

List of Figures

Figure No.	Title	Page No.
2.1	Types of block copolymers	10
2.2	Schematic diagrams of functionalized polymer micelles with active targeting to tumors and responsive drug release properties	14
3.1	Wavelength scan of ETO in ACN at concentration of 20 µg/ml	40
3.2	Regressed calibration curve of ETO in ACN	41
3.3	Regressed calibration curve of ETO in PBS pH 7.4	42
3.4	Typical chromatogram of cell lysis solution spiked with ETO along with internal standard (diazepam)	45
3.5	Regressed calibration curve of ETO in cell lysate	46
3.6	Regressed calibration curve of CH ₃ O-PEG-OH (M.W. 2000) at λ 525 nm	49
3.7	Regressed calibration curve of CH ₃ O-PEG-OH (M.W. 5000) at λ 525 nm	50
3.8	Regressed calibration curve of YIGSR-NH ₂ at λ 345 nm	52
3.9	Regressed calibration curve of EILDV-NH ₂ at λ 345 nm	52
4.1	Schematic representation of synthesis of PEG-PCL copolymer	56
4.2	Synthetic scheme of synthesis of MPEG-PCL di-block copolymer	56
4.3	Chemical structure of MPEG-PCL block copolymer	60
4.4	¹ H NMR spectrum of BCP 2-2 di-block copolymer	60
4.5	¹ H NMR spectrum of BCP 2-3.5 di-block copolymer	61
4.6	¹ H NMR spectrum of BCP 2-5 di-block copolymer	61
4.7	¹ H NMR spectrum of BCP 5-5 di-block copolymer	62
4.8	¹ H NMR spectrum of BCP 5-7 di-block copolymer	62
4.9	¹ H NMR spectrum of BCP 5-10 di-block copolymer	63
4.10	¹ H NMR spectrum of FBCP 2-3.5 di-block copolymer	63
4.11	¹ H NMR spectrum of FBCP 5-7 di-block copolymer	64
4.12	GPC chromatogram of BCP 2-2, BCP 2-3.5 and BCP 2-5 di-block copolymer	65

4.13	GPC chromatogram of BCP 5-5, BCP 5-7 and BCP 5-10 di-block copolymer	65
4.14	GPC chromatogram of FBCP 2-3.5 and FBCP 5-7 di-block copolymer	66
4.15	FTIR spectrum of BCP 2-2 di-block copolymer	67
4.16	FTIR spectrum of BCP 2-3.5 di-block copolymer	67
4.17	FTIR spectrum of BCP 2-5 di-block copolymer	68
4.18	FTIR spectrum of BCP 5-5 di-block copolymer	68
4.19	FTIR spectrum of BCP 5-7 di-block copolymer	69
4.20	FTIR spectrum of BCP 5-10 di-block copolymer	69
4.21	FTIR spectrum of FBCP 2-3.5 di-block copolymer	70
4.22	FTIR spectrum of FBCP 5-7 di-block copolymer	70
5.1	Effect of stirring speed on particle size and percent drug entrapment of MPCL micelles	81
5.2	Effect of rate of addition of organic solvent to aqueous phase on particle size and drug entrapment of MPCL micelles	82
5.3	Influence of ratio of drug to polymer on particle size and percent drug entrapment of MPCL220, MPCL235 and MPCL250 micelles	84
5.4	Influence of ratio of drug to polymer on particle size and percent drug entrapment of MPCL550, MPCL570 and MPCL5100 micelles	84
5.5	Influence of ratio of aqueous to organic phase on particle size and percent drug entrapment of MPCL220, MPCL235 and MPCL250 micelles	88
5.6	Influence of ratio of aqueous to organic phase on particle size and percent drug entrapment of MPCL550, MPCL570 and MPCL5100 micelles	88
5.7	Maximum practical percent drug loading achieved in various MPCL micelles	92
5.8	Typical particle size distributions of ETO loaded MPCL235 micelles	92
5.9	Zeta potential of ETO loaded MPCL 235 micelles	93
5.10	Excitation spectra of pyrene as a function of MPCL 250 micelle concentration in water at room temperature	94

