

List of Tables

Table 1.1 Different classes of drugs used in antiretroviral therapy	2
Table 1.2 Protease inhibitors approved as antiretroviral drugs.....	4
Table 2.1 Various fixed dose combinations approved by FDA for treatment of HIV infection	21
Table 2.2 Overview of the inhibitors of HIV protease approved for clinical use.....	24
Table 2.3 Different techniques employed for preparation of SLNs.....	37
Table 2.4 Various types of solid lipids used for SLNs preparation	39
Table 2.5 Commonly used stabilizers for SLN preparation	41
Table 3.1 Data for calibration plot of Darunavir in Methanol: DCM (7:3).....	84
Table 3.2 Intra-day and inter-day precision for determination of Darunavir in methanol: DCM (7:3).....	86
Table 3.3 Determination of accuracy of the method.....	86
Table 3.4 Optical characteristics of Darunavir in methanol: DCM (7:3)	87
Table 3.5 Data for calibration plot of Darunavir in SGF: methanol (1:0.5)	89
Table 3.6 Intra-day and inter-day precision for determination of Darunavir in SGF: methanol (1:0.5)	90
Table 3.7 Determination of accuracy of the method.....	90
Table 3.8 Optical characteristics of Darunavir in SGF: methanol (1:0.5).....	91
Table 3.9 Data for calibration plot of Darunavir in SIF:methanol (1:0.5).....	91
Table 3.10 Intra-day and inter-day precision for determination of Darunavir in SIF:methanol (1:0.5)	93
Table 3.11 Determination of accuracy of the method.....	93
Table 3.12 Optical characteristics of Darunavir in SGF: methanol (1:0.5).....	93
Table 3.13 Data for calibration plot of Darunavir using HPLC	94
Table 3.14 Intra-day and inter-day precision for determination of Darunavir using HPLC	95
Table 3.15 Accuracy determination of method.....	96
Table 3.16 Optical characteristics of Darunavir using HPLC method	96
Table 3.17 Calibration plot of Darunavir in plasma using LC/MS.....	97
Table 3.18 Optical characteristics of Darunavir in plasma using LCMS	100
Table 3.19 Data for calibration plot of Darunavir in spleen using LC/MS	100
Table 3.20 Optical characteristics of Darunavir in spleen using LCMS	102
Table 3.21 Data for calibration plot of ATZ in methanol: DCM (7:3).....	103
Table 3.22 Intra-day and inter-day precision for determination of ATZ in methanol: DCM (7:3).....	104
Table 3.23 Determination of accuracy of the method.....	104
Table 3.24 Optical characteristics of ATZ in methanol: DCM (7:3).....	105
Table 3.25 Data for calibration plot of ATZ in SGF:methanol (1:0.5).....	106

