Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Synthesis and Biological Evaluation of Dual Functionalized Glutathione Sensitive Poly(Ester-Urethane) Multiblock Polymeric Nanoparticles for Cancer Targeted Drug Delivery

Arun Kumar,[a,b] *Shantanu V. Lale,*[a,b] *Farhat Naz,*[c] *Veena Choudhary*[d] *and Veena Koul*[a,b*]

[a] Centre for Biomedical Engineering, Indian Institute of Technology Delhi, New Delhi 110016, India

[b] Biomedical Engineering Unit, All India Institute of Medical Sciences (AIIMS), New Delhi 110029, India

[c] Department of Pathology, All India Institute of Medical Sciences (AIIMS), New Delhi 110029, India

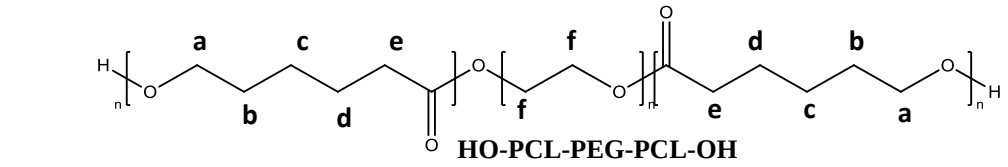
[d] Centre for Polymer Science and Engineering, Indian Institute of Technology Delhi, New Delhi 110016, India

[*]Corresponding author

Tel: +91 1126591041

E-mail: veenak_iitd@yahoo.com

[1]H NMR Tri block copolymer HO-PCL-PEG-PCL-OH



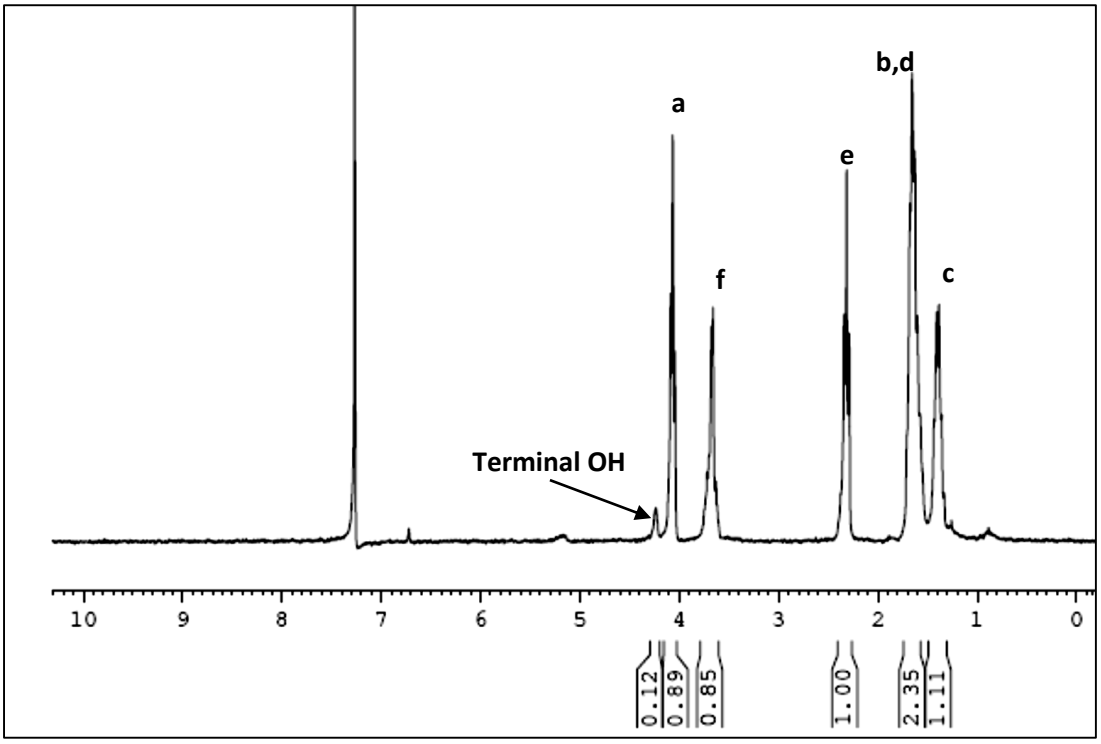
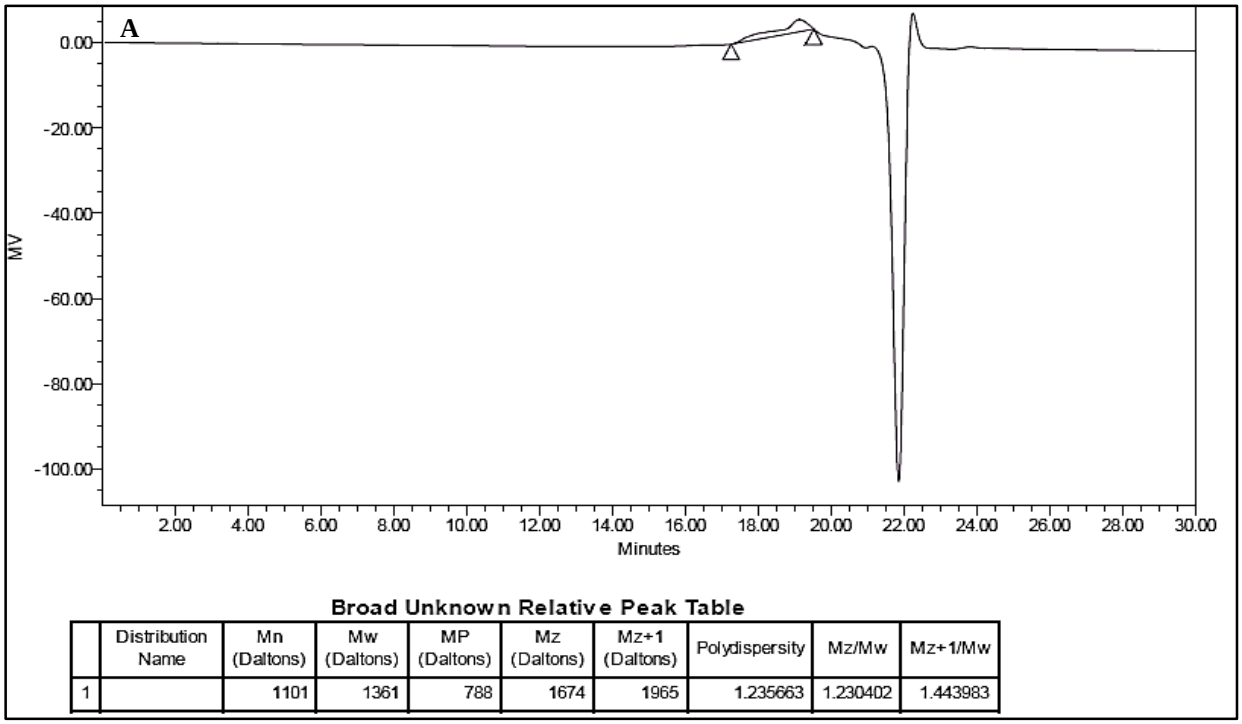