5.11	Plot of I_{338}/I_{335} (from pyrene excitation spectra) vs log C for MPCL220, MPCL235 and MPCL250 micelles	96
5.12	Plot of I_{338}/I_{335} (from pyrene excitation spectra) vs log C for MPCL550, MPCL570 and MPCL5100 micelles	96
5.13	Natural log of zeta potential vs. K of MPCL220, MPCL235 and MPCL250 micelles with and without drug	99
5.14	Natural log of zeta potential vs. K of MPCL220, MPCL235 and MPCL250 micelles with and without drug	100
5.15	Influence of serum proteins on block co-polymeric micelles as drug delivery systems	101
5.16	Effect on particle size of MPCL220, MPCL235 and MPCL250 micelles after incubation in presence and absence of BSA	104
5.17	Effect on particle size of MPCL550, MPCL570 and MPCL5100 micelles after incubation in presence and absence of BSA	104
5.18	Percent hemolysis ETO injection and placebo injections (ETO) after 30 min of incubation with erythrocyte dispersion	109
5.19	Percent hemolysis MPCL micelles after 30 min, 4 h and 24 h of incubation with erythrocyte dispersion	109
6.1	Differential scanning calorimetry thermograms of pure ETO and ETO loaded MPCL 235 and MPCL 570 micelles	125
6.2	Powder X-ray diffraction patterns of ETO and ETO loaded MPCL 235 and MPCL 570 micelles	126
6.3	TEM images of MPCL235 micelles after negative staining with 1% uranyl acetate	127
6.4	TEM images of MPCL570 micelles after negative staining with 1% uranyl acetate	127
6.5	Redispersibility index of micellar formulations at various weight ratios of total solid content to sucrose	129
6.6	Redispersibility index of micellar formulations at various weight ratios of total solid content to trehalose	130
6.7	Redispersibility index of micellar formulations using various ratio of total solid content to sucrose and poloxamer-188	133

6.8	<i>In vitro</i> release study profile of MPCL235, YPCL235 and EPCL235 micelles in PBS pH 7.4	135
6.9	<i>In vitro</i> release study profile of MPCL570, YPCL570 and EPCL570 micelles in PBS pH 7.4	136
7.1	Cell viability of B16F10 cells with ETO, MPCL235, YPCL235 and EPCL235 formulation after 24 h incubation period	150
7.2	Cell viability of B16F10 cells with ETO, MPCL570, YPCL570 and EPCL570 formulation after 24 h incubation period	151
7.3	Cell viability of B16F10 cells with ETO, MPCL235, YPCL235 and EPCL235 formulation after 48 h incubation period	152
7.4	Cell viability of B16F10 cells with ETO, MPCL570, YPCL570 and EPCL570 formulation after 48 h incubation period	153
7.5	Cell viability of B16F10 cells with ETO, MPCL 235, YPCL 235 and EPCL 235 formulation after 72 h incubation period	156
7.6	Cell viability of B16F10 cells with ETO, MPCL 570, YPCL 570 and EPCL 570 formulation after 72 hr incubation period	157
7.7	Cell viability of B16F10 cells after treatment with MPCL235-P for various time point incubation	158
7.8	Cell viability of B16F10 cells after treatment with MPCL570-P for various time point incubation	159
7.9	Morphological changes of B16F10 cells after treatment with ETO and untreated control (UC)	162
7.10	Morphological changes of B16F10 cells after treatment with MPCL 235 and YPCL235	163
7.11	Morphological changes of B16F10 cells after treatment with YPCL 235 and EPCL 235	164
7.12	Morphological changes of B16F10 cells after treatment with MPCL 570 and YPCL 570	165
7.13	Morphological changes of B16F10 cells after treatment with YPCL570 and EPCL570	166
7.14	Morphological changes of B16F10 cells after treatment with MPCL235-P and MPCL570- P	167
7.15	Typical images of colony formation	168

