

LIST OF FIGURES

Figure No.	Topic	Page No.
Figure 2.1	Physiological constraints leading to reduction in bioavailability through oral delivery	12
Figure 2.2	Role of nanocarrier based formulations in oral drug delivery	14
Figure 2.3	Schematic diagram of mechanisms of intestinal drug transport from lipid-based formulations	16
Figure 2.4	Transport mechanism across intestinal epithelium	23
Figure 2.5	Diagrammatic representation depicting the probable mechanistic pathways for transportation of drugs across the GI lumen using SEDDS	46
Figure 3.1	Overlay plot of Asenapine maleate in methanol	95
Figure 3.2	Standard calibration curve of Asenapine maleate in methanol	95
Figure 3.3	Overlay plot of Asenapine maleate in chloroform:methanol	97
Figure 3.4	Standard calibration curve of Asenapine maleate in chloroform: methanol	98
Figure 3.5	Overlay plot of Asenapine maleate in 0.1 N HCl	100
Figure 3.6	Standard calibration curve of Asenapine maleate in 0.1 N HCl	100
Figure 3.7	Overlay plot of Asenapine maleate in phosphate buffer pH 6.8	102
Figure 3.8	Standard calibration curve of Asenapine maleate in phosphate buffer pH 6.8	103
Figure 3.9	Overlay plot of Asenapine maleate in phosphate buffer pH 7.4	105
Figure 3.10	Standard calibration curve of Asenapine maleate in phosphate buffer pH 7.4	105
Figure 3.11	Overlay plot of Asenapine maleate in phosphate buffer:ACN	107
Figure 3.12	Calibration curve of Asenapine maleate in phosphate buffer: CAN	108
Figure 3.13	Overlay plot of Asenapine maleate in plasma	110
Figure 3.14	Calibration curve of Asenapine maleate in plasma	110
Figure 3.15	Overlay plot of Lurasidone HCl in methanol	112
Figure 3.16	Standard calibration curve of Lurasidone HCl in methanol	113

Figure 3.17	Standard calibration curve of Lurasidone HCl in chlorofom:methanol	115
Figure 3.18	Standard calibration curve of Lurasidone HCl in chlorofom:methanol	115
Figure 3.19	Overlay plot of Lurasidone HCl in 0.1 N HCl	117
Figure 3.20	Standard calibration curve of Lurasidone HCl in 0.1 N HCl	118
Figure 3.21	Overlay plot of Lurasidone HCl in phosphate buffer pH 6.8	120
Figure 3.22	Standard Calibration curve of Lurasidone HCl in phosphate buffer pH 6.8	120
Figure 3.23	Overlay plot of Lurasidone HCl in phosphate buffer pH 7.4	123
Figure 3.24	Standard Calibration curve of Lurasidone HCl in phosphate buffer pH 7.4	123
Figure 3.25	Overlay plot of Lurasidone HCl in phosphate buffer:ACN	125
Figure 3.26	Standard calibration curve of Lurasidone HCl in Phosphate buffer:ACN	126
Figure 3.27	Overlay plot of Lurasidone HCl in Plasma	128
Figure 3.28	Standard calibration curve of Lurasidone HCl in Plasma	128
Figure 4.1	Solubility of Asenapine maleate in various lipids	140
Figure 4.2	Ishikawa diagram for (a) Particle size and (b) Entrapment efficiency of AM-SLNs	141
Figure 4.3	Main effect plot for Particle size of AM-SLNs	150
Figure 4.4	(a) Pareto chart (b) Half normal plot and (c) Normal plot for particle size of AM-SLNs	152
Figure 4.5	Main effect plots for entrapment efficiency of AM-SLNs	153
Figure 4.6	(a) Pareto chart (b) Half normal plot and (c) Normal plot for entrapment efficiency of AM-SLNs	155
Figure 4.7	(a) Contour and (b) Response surface plot showing effect of lipid concentration and surfactant concentration on particle size of AM-SLNs	158
Figure 4.8	(a) Contour and (b) Response surface plot showing effect of lipid concentration and sonication time on particle size of AM-SLNs	158