Figure S1. [1]H NMR Spectrum of HO-PCL-PEG-PCL-OH triblock copolymer

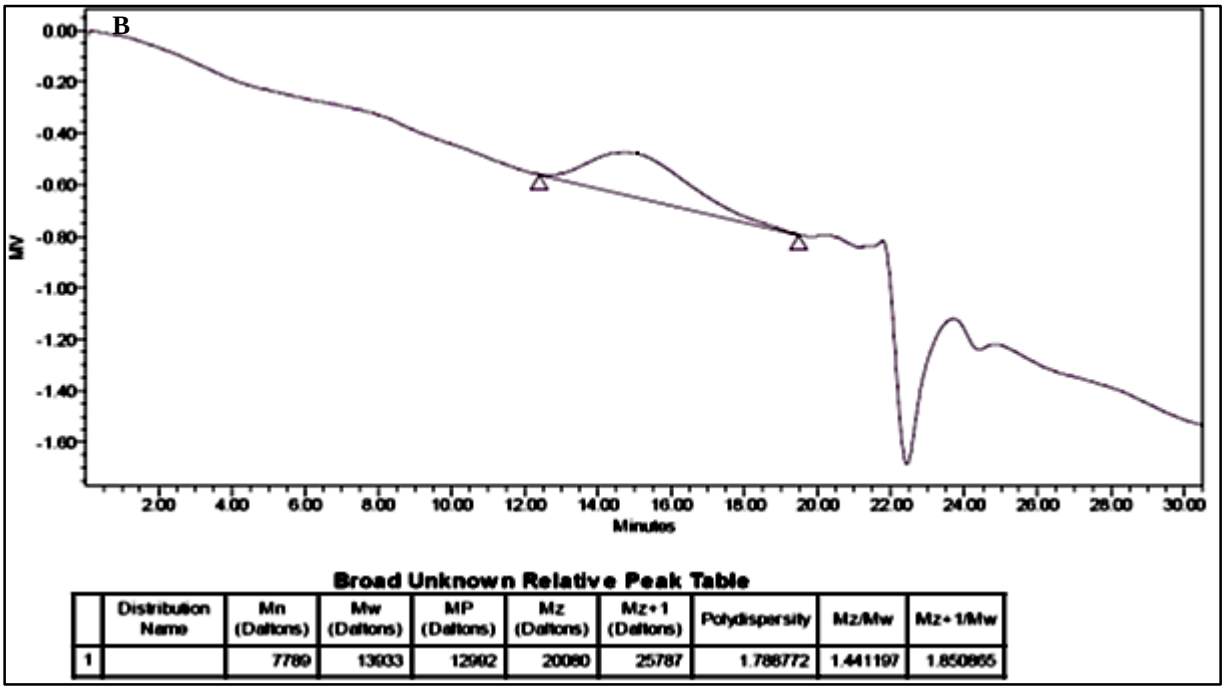
[1]H NMR (300 MHz, $CDCl_3$, δ (ppm) – 1.34-1.41 (m,-OCH_2CH_2***CH_2***CH_2CH_2CO-), 1.60-1.67 (m, OCH_2***CH_2***CH_2***CH_2***CH_2CO-), 2.29-2.34 (t, $OCH_2CH_2CH_2CH_2$***CH_2***CO-), 3.63-3.72 (-OCH_2-CH_2-O, PEG unit), 4.04-4.09 (t, -O***CH_2***$CH_2CH_2CH_2CH_2CO$-), 4.24 (t, -***CH_2***OH) terminal OH groups of polycaprolactone.

M_n (GPC) = 1101 Da; molecular weight distribution (MWD) 1.24.



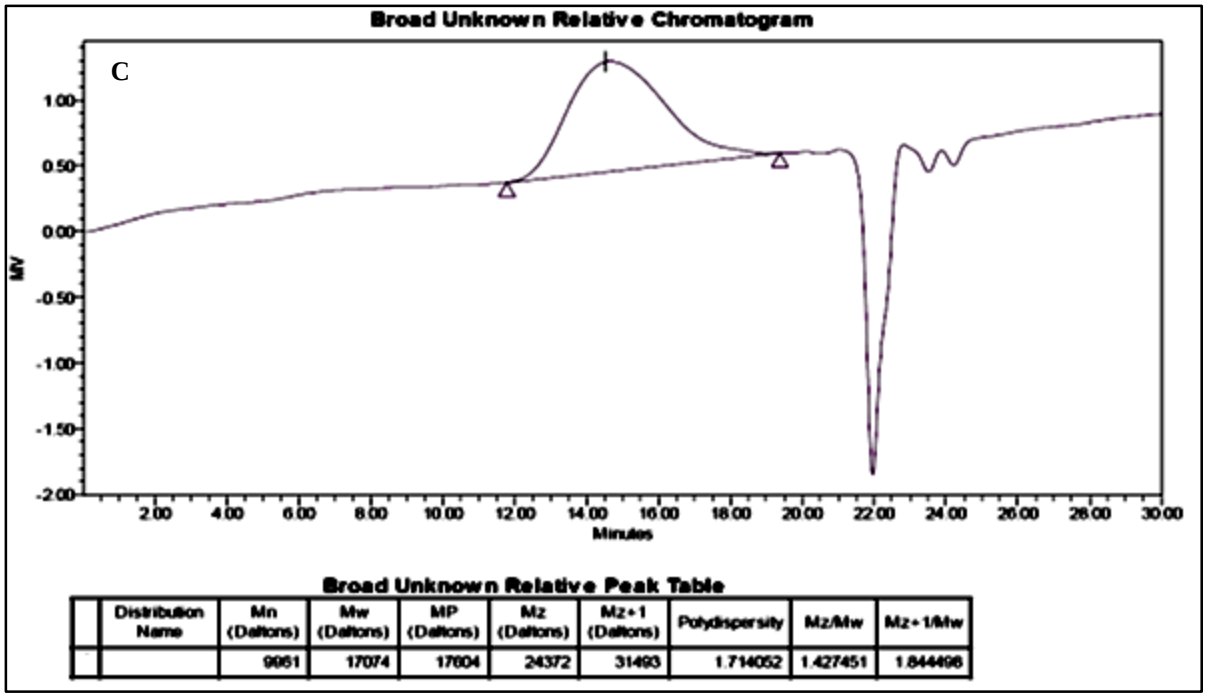
Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
1		1101	1361	788	1674	1965	1.235663	1.230402	1.443983



