



LIST OF FIGURES

Fig. No.	Title	Page No.
2.1	A representative cross-section of a cerebral capillary of the BBB	13
2.2	Schematic representation of emulsion polymerization technique	31
2.3	Schematic representation of emulsion-evaporation technique	32
2.4	Schematic representation of (A) Single and (B) Double emulsion technique for preparation of nanoparticles	33
2.5	Schematic description of the proposed formulation mechanism of nanocapsules by emulsification/ solvent diffusion.	34
2.6	Schematic representation of formation of nanoparticles by solvent displacement technique	35
2.7	Pathophysiologic connection between nose and brain.	41
4.1	FTIR spectrum of Pioglitazone HCl (Standard)	117
4.2	FTIR spectrum of Pioglitazone HCl (Sample)	117
4.3	FTIR spectrum of Rosiglitazone maleate (Standard)	118
4.4	FTIR spectrum of Rosiglitazone maleate (Sample)	118
4.5	FTIR spectrum of Rosiglitazone base (Standard)	119
4.6	FTIR spectrum of Rosiglitazone base (Sample)	119
4.7	Ultraviolet absorption spectrum of Pioglitazone HCl in Methanol:Acetonitrile	120
4.8	Ultraviolet absorption spectrum of Pioglitazone HCl in Methanol:Acetonitrile:PBS (pH 7.4):0.1 N NaOH Solution	120
4.9	Ultraviolet absorption spectrum of Roseglitazone maleate in Methanol	121
4.10	Ultraviolet absorption spectrum of Rosiglitazone base in Acetonitrile:PBS (pH 7.4)	121
4.11	Linearly regressed calibration curve of Pioglitazone HCl in MeOH-ACN at $\lambda_{\max} = 268.0$ nm	122
4.12	Linearly regressed calibration curve of Pioglitazone HCl in MeOH - ACN - PBS(pH 7.4) - 0.1 N NaOH at $\lambda_{\max} = 266.0$ nm	124
4.13	Linearly regressed calibration curve of Rosiglitazone maleate in MeOH at $\lambda_{\max} = 246.8$ nm	126
4.11	Linearly regressed calibration curve of Rosiglitazone base in ACN-PBS(pH 7.4) at $\lambda_{\max} = 246.2$ nm	128
5.1	Optimization of PLGA concentration with respect to particle size and PDI	143
5.2	Optimization of PLGA concentration with respect to entrapment efficiency	143
5.3	Optimization of loading amount of drug with respect to particle	144

	size and PDI	
5.4	Optimization of loading amount of drug with respect to entrapment efficiency	144
5.5	Optimization of surfactant concentration with respect to particle size and PDI	145
5.6	Optimization of surfactant concentration with respect to entrapment efficiency	145
5.7	Optimization of PVA concentration with respect to particle size and PDI	146
5.8	Optimization of PVA concentration with respect to entrapment efficiency	146
5.9	Optimization of volume of organic phase for polymer with respect to particle size and PDI	147
5.10	Optimization of volume of organic phase for polymer with respect to entrapment efficiency	147
5.11	Optimization of volume of organic phase for drug with respect to particle size and PDI	148
5.12	Optimization of volume of organic phase for drug with respect to entrapment efficiency	148
5.13	Optimization of PLGA concentration with respect to particle size and PDI	153
5.14	Optimization of PLGA concentration with respect to entrapment efficiency	153
5.15	Optimization of loading amount of drug with respect to particle size and PDI	154
5.16	Optimization of loading amount of drug with respect to entrapment efficiency	154
5.17	Optimization of surfactant concentration with respect to particle size and PDI	155
5.18	Optimization of surfactant concentration with respect to entrapment efficiency	155
5.19	Optimization of PVA concentration with respect to particle size and PDI	156
5.20	Optimization of PVA concentration with respect to entrapment efficiency	156
5.21	Optimization of Polaxamer concentration with respect to particle size and PDI	157
5.22	Optimization of Polaxamer concentration with respect to entrapment efficiency	157
5.23	Optimization of volume of organic phase for polymer with respect to particle size and PDI	158