Figure 4.9	(a) Contour and (b) Response surface plot showing effect of surfactant concentration and sonication time on particle size of AM-SLNs	159
Figure 4.10	(a) Contour and (b) Response surface plot showing effect of lipid concentration and surfactant concentration on entrapment efficiency of AM-SLNs	161
Figure 4.11	(a) Contour and (b) Response surface plot showing effect of lipid concentration and sonication time on entrapment efficiency of AM-SLNs	161
Figure 4.12	(a) Contour and (b) Response surface plot showing effect of surfactant concentration and sonication time on entrapment efficiency of AM-SLNs	162
Figure 4.13	Desirability plot for optimized batch of AM-SLNs	163
Figure 4.14	Overlay plot showing robustness of design space of AM-SLNs	164
Figure 4.15	Particle size of optimized batch of AM-SLNs	165
Figure 4.16	Zeta potential of optimized batch of AM-SLN	166
Figure 4.17	FTIR spectrum of (a) AM (b) GMS (c) Physical mixture and (d) lyophilized AM-SLNs	168
Figure 4.18	DSC thermogram of (a) AM (b) GMS (c) Physical mixture of AM and GMS (d) lyophilized AM-SLNs	171
Figure 4.19	XRD of (a) AM (b) GMS (c) physical mixture of AM and GMS (d) lyophilized AM-SLNs	173
Figure 4.20	TEM image of optimized batch of AM-SLNs	174
Figure 4.21	In vitro drug release profile of AM-SLNs and drug suspension	175
Figure 4.22	Ex vivo drug release profile of AM-SLNs and drug suspension	176
Figure 5.1	Solubility of Asenapine maleate in various oils	190
Figure 5.2	Solubility of Asenapine maleate in various surfactants	190
Figure 5.3	Solubility of Asenapine maleate in various co-surfactants	191
Figure 5.4	Emulsification study of Asenapine maleate in surfactants	192
Figure 5.5	Emulsification study of Asenapine maleate in co-surfactants	193
Figure 5.6	Ternary diagrams of Capryol 90 with different ratio of Cremophor EL and Transcutol HP (a)1:0, (b)1:1, (c)2:1, (d)3:1, (e)1:2 and (f)1:3	195

Figure 5.7	Two-component mixture plot for the effect of varying ratio of two components with a fixed amount of the other component for globule size of AM-SMEDDS	199
Figure 5.8	(a) Contour and (b) Response surface plot showing effect of independent variables on globule size of AM-SMEDDS	199
Figure 5.9	Two-component mixture plot for the effect of varying ratio of two components with a fixed amount of the other component for % transmittance of AM-SMEDDS	202
Figure 5.10	(a) Contour and (b) Response surface plot showing effect of independent variables on %transmittance of AM-SMEDDS	203
Figure 5.11	Two-component mixture plot for the effect of varying ratio of two components with a fixed amount of the other component for self-emulsification time of AM-SMEDDS	206
Figure 5.12	(a) Contour and (b) Response surface plot showing effect of independent variables on self-emulsification time of AM-SMEDDS	206
Figure 5.13	Desirability plot of optimized batch of AM-SMEDDS	208
Figure 5.14	Overlay plot depicting the design space of AM-SMEDDS	209
Figure 5.15	Globule size of optimized batch of AM-SMEDDS	210
Figure 5.16	Zeta potential of optimized batch of AM-SMEDDS	211
Figure 5.17	FTIR spectrum of (a) drug (b) Capryol 90 (c) Cremophor EL (d) Transcutol HP (e) Physical mixture of drug and excipients (f) AM-SMEDDS	214
Figure 5.18	TEM image of optimized batch of AM-SMEDDS	214
Figure 5.19	In vitro drug release profile of AM-SMEDDS and AM suspension	215
Figure 5.20	Ex vivo permeation study of AM-SMEDDS and AM suspension	216
Figure 6.1	Solubility of Lurasidone HCl in various lipids	229
Figure 6.2	Ishikawa diagram illustrating factors that may have impact on the particle size of LH-SLNs	230
Figure 6.3	Ishikawa diagram illustrating factors that may have impact on the entrapment efficiency of LH-SLNs	230

