Figure No.	Title	Page No.
2.1	Barriers to brain delivery	17
2.2	Efflux transporters at Blood Brain Barrier	19
2.3	Transport routes across the Blood Brain Barrier	21
2.4	Schematic representation of the transferrin receptors	29
2.5	Structure of human transferring	30
2.6	TfR internalization upon binding of Tf to its receptors	31
2.7	Techniques to characterize Nanoparticles	38
2.8	Possible Transport pathways: nasal mucosa to brain/CNS	42
2.9	Critical physicochemical factors need to be considered prior to designing intranasal drug delivery systems	44
2.10	O/W type, W/O type and bicontinuous microemulsion	45
2.11	Different regions of phase diagrams	48
2.12	Ternary systems	48
3.1	Regressed calibration curve for estimation of TMD in acetonitrile	80
3.2	Regressed calibration curve for estimation of TMD in methanol	82
3.3	Regressed calibration curve for estimation of TMD in PBS pH 5 with 2% Tween-80	85
3.4	Regressed calibration curve for estimation of LTG in acetonitrile	88
3.5	Regressed calibration curve for estimation of LTG in methanol	90
3.6	Regressed calibration curve for estimation of LTG in PBS pH 5 with 1% SLS	93
3.7	Regressed calibration curve for estimation of residual PVA in water	96
3.8	Regressed calibration curve of Tf and Lf by BCA method	97
4.1	Schematic representation of the nanoprecipitation process	103
4.2	Schematic diagram of conjugation of Tf/Lf to nanoparticle surface	106
4.3	Schematic diagram for the method of preparation of NPs	112
4.4	Contour plots of TMD-NPs: Effect of polymer concentration (X_2) and volume of organic phase (X_3) on PS	121
4.5	Response surface plots of TMD-NPs: Effect of polymer concentration (X_2) and volume of organic phase (X_3) on PS	122
4.6	Contour plots of LTG-NPs: Effect of polymer concentration (X_2) and volume of organic phase (X_3) on PS	123
4.7	Response surface plots of LTG-NPs: Effect of polymer concentration (X_2) and volume of organic phase (X_3) on PS	124
4.8	Overlay of contour plots of PS and EE for TMD-NPs at 0 level of stabilizer concentration (X_1)	125
4.9	Overlay of contour plots of PS and EE for LTG-NPs at 0 level of stabilizer concentration (X_1)	125

LIST OF FIGURES

-		Influence of the concentration of the activating agent SR-4GL on Tf/Lf density	
	4.10	and PS of TMD-NPs (A) Tf-TMD-NPs (B) Lf-TMD-NPs	132
	4.11	Influence of the Tf/Lf concentration on Tf/Lf density and PS of TMD-NPs (A) Tf-TMD-NPs (B) Lf-TMD-NPs	132
,	4.12	Influence of the concentration of the activating agent SR-4GL on Tf/Lf density and PS of LTG-NPs (A) Tf-LTG-NPs (B) Lf-LTG-NPs	133
	4.13	Influence of the Tf/Lf concentration on Tf/Lf density and PS of LTG-NPs (A) Tf-LTG-NPs (B) Lf-LTG-NPs	13:
	4.14	¹ H-NMR of (A) Tf -TMD-NPs and (B) Lf-TMD-NPs	13
	4.15	¹ H-NMR of (A) Tf -LTG-NPs and (B) Lf-LTG-NPs	13
	4.16	Effect of different lyoprotectants and its concentration on the particle size and redispersibility of TMD-NPs	13
	4.17	TEM images of (A) TMD-NPs, (B) Lf-TMD-NPs and (C) Tf-TMD-NPs.	14
	4.18	TEM images of (A) LTG-NPs, (B) Lf-LTG-NPs and (C) Tf-LTG-NPs	14
	4.19	DSC thermogram of (A) TMD-NPs (B) TMD (C) PLGA and (D) PVA.	14
	4.20	DSC thermogram of (A) LTG-NPs (B) LTG (C) PLGA and (D) PVA	14
	4.21	In vitro release profile of TMD from conjugated and unconjugated NPs	14
	4.22	In vitro release profile of LTG from conjugated and unconjugated NPs	14
	5.1	Phase diagram of TME with varying surfactant: cosurfactant ratio (A) 1:1 (B) 2:1 (C) 3:1	16
	5.2	Phase diagram of LME with varying surfactant: cosurfactant ratio (A) 1:1 (B) 2:1 (C) 3:1 (D) 4:1	16
	5.3	TEM image of (A) TME (B) TNE	17
	5.4	TEM image of (A) LME (B) LNE	17
	5.5	In vitro release profile of TMD from TS, TME and TNE	17
	5.6	In vitro release profile of LTG from LS, LME and LNE	17
	5.7	Optical images of nasal mucosa treated with emulsion formulations	17
	6.1	Comparison of PS at initial and different stability conditions of formulations (Tf-TMD-NPs and Lf-TMD-NPs)	18
	6.2	Comparison of ZP at initial and different stability conditions of formulations (Tf-TMD-NPs and Lf-TMD-NPs)	18
	6.3	Comparative release profile of Tf-TMD-NPs after 6M at $5^{\circ}C \pm 3^{\circ}C$	18
	6.4	Comparative release profile of Lf-TMD-NPs after 6M at $5^{\circ}C \pm 3^{\circ}C$	18
	6.5	Comparison of PS at initial and different stability conditions of formulations (Tf-LTG-NPs and Lf-LTG-NPs)	19
	6.6	Comparison of ZP at initial and different stability conditions of formulations (Tf-LTG-NPs and Lf-LTG-NPs)	19
	6.7	Comparative release profile of Tf-LTG-NPs after 6M at $5^{\circ}C \pm 3^{\circ}C$	19
	6.8	Comparative release profile of Lf-LTG-NPs after 6M at $5^{\circ}C \pm 3^{\circ}C$	19
	6.9	Comparison of GS at initial and different stability conditions of formulations	19