Table 3.26 Intra-day and inter-day precision for determination of ATZ in SGF:methanol (1:0.5)	108
Table 3.27 Determination of accuracy of the method.....	108
Table 3.28 Optical characteristics of ATZ in SGF: methanol (1:0.5)	109
Table 3.29 Data for calibration plot of ATZ in SIF:methanol (1:0.5).....	109
Table 3.30 Intra-day and inter-day precision for determination of ATZ in SGF:methanol (1:0.5)	111
Table 3.31 Determination of accuracy of the method.....	111
Table 3.32 Optical characteristics of ATZ in SIF: methanol (1:0.5).....	112
Table 3.33 Data for calibration plot of Atazanavir sulfate using HPLC	112
Table 3.34 Intra-day and inter-day precision for determination of Atazanavir sulfate using HPLC.....	113
Table 3.35 Accuracy determination of method.....	114
Table 3.36 Optical characteristics of ATZ using HPLC.....	114
Table 3.37 Data for calibration plot of Atazanavir sulfate in plasma.....	115
Table 3.38 Intra-day and inter-day precision for determination of Atazanavir sulfate in plasma using HPLC	116
Table 3.39 Accuracy determination of method.....	117
Table 3.40 Optical characteristics of ATZ in plasma using HPLC	117
Table 3.41 Data for calibration plot of Atazanavir sulfate for estimation in spleen.....	118
Table 3.42 Intra-day and inter-day precision for determination of Atazanavir sulfate in spleen using HPLC	119
Table 3.43 Accuracy determination of method.....	119
Table 3.44 Optical characteristics of ATZ in spleen using HPLC	120
Table 4.1 Composition of various batches of nanoemulsion of Darunavir	131
Table 4.2 Effect of ultraturrax speed and homogenization on particle size and PDI of placebo nanoparticles.....	135
Table 4.3 Effect of ratio of aqueous phase: organic phase on particle size and PDI of placebo nanoparticles.....	135
Table 4.4 Effect of sonication cycle on particle size and PDI of placebo nanoparticles	136
Table 4.5 Effect of type of organic solvent on particle size and PDI of placebo nanoparticles	137
Table 4.6 Effect of pluronic F68 on particle size and PDI of solid lipid nanoparticles...	138
Table 4.7 Effect of polyvinyl alcohol on particle size and PDI of solid lipid nanoparticles	138
Table 4.8 Effect of sodium oleate on particle size and PDI of solid lipid nanoparticles	139
Table 4.9 Effect of various formulation parameters on particle size, PDI and drug entrapment efficiency of Darunavir loaded solid lipid nanoparticles.....	140
Table 4.10 Effect of lipid and surfactant concentration on particle size, PDI and drug entrapment efficiency of Darunavir loaded solid lipid nanoparticles.....	142

Table 4.11 Final optimized Darunavir loaded solid lipid nanoparticles	143
Table 4.12 Results of cryoprotectant effect on the optimized Darunavir loaded solid lipid nanoparticles	144
Table 4.13 Results of solubility study of Darunavir in various oils/surfactants	146
Table 4.14 Results of evaluation parameters of various batches of nanoemulsion of Darunavir	147
Table 4.15 Results of globule size of different batches of nanoemulsion upon storage at 4°C and 25 °C.	148
Table 4.16 Results of zeta potential of different batches of nanoemulsion upon storage at 4°C and 25°C.	149
Table 4.17 Effect of various formulation parameters on particle size, PDI and drug entrapment efficiency of Atazanavir sulfate loaded solid lipid nanoparticles	150
Table 4.18 Effect of lipid and surfactant concentration on particle size, PDI and drug entrapment efficiency of ATZ loaded solid lipid nanoparticles	151
Table 4.19 Results of cryoprotectant effect on the optimized ATZ loaded solid lipid nanoparticles	153
Table 5.1 Composition of 10 ml of stacking gel.....	162
Table 5.2 Composition of 10 ml of resolving gel	163
Table 5.3 Characteristic peaks of Darunavir observed in various samples	181
Table 5.4 Characteristics FT-IR peaks of lipid observed in various samples.....	181
Table 5.5 In-vitro drug release profile of plain Darunavir suspension and Darunavir loaded nanoparticles.....	182
Table 5.6 Calibration plot of BSA	185
Table 5.7 Results of quantitative estimation of bound peptide in Pept-Dar-SLN formulation.....	185
Table 5.8 <i>In-vitro</i> drug release profile of peptide grafted Darunavir SLNs (Pept-Dar-SLN) in comparison to non-peptide grafted Darunavir SLNs (Dar-SLN2).....	186
Table 5.9 <i>In-vitro</i> drug release of Darunavir loaded nanoemulsion (DNE3) in comparison with plain Darunavir suspension	188
Table 5.10 Release kinetics of optimized Darunavir loaded nanoemulsion (DNE3) formulation.....	189
Table 5.11 Characteristic peaks of ATZ observed in various samples.....	195
Table 5.12 Characteristics peaks of lipid observed in various samples.....	196
Table 5.13 Results of quantitative estimation of bound peptide in Pept-ATZ-SLN formulation.....	197
Table 5.14 <i>In-vitro</i> drug release profile of plain ATZ suspension and ATZ loaded nanoparticles	198
Table 6.1 MTT assay results of control sample, placebo SLNs and Darunavir loaded SLNs	216