Figure 6.4	Main effect plot for particle size of LH-SLNs	239
Figure 6.5:	(a) Pareto chart (b) Half normal plot and (c) Normal plot for particle size of LH-SLNs	241
Figure 6.6	Main effect plot for entrapment efficiency of LH-SLNs	242
Figure 6.7	(a) Pareto chart (b) Half normal plot and (c) Normal plot for entrapment efficiency of LH-SLNs	244
Figure 6.8	(a) Contour and (b) Response surface plot showing effect of lipid concentration and homogenization pressure on particle size of LH-SLNs	247
Figure 6.9	(a) Contour and (b) Response surface plot showing effect of lipid concentration and homogenization cycle on particle size of LH-SLNs	247
Figure 6.10	(a) Contour and (b) Response surface plot showing effect of homogenization pressure and homogenization cycle on particle size of LH-SLNs	247
Figure 6.11	(a) Contour and (b) Response surface plot showing effect of lipid concentration and homogenization pressure on entrapment efficiency of LH-SLNs	249
Figure 6.12	(a) Contour and (b) Response surface plot showing effect of lipid concentration and homogenization cycle on entrapment efficiency of LH-SLNs	249
Figure 6.13	(a) Contour and (b) Response surface plot showing effect of homogenization pressure and homogenization cycle on entrapment efficiency of LH-SLNs	250
Figure 6.14	Desirability plot of optimized batch of LH-SLNs	251
Figure 6.15	Overlay plot depicting the design space for optimized batch of LH-SLNs	252
Figure 6.16	Particle size of optimized batch of LH-SLNs	253
Figure 6.17	Zeta potential of optimized batch of LH-SLNs	254
Figure 6.18	FTIR spectrum of (a) LH (b) GMS (c) Physical mixture of LH and GMS and (d) lyophilized LH-SLNs	256
Figure 6.19	DSC thermogram of (a) LH (b) GMS (c) Physical mixture of LH and GMS (d) lyophilized LH-SLNs	258

Figure 6.20	XRD of (a) LH (b) GMS (c) physical mixture of LH and GMS (d) lyophilized LH-SLNs	261
Figure 6.21	TEM image of optimized batch of LH-SLNs	261
Figure 6.22	In vitro drug release profile of LH-SLNs and drug suspension	263
Figure 6.23	Ex vivo drug diffusion profile of LH-SLNs and drug suspension	264
Figure 7.1	Solubility of Lurasidone HCl in various oils	273
Figure 7.2	Solubility of Lurasidone HCl in various surfactants	274
Figure 7.3	Solubility of Lurasidone HCl in various co-surfactants	274
Figure 7.4	Emulsification study of Lurasidone HCl in surfactants	275
Figure 7.5	Emulsification study of Lurasidone HCl in co-surfactants	275
Figure 7.6	Ternary diagrams of Capmul MCM C8 with different ratio of Cremophor EL and Transcutol HP (a)1:0, (b)1:1, (c)2:1, (d)3:1, (e)4:2, (f)1:2 and (g)1:3 of LH-SMEDDS	278
Figure 7.7	(a) Contour and (b) Response surface plot showing effect of independent variables on globule size of LH-SMEDDS	281
Figure 7.8	(a) Contour and (b) Response surface plot showing effect of independent variables on %transmittance of LH-SMEDDS	282
Figure 7.9	(a) Contour and (b) Response surface plot showing effect of independent variables on self-emulsification time of LH-SMEDDS	284
Figure 7.10	Desirability plot of optimized batch of LH-SMEDDS	286
Figure 7.11	Overlay plot depicting the design space for optimized batch of LH-SMEDDS	287
Figure 7.12	Globule size of optimized batch of LH-SMEDDS	288
Figure 7.13	Zeta potential of optimized batch of LH-SMEDDS	289
Figure 7.14	FTIR spectrum of (a)LH (b) Capmul MCM C8 (c) Cremophor EL (d) Transcutol HP (e) Physical mixture of drug and excipients (f) LH-SMEDDS	291
Figure 7.15	TEM of optimized batch of LH-SMEDDS	292
Figure 7.16	In-vitro drug release profile of LH-SMEDDS and LH suspension	293

Figure 7.17	Ex vivo permeation study of LH-SMEDDS and LH suspension	294
Figure 8.1	Cell viability assay of the AM-SLNs in Caco-2 cell line	305
Figure 8.2	Cell viability assay of the LH-SLNs in Caco-2 cell line	305
Figure 8.3	Cell viability assay of the AM-SMEDDS in Caco-2 cell line	306
Figure 8.4	Cell viability assay of the LH-SMEDDS in Caco-2 cell line	307
Figure 8.5	Confocal microscopic images of Caco-2 cells (a) without any treatment (Control) (b) DAPI stained nuclei (c) Overlapped image	309
Figure 8.6	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C with (a) dye solution (b) DAPI stained nuclei (c) Overlapped image showing no internalization of dye solution in cells for AM	309
Figure 8.7	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) dye solution (b) DAPI stained nuclei (c) Overlapped image showing no internalization of dye solution in cells for AM	309
Figure 8.8	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C (a) 6- coumarin loaded SLNs (b) DAPI stained nuclei (c) Overlapped image showing internalization of SLNs in cells for AM	310
Figure 8.9	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) Coumarin-6 loaded SLNs (b) DAPI stained nuclei (c) Overlapped image showing internalization of SLNs in cells for AM	310
Figure 8.10	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C with (a) Coumarin-6 loaded SMEDDS (b) DAPI stained nuclei (c) Overlapped image showing internalization of SMEDDS in cells for AM	311
Figure 8.11	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) Coumarin-6 loaded SMEDDS (b) DAPI stained nuclei (c) Overlapped image showing internalization of SMEDDS in cells for AM	311

