LIST OF FIGURES

Figure No.	Figure Caption	Page No.
Chapter 2: Literature Review		
2.1	Airflow Limitation in Asthma and COPD	17
2.2	Production of brain-derived neurotrophic factor (BDNF)	20
2.3	Neurotrophins and their receptors	20
2.4	BDNF signalling	20
2.5	RNA interference mechanism	25
2.6	Intracellular and extracellular barriers in pulmonary delivery	29
2.7	siRNA therapeutics delivery via pulmonary route	30
2.8	Particles depositions mechanism in pulmonary delivery	33
Chapter 3: siRNA Profiling and Analytical Method Development		
3.1	Genomic regions detail of brain derived neurotrophic factor (Mus musculus (house mouse))	63
3.2	siRNA concentration estimation by Nanodrop UV spectrophotometer	65
3.3	Known concentration of siRNA Vs Nanodrop concentration correlation	65
3.4	Estimation of minimum quantity of siRNA by gel retardation assay	68
3.5	Determination of Quantifiable range of siRNA	69
3.6	Gel electrophoresis band densities at different siRNA concentrations	69
3.7	Calibration curve of siRNA gel retardation	70
3.8	Accuracy and precision of gel electrophoresis method for siRNA quantification	71
Chapter 4: Development of Chitosan based non viral Vectors		
4.1	Synthesis steps of N,N,N-Trimethylated chitosan	75
4.2	Reaction of TNBS with a primary amine containing molecule to produce a chromogenic derivative	79
4.3	^{1}H-NMR spectrum of Trimethylated chitosan-1 (TMC-1)	81
4.4	^{1}H-NMR spectrum of Trimethylated chitosan-2 (TMC-2)	82

4.5	^{1}H-NMR spectrum of Trimethylated chitosan-3 (TMC-3)	82
4.6	^{1}H-NMR spectrum of Trimethylated chitosan-4 (TMC-4)	83
4.7	FTIR spectrum of Trimethylated chitosan-1	84
4.8	FTIR spectrum of Trimethylated chitosan-2	84
4.9	FTIR spectrum of chitosan	85
4.10	Plot of Degree of quarterisation Vs. reaction time	86
4.11	Solubility profile of Trimethylated chitosan with different DOQ	87
4.12	*In vitro* cytotoxicity MTT assay of Trimethylated chitosans	88
4.13	^{1}H-NMR spectrum of the Urocanic acid conjugated TMC-31	89
4.14	^{1}H-NMR spectrum of the Piperazine 2-carboxylic acid conjugated TMC-31	90
4.15	^{1}H-NMR spectrum of the 3- Pyridyl acetic acid conjugated TMC-31	90
4.16	FTIR spectrum of Urocanic acid conjugated tmc-31	91
4.17	FTIR spectrum of Piperazine 2-carboxylic acid conjugated TMC-31	91
4.18	FTIR spectrum of 3- Pyridyl acetic acid conjugated TMC-31	92
4.19	Degree of conjugation of heterocyclic moieties on TMC	93
4.20	Acid/base titration of different modified TMCs	94
4.21	% Haemolysis of different modified TMCs	95
4.22	Erythrocyte aggregations by different modified TMCs	98
4.23	Cell viability of modified TMCs	99
Chapter 5: Development of Polyethylenimine based non viral vectors		
5.1	^{1}H-NMR spectrum of Urocanic acid conjugated Polyethylenimine	107
5.2	^{1}H-NMR spectrum of Unmodified 25kDa branched Polyethylenimine	108
5.3	FTIR spectrum of Polyethylenimine	109
5.4	FTIR spectrum of Urocanic acid conjugated Polyethylenimine (PEI-UA)	109
5.5	UV spectra of calibration for TNBS assay	110
5.6	Acid/base titration of modified Polyethylenimines	112
5.7	% Haemolysis of different modified Polyethylenimines	113