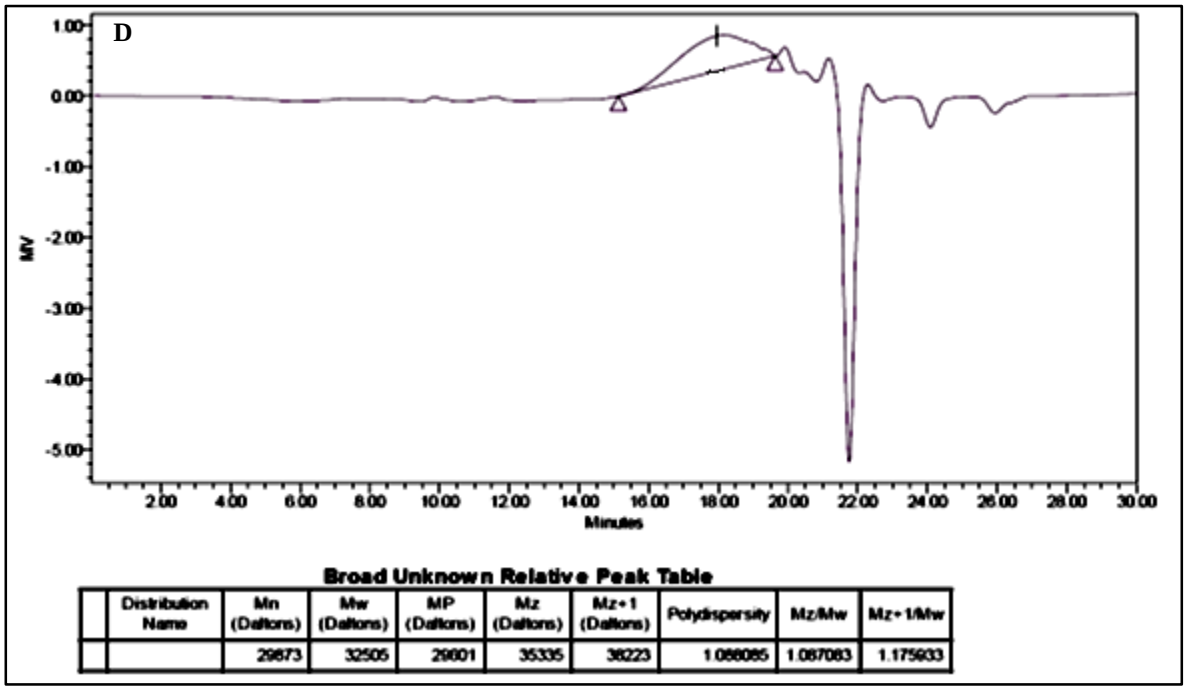
Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
1		7789	13033	12992	20080	25787	1.788772	1.441197	1.850865



Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
		9951	17074	17604	24372	31493	1.714052	1.427451	1.844498



Broad Unknown Relative Peak Table

	Distribution Name	Mn (Daltons)	Mw (Daltons)	MP (Daltons)	Mz (Daltons)	Mz+1 (Daltons)	Polydispersity	Mz/Mw	Mz+1/Mw
		29873	32505	29901	35335	38223	1.088085	1.087083	1.175933

Figure S2. GPC data of **(A)** triblock copolymer, **(B)** multiblock copolymer (MB-30-ss-PCL) **(C)** multiblock copolymer (MB-50-ss-PCL), **(D)** multiblock copolymer (MB-70-ss-PCL)