5.24	Optimization of volume of organic phase for polymer with respect to entrapment efficiency	158
5.25	Optimization of volume of organic phase for drug with respect to particle size and PDI for Pioglitazone	159
5.26	Optimization of volume of organic phase for drug with respect to particle size and PDI for Rosiglitazone	159
5.27	Optimization of volume of organic phase for drug with respect to entrapment efficiency of Pioglitazone	160
5.28	Optimization of volume of organic phase for drug with respect to entrapment efficiency of Rosiglitazone	160
5.29	FTIR spectrum of PIO-NP	170
5.30	FTIR spectrum of Tf-PIO-NP	170
5.31	FTIR spectrum of ROS-NP	171
5.32	FTIR spectrum of Tf-ROS-NP	171
5.33	TEM photomicrograph of PIO-NP	172
5.34	TEM photomicrograph of Tf-PIO-NP	172
5.35	TEM photomicrograph of ROS-NP	173
5.36	TEM photomicrograph of Tf-ROS-NP	173
5.37	Thermogravimetric analysis of Pioglitazone	174
5.38	Thermogravimetric analysis of Rosiglitazone	174
5.39	Thermogravimetric analysis of PLGA	175
5.40	Thermogravimetric analysis of Tf-PIO-NP	175
5.41	Thermogravimetric analysis of Tf-ROS-NP	176
5.42	X-Ray diffractogram of polymer (PLGA)	176
5.43	X-Ray diffractogram of Pioglitazone HCl	177
5.44	X-Ray diffractogram of Pioglitazone-PLGA physical mixture	177
5.45	X-Ray diffractogram of PIO-NP	178
5.46	X-Ray diffractogram of Tf-PIO-NP	178
5.47	X-Ray diffractogram of Rosiglitazone base	179
5.48	X-Ray diffractogram of Rosiglitazone-PLGA physical mixture	179
5.49	X-Ray diffractogram of ROS-NP	180
5.50	X-Ray diffractogram of Tf-ROS-NP	180
5.51	<i>In vitro</i> release profile of Pioglitazone loaded formulations	181
5.52	<i>In vitro</i> release profile of Rosiglitazone loaded formulations	181
6.1	Effect on particle size of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 5°C±2°C.	213
6.2	Effect on particle size of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 25°C±2°C & 60±5% RH.	213
6.3	Effect on PDI of optimized nanoparticulate formulations of	214

	Pioglitazone and Rosiglitazone during 6 months storage 5°C±2°C.	
6.4	Effect on PDI of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage 25°C±2°C at 60±5% RH.	214
6.5	Effect on zeta potential of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 5°C±2°C.	215
6.6	Effect on zeta potential of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 25°C±2°C & 60±5% RH.	215
6.7	Effect on drug content of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 5°C±2°C.	216
6.8	Effect on drug content of optimized nanoparticulate formulations of Pioglitazone and Rosiglitazone during 6 months storage at 25°C±2°C at 60±5% RH.	216
7.1	Cytoprotective activity of various Pioglitazone formulations (concentration equivalent to 0.5 µM, 1.25 µM and 5.0 µM) after 48 h incubation with β-Amyloid	230
7.2	Cytoprotective activity of various Rosiglitazone formulations (concentration equivalent to 0.5 µM, 1.25 µM and 5.0 µM) after 48 h incubation with β-Amyloid	230
7.3	Photomicrograph of neuro-2a cells after 48 hrs incubation with PIO-S (equivalent to 5 µM of Pioglitazone)	231
7.4	Photomicrograph of neuro-2a cells after 48 hrs incubation with PIO-NP (equivalent to 5 µM of Pioglitazone)	231
7.5	Photomicrograph of neuro-2a cells after 48 hrs incubation with Tf-PIO-NP (equivalent to 5 µM of Pioglitazone)	232
7.6	Photomicrograph of neuro-2a cells after 48 hrs incubation with ROS-NP (equivalent to 5 µM of Pioglitazone)	232
7.7	Photomicrograph of neuro-2a cells after 48 hrs incubation with ROS-NP (equivalent to 5 µM of Pioglitazone)	233
7.8	Photomicrograph of neuro-2a cells after 48 hrs incubation with Tf-ROS-NP (equivalent to 5 µM of Pioglitazone)	233
8.1	Effect of amount of stannous chloride on labeling efficiency of Pioglitazone and its nanoparticulate formulation with ^{99m} Tc	260
8.2	Effect of amount of stannous chloride on labeling efficiency of Rosiglitazone and its nanoparticulate formulation with ^{99m} Tc	260
8.3	Effect of pH on labeling efficiency of Pioglitazone and its nanoparticulate formulation with ^{99m} Tc	261

