Shelf life and E ₁) Activation energy and 3D plot for A ₂) % Drug, B ₂) Rate Constant, C ₂) Half life, D ₂) Shelf life and E ₂) Activation energy	312
Fig. 5.27 Predication of degradation kinetic parameters A) % drug B) rate constant C) half life D) shelf life E) activation energy	313
Fig. 5.28 DP-6 confirmation by A) RP-HPLC B) UPLC and C) ESI/MS spectrum	317
Fig. 5.29 Chemical structure of A) rifabutin and B) DP-6 with atom number	319
Fig. 5.30 NMR spectrum for A) proton NMR B) Carbon-13 NMR and C) APT NMR	322
Fig. 5.31 IR spectrum of alkali DP of rifabutin	326
Fig. 5.32 DP confirmation by A) RP-HPLC B) UPLC and C) ESI/MS spectrum	328
Fig. 5.33 A) Q1 Ms spectrum for DP B) Q3 MS spectrum for acid DP of rifabutin	329
Fig.5.34 Fragmentation pathway for acid DP of rifabutin	330
Fig. 5.35 Chemical structure of A) rifabutin and B) DP with atom number	331
Fig.5.36 IR spectrum of isolated DP A5 of acid degradation of rifabutin	332
Fig. 5.37 Rifabutin bulk drug chromatogram	334
Fig. 5.38 A) UPLC chromatogram B) ESI-MS spectrum of rifabutin	335
Fig.5.39 MS ionization of rifabutin	336
Fig.5.40 Proton NMR of rifabutin bulk drug	337
Fig. 5.41 UPLC chromatogram for mixture of alkaline degradation products	340

Appendix-I

Fig. 5.42 ESI/MS spectrum of rifabutin DPs in alkaline medium in order of elution	342
Scheme-1. Proposed degradation pathway for rifabutin in alkaline media	345
Fig. 5.43 A) UPLC chromatogram of mixture of DPs in acidic medium B) ESI/MS spectrum DPs at Rt 0.16 C) DPs at Rt 1.35 D) DPs at Rt 1.39 E) DPs at Rt 1.7 F) rifabutin bulk drug at Rt 1.9 G) DP at Rt 2.14 H) DP at Rt 2.25	349
Scheme-2. Proposed degradation pathway for rifabutin in alkaline media	356
Fig. 5.44 A) UPLC chromatogram B) ESI/MS spectrum of oxidative sample DP mixture	358