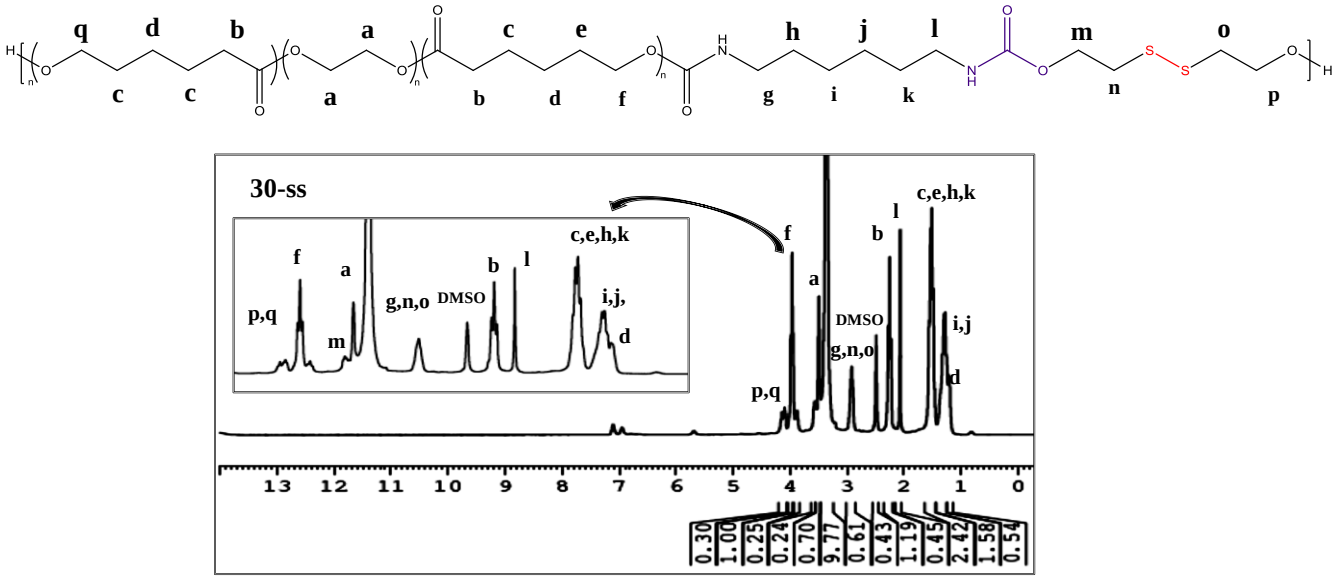
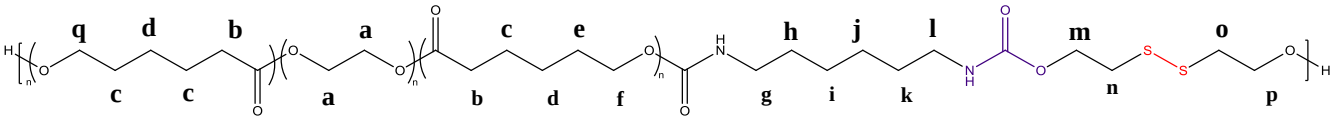


Figure S3A. ^{1}H NMR Spectrum of multiblock copolymer based on PCL-PEG-PCL

^{1}H NMR (300 MHz, DMSO, δ (ppm)) – 1.32-1.30 (m,-OCH$_2$CH$_2$***CH$_2$***CH$_2$CH$_2$CO- and (–HN-CH$_2$CH$_2$**CH$_2$CH$_2$**CH$_2$CH$_2$-NH-) of hexamethylene group), 1.49-1.56 (m, OCH$_2$***CH$_2$***CH$_2$***CH$_2$***CH$_2$CO-), 2.07 (–HN-CH$_2$***CH$_2$***CH$_2$CH$_2$***CH$_2$***CH$_2$-NH- of hexamethylene group), 2.23-2.28 (t, OCH$_2$CH$_2$CH$_2$CH$_2$***CH$_2$***CO-) of polycaprolactone, 2.92 (m, -CH$_2$***CH$_2$*** -SS-***CH$_2$***CH$_2$-) and (–HN-***CH$_2$***CH$_2$CH$_2$CH$_2$CH$_2$***CH$_2$***-NH- of hexamethylene group), 3.49 (-OCH$_2$-CH$_2$-O, PEG unit), 3.95 (t, (-O-***CH$_2$***CH$_2$ -SS-CH$_2$***CH$_2$***-O-) of 2-hydroxyethyl sulphide, 3.95-3.97 (t, O***CH$_2$***CH$_2$CH$_2$CH$_2$CH$_2$CO-) of polycaprolactone, 4.12-4.18 (t, -***CH$_2$***OH) terminal OH groups of polycaprolactone.