8.4	Effect of pH on labeling efficiency of Rosiglitazone and its nanoparticulate formulation with ^{99m} Tc	261
8.5	Effect of incubation time of stannous chloride on labeling efficiency of Pioglitazone and its nanoparticulate formulation with ^{99m} Tc	262
8.6	Effect of incubation time of stannous chloride on labeling efficiency of Rosiglitazone and its nanoparticulate formulation with ^{99m} Tc	262
8.7	Biodistribution of PIO-D (oral)	263
8.8	Biodistribution of PIO-S (nasal)	263
8.9	Biodistribution of PIO-NP (i.v.)	264
8.10	Biodistribution of Tf-PIO-NP (i.v.)	264
8.11	Biodistribution of different Pioglitazone formulations in brain	265
8.12	Biodistribution of ROS-S (oral)	265
8.13	Biodistribution of ROS-S (nasal)	266
8.14	Biodistribution of ROS-S (i.v.)	266
8.15	Biodistribution of ROS-NP (i.v.)	267
8.16	Biodistribution of Tf-ROS-NP (i.v.)	267
8.17	Biodistribution of different Rosiglitazone formulations in brain	268
8.18	Gamma Scintigraphs of swiss albino mice after administration of radiolabeled formulations at 30 min	269
8.19	Gamma Scintigraphs of swiss albino mice after administration of radiolabeled formulations at 1 Hr	270
8.20	Gamma Scintigraphs of swiss albino mice after administration of radiolabeled formulations at 2 Hr	271
8.21	Gamma Scintigraphs of swiss albino mice after administration of radiolabeled formulations at 6 Hr	272



LIST OF INSTRUMENTS USED

Instrument	Company
Refrigerated centrifuge	Sigma 3K30 refrigerated high speed laboratory centrifuge; Sigma Instruments, Osterode, Germany
Zetasizer	Malvern Zetasizer 3000 HS _A Nanoseries Nano-ZS (Malvern Instruments Ltd, Worcestershire, UK)
Thermogravimetric Analyzer	Exstar TG/DTA 6300
pH meter	LabIndia PICO ⁺ pH meter
Vortex mixer	Spinix Vortex mixer
Lyophilizer	DW1, 0-60E, Heto Dry Winner, Denmark
Spectrophotometer	680 XR BioRad France
Probe Sonicator	Sartorius Labsonic [®] M Probe Sonicator
Microplate Reader	ELISA plate reader BioRad, 680 XR
Vacuum Pump	Vacuum Pump F16, Bharat Vacuum Pumps, Bangalore
Bath Sonicator	Bath Sonicator, DTC 503, Ultra Sonics
Oven	Stability Oven, Shree Kailash Industries, Vadodara
Analytical Balance	Analytical Balance – AX 120, EL 8300, Shimadzu Corporation, Japan
Transmission Electron Microscope	Philips – Morgagni 268-D, Netherland
X-Ray Diffractometer	Shimadzu XRD-6000, Japan
Inverted Microscope	Olympus CKX-41 Inverted Microscope, Camera – DP12 fitted with adaptor
Rotary vacuum evaporator	Buchi, German
UV-Vis Spectrophotometer	Shimadzu UV 1601; Shimadzu, Kyoto, Japan UV-1700 PharmaSpec
FTIR	Bruker Alpha T FTIR
Magnetic Stirrer	Spectralab Whirlmatic Mega Stirrer