7.16	Percent colony inhibition of B16F10 cells after treatment with two subtoxic doses of ETO, MPCL235, YPCL235, EPCL235 and MPCL235-P-A	170
7.17	Percent colony inhibition of B16F10 cells after treatment with two subtoxic doses of ETO, MPCL570, YPCL570, EPCL570 and MPCL570-P-A	170
7.18	Microscopic wound images of Zero hr reference plate, Untreated control and Plain ETO-A	172
7.19	Microscopic wound images of MPCL235-A, YPCL235-A, EPCL235-A and MPCL235-P-A	172
7.20	Microscopic wound images of MPCL570-A, YPCL570-A, EPCL570-A and MPCL570-P-A	173
7.21	Percent cell migration of B16F10 cells treated with ETO, MPCL235, YPCL235, EPCL235 and MPCL235-P	173
7.22	Percent cell migration of B16F10 cells treated with ETO, MPCL570, YPCL570, EPCL570 and MPCL570-P	174
7.23	Percent cell adhesion of B16F10 cells after treatment with micellar formulations to YIGSR-NH ₂ coated plate	176
7.24	Percent cell adhesion of B16F10 cells after treatment with micellar formulations to EILDV-NH ₂ coated plate	177
7.25	Confocal fluorescence images of MPCL235, YPCL235 and EPCL235 micelles after incubation of 1 and 3 h	179
7.26	Confocal fluorescence images of MPCL570, YPCL570 and EPCL570 micelles after incubation of 1 and 3 h	180
7.27	Percent cellular uptake of ETO, MPCL235, YPCL235 and EPCL235	182
7.28	Percent cellular uptake of ETO, MPCL570, YPCL570 and EPCL570 micelles	182
7.29	Cell cycle analysis of untreated control and ETO treated B16F10 cells	185
7.30	Cell cycle analysis of B16F10 cells after treatment with MPCL235, YPCL235 and EPCL235 micelles	185

7.31	Cell cycle analysis of B16F10 cells after treatment with MPCL570, YPCL570 and EPCL570 micelles	186
7.32	Cell cycle analysis of B16F10 cells after treatment with MPCL235-P and MPCL570-P micelles	186
8.1	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in blood of EAT tumor bearing mice after i.v. administration	205
8.2	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in liver of EAT tumor bearing mice after i.v. administration	206
8.3	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in spleen of EAT tumor bearing mice after i.v. administration	206
8.4	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in lung of EAT tumor bearing mice after i.v. administration	208
8.5	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in kidney of EAT tumor bearing mice after i.v. administration	208
8.6	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in heart of EAT tumor bearing mice after i.v. administration	210
8.7	Biodistribution profile of ^{99m} Tc labeled ETO and micellar formulations in tumor of EAT tumor bearing mice after i.v. administration	210
8.8	Effect of <i>in vitro</i> ETO and ETO loaded micelles treated B16F10 cells on inhibition of nodule formation in C57BL/6 mice	212
8.9	Appearance of lungs after 21 st day of invitro treated B16F10 cells inoculation	214
8.10	Effect of intravenous treatment of ETO and ETO loaded micellar formulations on inhibition of pulmonary metastatic nodule formation of B16F10 cells inoculated mice	215

8.11	Appearance of lungs after 21 st day of B16F10 cells inoculations followed by intravenous treatment of formulations	217
8.12	Histopathological studies of lung tissues showing reduction in tumor islands by invitro treated B16F10 cells with various formulations (Pre-treatment)	218
8.13	Histopathological studies of lung tissues showing reduction in tumor islands by invitro treated B16F10 cells with various formulations (Post-treatment)	219