Table 6.2 Relative Caco-2 cell uptake efficiency of Darunavir and Atazanavir sulfate in absence or presence of various endocytic inhibitors	217
Table 6.3 Drug transfer across Caco-2 cell line for Darunavir loaded SLNs and plain Darunavir solution	219
Table 6.4 Drug transfer across Caco-2 cell line for ATZ loaded SLNs and plain ATZ solution.....	220
Table 7.1 Plasma concentration profile after oral administration of Darunavir suspension, marketed tablet, Dar-SLN1, Dar-SLN2 and Dar-SLN3 to rats (n=3).....	234
Table 7.2 Pharmacokinetic parameters after oral administration of Darunavir suspension, marketed tablet, Dar-SLN1, Dar-SLN2 and Dar-SLN3 to rats (n=3).....	235
Table 7.3 Mean plasma Darunavir concentration after intragastric administration of Darunavir suspension and optimized Darunavir loaded SLNs (Dar-SLN2).....	238
Table 7.4 Mean plasma Darunavir concentration after intraduodenal administration of Darunavir suspension and optimized Darunavir loaded SLNs (Dar-SLN2).....	239
Table 7.5 Plasma concentration of Darunavir from Dar-SLN2 in presence and absence of cycloheximide	241
Table 7.6 Results of biodistribution study in different organs upon administration of Darunavir suspension.....	243
Table 7.7 Results of biodistribution study in different organs upon administration of Darunavir loaded SLNs.....	243
Table 7.8 Distribution of Darunavir in PP and Non-PP region upon oral administration of Dar-SLNs.....	248
Table 7.9 Plasma concentration vs time profile after oral administration of peptide grafted Darunavir SLNs (Pept-Dar-SLN) and non-peptide grafted Darunavir SLNs (Dar-SLN2) to rats (n=3).....	249
Table 7.10 Pharmacokinetic parameters after oral administration of peptide grafted Darunavir SLNs (Pept-Dar-SLN) and non-peptide grafted Darunavir SLNs (Dar-SLN2) rats (n=3)	250
Table 7.11 Results of biodistribution study in different organs upon administration of peptide grafted Darunavir loaded SLNs	251
Table 7.12 Plasma concentration profile after oral administration of Darunavir nanoemulsion in comparison to its suspension form and Marketed tablet (n=3)	254
Table 7.13 Pharmacokinetic parameters after oral administration of Darunavir nanoemulsion in comparison to its suspension form and marketed tablet (n=3).....	255
Table 7.14 Results of biodistribution study in different organs upon administration of Darunavir loaded lipid nanoemulsion.....	256

Table 7.15 Plasma concentration vs time profile after oral administration of peptide grafted ATZ loaded SLNs (Pept-ATZ-SLN) and non-peptide grafted ATZ loaded SLNs (ALN-23) to rats (n=3).....	261
Table 7.16 Results of pharmacokinetic parameters upon oral administration of Atazanavir loaded SLNs and plain drug suspension to rats (n=3).....	262
Table 7.17 Results of biodistribution study in different organs upon administration of ATZ suspension	263
Table 7.18 Results of biodistribution study in different organs upon administration of ATZ loaded SLNs	264
Table 7.19 Results of biodistribution study in different organs upon administration of peptide grafted ATZ loaded SLNs	264
Table 8.1 Stability data of Dar-SLN2	272
Table 8.2 Stability data of Pept-Dar-SLN.....	273
Table 8.3 Stability data of Darunavir loaded nanoemulsion (DNE-3) at $5 \pm 3^{\circ}\text{C}$	274
Table 8.4 Stability data of Pept-ATZ-SLN.....	275