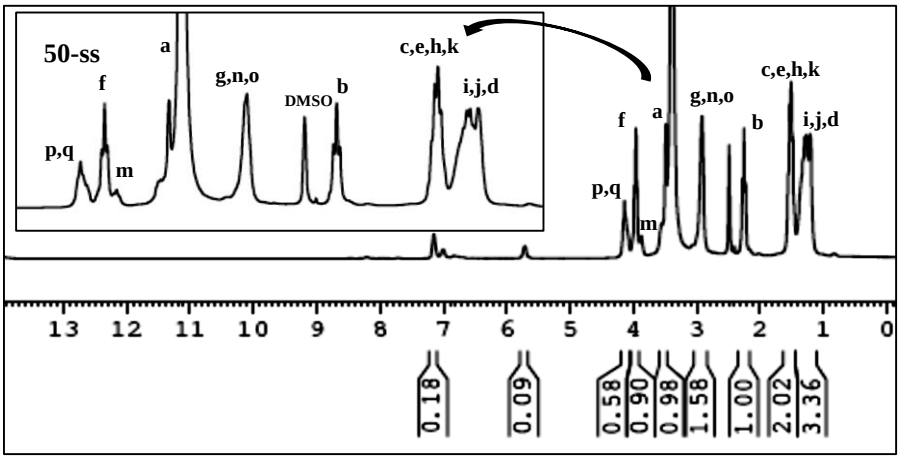


Figure S3B. ^{1}H NMR Spectrum of multiblock copolymer based on PCL-PEG-PCL

^{1}H NMR (300 MHz, DMSO, δ (ppm)) – 1.32-1.30 (m,-OCH$_2$CH$_2$***CH$_2$***CH$_2$CH$_2$CO- and (–HN-CH$_2$CH$_2$**CH$_2$CH$_2$**CH$_2$CH$_2$-NH-) of hexamethylene group), 1.49-1.56 (m, OCH$_2$***CH$_2$***CH$_2$***CH$_2$***CH$_2$CO-), 2.07 (–HN-CH$_2$***CH$_2$***CH$_2$CH$_2$***CH$_2$***CH$_2$-NH- of hexamethylene group), 2.23-2.28 (t, OCH$_2$CH$_2$CH$_2$CH$_2$***CH$_2$***CO-) of polycaprolactone, 2.92 (m, -CH$_2$***CH$_2$*** -SS-***CH$_2$***CH$_2$-) and (–HN-***CH$_2$***CH$_2$CH$_2$CH$_2$CH$_2$***CH$_2$***-NH- of hexamethylene group), 3.49 (-OCH$_2$-CH$_2$-O, PEG unit), 3.95 (t, (-O-***CH$_2$***CH$_2$ -SS-CH$_2$***CH$_2$***-O-) of 2-hydroxyethyl sulphide, 3.95-3.97 (t, O***CH$_2$***CH$_2$CH$_2$CH$_2$CH$_2$CO-) of polycaprolactone, 4.12-4.18 (t, -***CH$_2$***OH) terminal OH groups of polycaprolactone.