5.8	Erythrocyte aggregations by (a) PEI (b)PEI-UAA(c) PEI-UAB(d) PEI-UAC	114
5.9	Cell viability of different modified PEIs	115
Chapter 6: Formulation Development and Characterization		
6.1	Gel electrophoresis of siRNA-TMC	131
6.2	Gel electrophoresis of siRNA-TMC-UAA	131
6.3	Gel electrophoresis of siRNA-TMC-UAB	132
6.4	Gel electrophoresis of siRNA-TMC-UAC	132
6.5	Gel electrophoresis of siRNA-TMC-PCA	132
6.6	Gel electrophoresis of siRNA-TMC-PCB	133
6.7	Gel electrophoresis of siRNA-TMC-PCC	133
6.8	Gel electrophoresis of siRNA-TMC-PAA	133
6.9	Gel electrophoresis of siRNA-TMC-PAB	134
6.10	Gel electrophoresis of siRNA-TMC-PAC	134
6.11	Gel electrophoresis of siRNA-bPEI	134
6.12	Gel electrophoresis of siRNA-PEI-UAA	135
6.13	Gel electrophoresis of siRNA-PEI-UAB	135
6.14	Gel electrophoresis of siRNA-PEI-UAC	135
6.15	siRNA integration after complexation	137
6.16	siRNA integration after complexation	137
6.17 (a-n)	Particle size of different polyplex formulations	142
6.18	Cytotoxicity of siRNA-TMC-UAA, siRNA-TMC-UAB and siRNA-TMC-UAC	144
6.19	Cytotoxicity of siRNA-TMC, siRNA-TMC-PCA, siRNA-TMC-PCB and siRNA-TMC-PCC	145
6.20	Cytotoxicity of siRNA-TMC-PAA, siRNA-TMC-PAB and siRNA-TMC-PAC	145
6.21	Cytotoxicity of siRNA-bPEI, siRNA-PEI-UAA, siRNA-PEI-UAB and siRNA-PEI-UAC	145

6.22	Cell uptake of (a) Naked siRNA(b) siRNA-TMC (c) siRNA-TMC-UAA(d) siRNA-TMC-UAB(e) siRNA-TMC-UAC by confocal microscopy	148
6.23	Cell uptake of (a) siRNA-TMC-PCA(b) siRNA-TMC-PCB(c) siRNA-TMC-PCC by confocal microscopy	148
6.24	Cell uptake of (a) siRNA-TMC-PAA(b) siRNA-TMC-PAB(c) siRNA-TMC-PAC by confocal microscopy	149
6.25	Cell uptake of (a)siRNA-BPEI, (b)siRNA-PEI-UAA, (c) siRNA-PEI-UAB (d) siRNA-PEI-UAC(e)L2KL by confocal microscopy	150
6.26	FACS analysis of FAM-NC-siRNA and L2KL	151
6.27	FACS analysis of siRNA-TMC-UAA, siRNA-TMC-UAB and siRNA-TMC-UAC	151
6.28	FACS analysis of siRNA-TMC-PCA, siRNA-TMC-PCB and siRNA-TMC-PCC	152
6.29	FACS analysis of siRNA-TMC-PAA, siRNA-TMC-PAB and siRNA-TMC-PAC	152
6.30	FACS analysis of siRNA-PEI-UAA, siRNA-PEI-UAB and siRNA-PEI-UAC	152
6.31	FACS analysis of siRNA-BPEI and siRNA-TMC	153
6.31(a)	Mean fluorescent intensity of different polyplexes formulations	154
6.32	Electrolyte induced flocculation of polyplexes	156
6.33	Heparin competition of siRNA-TMC-UAA	157
6.34	Heparin competition of siRNA-TMC-PCA	157
6.35	Heparin competition of siRNA-TMC-PAA	158
6.36	Heparin competition of siRNA-PEI-UAA	158
6.37	Serum stability of polyplexes	161
6.38	Stability of polyplexes in bronchoalveolar lavage fluid	162
6.39	TEM image of siRNA-TMC-UAA Polyplexes	163
6.40	TEM image of siRNA-TMC-PCA Polyplexes	163
6.41	TEM image of siRNA-TMC-PAA Polyplexes	164

6.42	TEM image of siRNA-PEI-UAA Polyplexes	164
Chapter 7: Nebulized siRNA delivery and Characterization		
7.1	Schematic representation of Twin stage apparatus	170
7.2	siRNA integrity post nebulization	173
7.3	Cell uptake of TMC, TMC-UAA, TMC-PCA, TMC-PAA, PEI and PEI-UAA based polyplexes post nebulization	174
7.4	Particle size of polyplexes at pre-nebulization and post nebulization	176
7.5	Zeta potential of polyplexes at pre-nebulization and post nebulization	176
7.6	Particle size of different polyplexes post nebulization	177
Chapter 8: Animal studies		
8.1	Gene expression (%) of BDNF mRNA in OVA induced inflammatory mice	189
8.2	Amplification plot of BDNF mRNA(green) and GAPDH (yellow)	190
8.3	Melt curve of (a) BDNF and (b) GAPDH	190
8.4	Total cell counts and differential cell counts in BALF	191
8.5	Histopathology of lung of control and after treatment with formulations	193