Figure 8.12	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C with (a) dye solution (b) DAPI stained nuclei (c) Overlapped image showing no internalization of dye solution in cells for LH	313
Figure 8.13	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) dye solution (b) DAPI stained nuclei (c) Overlapped image showing no internalization of dye solution in cells for LH	313
Figure 8.14	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C with (a) Coumarin-6 loaded SLNs (b) DAPI stained nuclei (c) Overlapped image showing internalization of SLNs in cells for LH	314
Figure 8.15	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) coumarin 6-loaded SLNs (b) DAPI stained nuclei (c) Overlapped image showing internalization of SLNs in cells for LH	314
Figure 8.16	Confocal microscopic images of Caco-2 cells after 1 h incubation at 37 °C with (a) Coumarin-6 loaded SMEDDS (b) DAPI stained nuclei (c) Overlapped image showing internalization of SMEDDS in cells for LH	315
Figure 8.17	Confocal microscopic images of Caco-2 cells after 4 h incubation at 37 °C with (a) Coumarin-6 loaded SMEDDS (b) DAPI stained nuclei (c) Overlapped image showing internalization of SMEDDS in cells for LH	315
Figure 8.18	Comparative dot plot showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for AM	317
Figure 8.19	Mean fluorescence intensity graph showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for AM	318

Figure 8.20	Histogram showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for AM	319
Figure 8.21	Mean fluorescence Intensity plot of dye solution, Coumarin-6 loaded SLN and Coumarin-6 loaded SMEDDS for AM	320
Figure 8.22	Comparative dot plot showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for LH	321
Figure 8.23	Mean fluorescent intensity graphs showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for LH	322
Figure 8.24	Histogram showing uptake of Coumarin-6 solution, Coumarin-6 loaded SLNs, and Coumarin-6 loaded SMEDDS at 1 h (a,c,e) and 4 h (b,d,f) in Caco-2 cells for LH	323
Figure 8.25	Mean fluorescence Intensity of dye solution, Coumarin-6 loaded SLN and Coumarin-6 loaded SMEDDS for LH	324
Figure 8.26	Intracellular uptake of SLNs and Drug suspension in presence of specific inhibitors	325
Figure 9.1	Plasma concentration vs time profile after oral administration of AM-SLN and AM suspension	341
Figure 9.2	Plasma concentration vs time profile after oral administration of LH-SLN and LH suspension	343
Figure 9.3	Plasma concentration vs time profile after oral administration of AM-SMEDDS and AM suspension	345
Figure 9.4	Plasma concentration vs time profile after oral administration of LH-SMEDDS and LH suspension	346
Figure 9.5	Plasma concentration vs time profile after oral administration of AM-SLNs to cycloheximide treated and non-treated (control) rats	348
Figure 9.6	Plasma concentration vs time profile after oral administration of AM-SMEDDS to cycloheximide treated and non-treated (control) rats	349

Figure 9.7	Plasma concentration vs time profile after oral administration of LH-SLNs to cycloheximide treated and non-treated (control) rats	350
Figure 9.8	Plasma concentration vs time profile after oral administration of LH-SMEDDS to cycloheximide treated and non-treated (control) rats	350
Figure 9.9	Cataleptic behavior of rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM-SLNs (f) LH-SLNs (g) AM-SMEDDS (h) LH-SMEDDS	352
Figure 9.10	Motor coordination study in rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM SLN (f) LH SLN (g) AM SMEDDS (h) LH SMEDDS	353
Figure 9.11	Nootropic study in rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM SLN (f) LH SLN (g) AM SMEDDS (h) LH SMEDDS	354
Figure 9.12	Behavioral parameter showing locomotion score in rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM-SLNs (f) LH-SLNs (g) AM-SMEDDS (h) LH-SMEDDS	355
Figure 9.13	Behavioral parameter showing Stereotypy score in rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM-SLNs (f) LH-SLNs (g) AM-SMEDDS (h) LH-SMEDDS	355
Figure 9.14	Behavioral parameter showing Ataxia in rats treated with (a) saline (b) MK-801 (c) AM suspension (d) LH suspension (e) AM-SLNs (f) LH-SLNs (g) AM-MEDDS (h) LH-SMEDDS	356