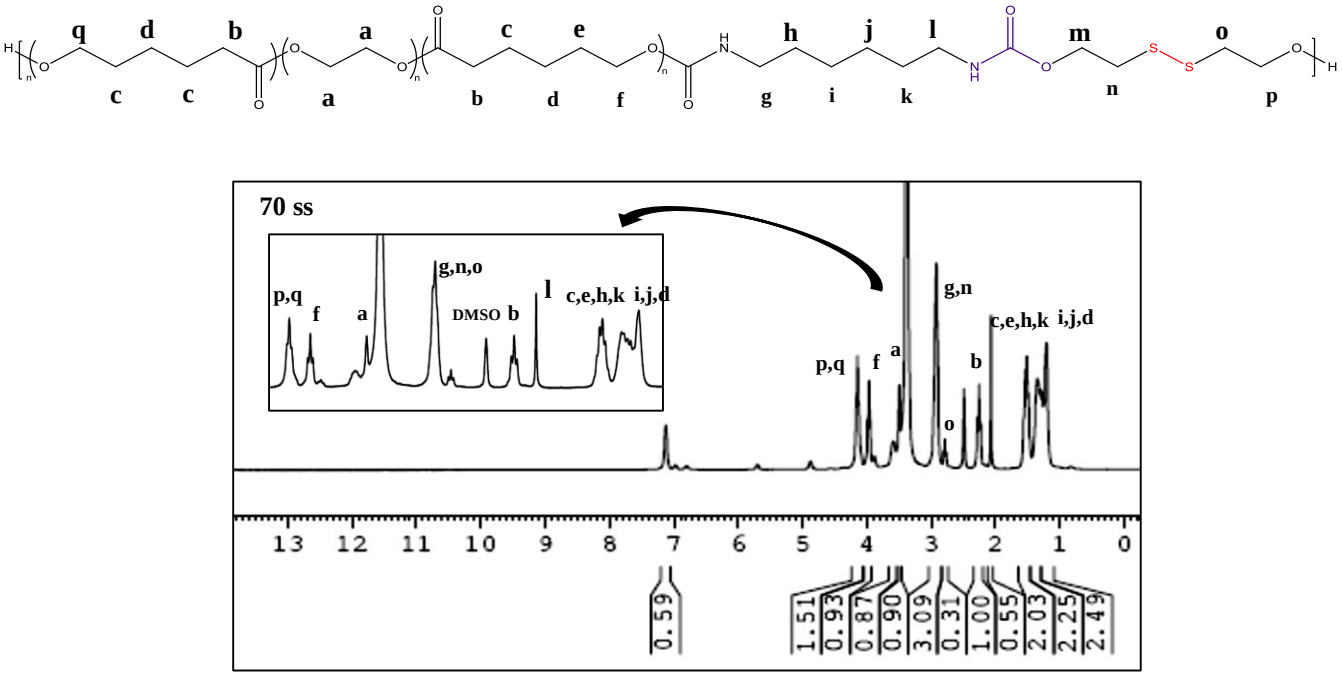


Figure S3C. ^{1}H NMR Spectrum of multiblock copolymer based on PCL-PEG-PCL

^{1}H NMR (300 MHz, DMSO, δ (ppm)) – 1.32-1.30 (m,-OCH_2CH_2***CH_2***CH_2CH_2CO- and (–HN-CH_2CH_2**CH_2CH_2**CH_2CH_2-NH-) of hexamethylene group), 1.49-1.56 (m, OCH_2***CH_2***CH_2***CH_2***CH_2CO-), 2.07 (–HN-CH_2***CH_2***CH_2CH_2***CH_2***CH_2-NH- of hexamethylene group), 2.23-2.28 (t, $OCH_2CH_2CH_2CH_2$***CH_2***CO-) of polycaprolactone, 2.92 (m, -CH_2***CH_2*** -SS-***CH_2***CH_2-) and (–HN-***CH_2***$CH_2CH_2CH_2CH_2$***CH_2***-NH- of hexamethylene group), 3.49 (-OCH_2-CH_2-O, PEG unit), 3.95 (t, (-O-***CH_2***CH_2 -SS-CH_2***CH_2***-O-) of 2-hydroxyethyl sulphide, 3.95-3.97 (t, O***CH_2***$CH_2CH_2CH_2CH_2CO$-) of polycaprolactone, 4.12-4.18 (t, -***CH_2***OH) terminal OH groups of polycaprolactone.

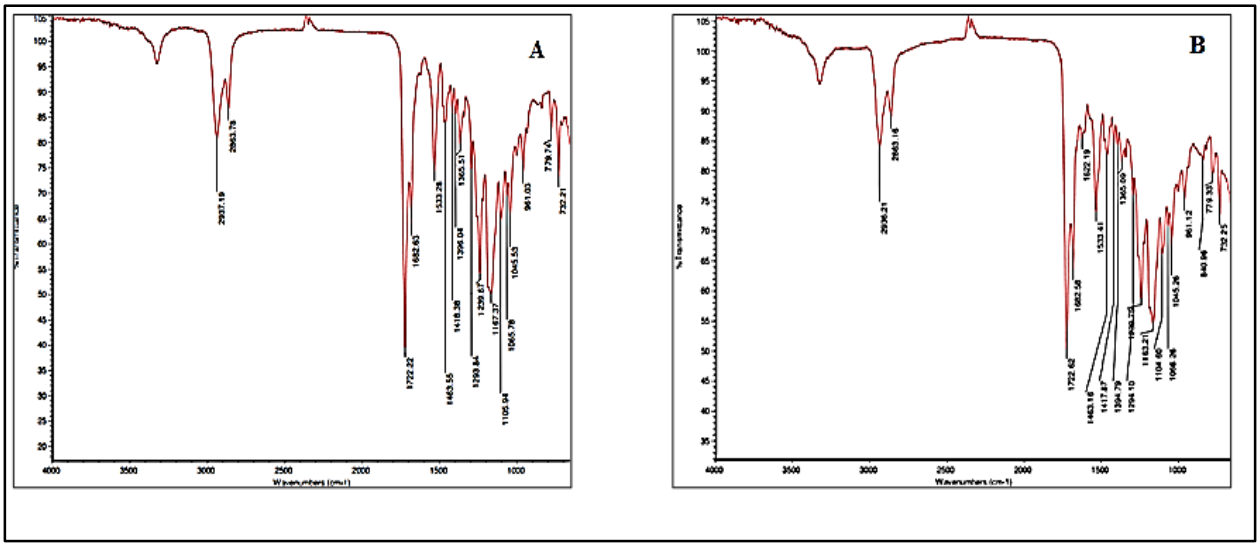


Figure S4. FTIR spectrum of (A) multiblock copolymer and (B) folate conjugated multiblock copolymer