	(TME and LME)	
•	Comparison of ZP at initial and different stability conditions of formulations	
6.10	(TME and LME)	194
6.11	Comparison of GS at initial and different stability conditions of formulations	195
0.11	(TNE and LNE)	195
6.12	Comparison of ZP at initial and different stability conditions of formulations (TNE and LNE)	196
7.1	Influence of the Amount of Stannous Chloride on the Labelling Efficiency of TMDS and TMD-NPs formulations	205
7.2	Influence of the Amount of Stannous Chloride on the Labelling Efficiency of LTGS and LTG-NPs formulations	207
7.3	Influence of the Amount of Stannous Chloride on the Labelling Efficiency of TS, TME and TNE	210
7.4	Influence of the Amount of Stannous Chloride on the Labelling Efficiency of LS, LME and LNE	212
8.1	Pharmacokinetic profiles of ^{99m} Tc labelled TMDS and TMD NPs formulations in blood	221
8.2	Distribution of ^{99m} Tc labelled TMDS and TMD NPs formulations in brain	221
8.3	Distribution of ^{99m} Tc labelled TMDS and TMD NPs formulations in (A) Liver (B) Spleen (C) Kidney (D) Heart (E) Lung	222
8.4	Distribution of ^{99m} Tc labelled LTGS and LTG NPs formulations in blood	226
8.5	Pharmacokinetic profiles of ^{99m} Tc labelled LTGS and LTG NPs formulations in brain	226
8.6	Distribution of ^{99m} Tc labelled LTGS and LTG NPs formulations in (A) Liver (B) Spleen (C) Kidney (D) Heart (E) Lung	227
8.7	Gamma Scintigraphy image of mice after 2 h of iv administration of (A) TMDS (B) Tf-TMD-NPs (C) Lf-TMD-NPs.	229
8.8	Pharmacokinetic profiles of ^{99m} Tc labelled TS, TME and TNE in blood	235
8.9	Distribution of ^{99m} Tc labelled TS, TME and TNE in brain	235
8.10	Distribution of ^{99m} Tc labelled TS, TME and TNE in (A) Liver (B) Spleen (C) Kidney (D) Lung (E) Stomach (F) Intestine	236
8.11	Pharmacokinetic profiles of ^{99m} Tc labelled LS, LME and LNE in blood	240
8.12	Distribution of ^{99m} Tc labelled LS, LME and LNE in brain	240
8.13	Distribution of ^{99m} Tc labelled LS, LME and LNE in various organs (Å) Liver (B) Spleen (C) Kidney (D) Lung (E) Stomach (F) Intestine	241
9.1	Influence on paw withdrawal latency measured in hot plate test by i.v. administration of TMDS, TMD-NPs, Tf-TMD-NPs and Lf-TMD-NPs in mice	253
9.2	Antinociceptive effect exerted by i.v. administration of TMDS, TMD-NPs, Tf- TMD-NPs and Lf-TMD-NPs in mice.	254

9.3	Influence on paw withdrawal latency measured in hot plate test by TS_{iv} , TS_{in} ,	255
2.5	TME and TNE in mice	200
		-
9.4	Antinociceptive effect exerted by administration of TS_{iv} , TS_{in} , TME and TNE in	256
	mice	
9.5	Time course of thermal hyperalgesia in control, sham operated and neuropathic	256
	mice (PSI).	
9.6	Influence on paw withdrawal latency measured in hot plate test by i.v.	258
7.0	administration of LTGS, LTG-NPs, Tf-LTG-NPs and Lf-LTG-NPs in rats	250
9.7	Antinociceptive effect exerted by i.v. administration of LTGS, LTG-NPs, Tf-	258
	LTG-NPs and Lf-LTG-NP in rats	
9.8	Influence on paw withdrawal latency measured in hot plate test by LSiv, LSin,	259
	LME and LNE in rats	
9.9	Antinociceptive effect exerted by administration of LSiv, LSin, LME and LNE	250
	in rats	259