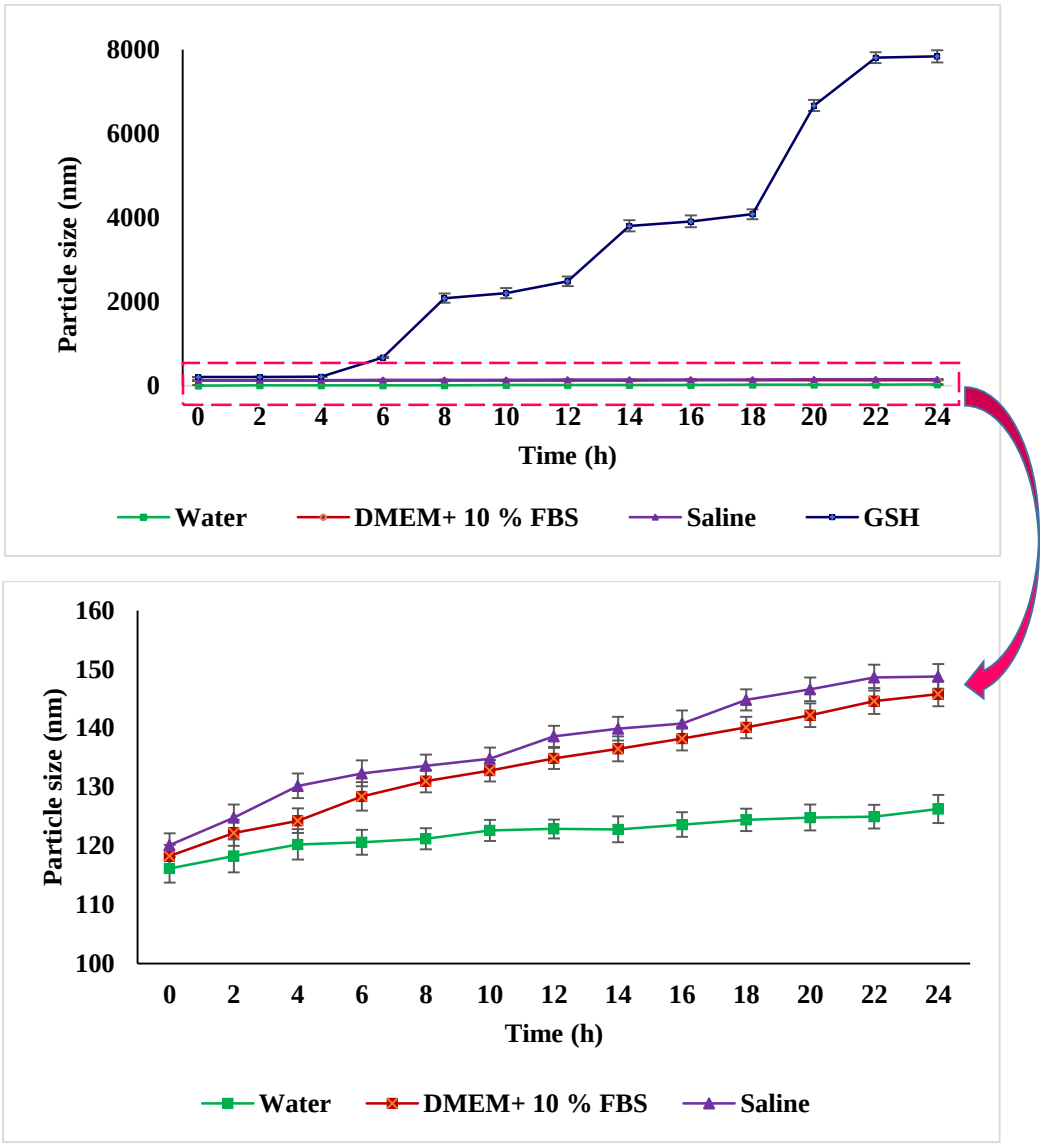


Figure S5. Colloidal stability of polymeric nanoparticles (MB-30-ss-FA-NPs)

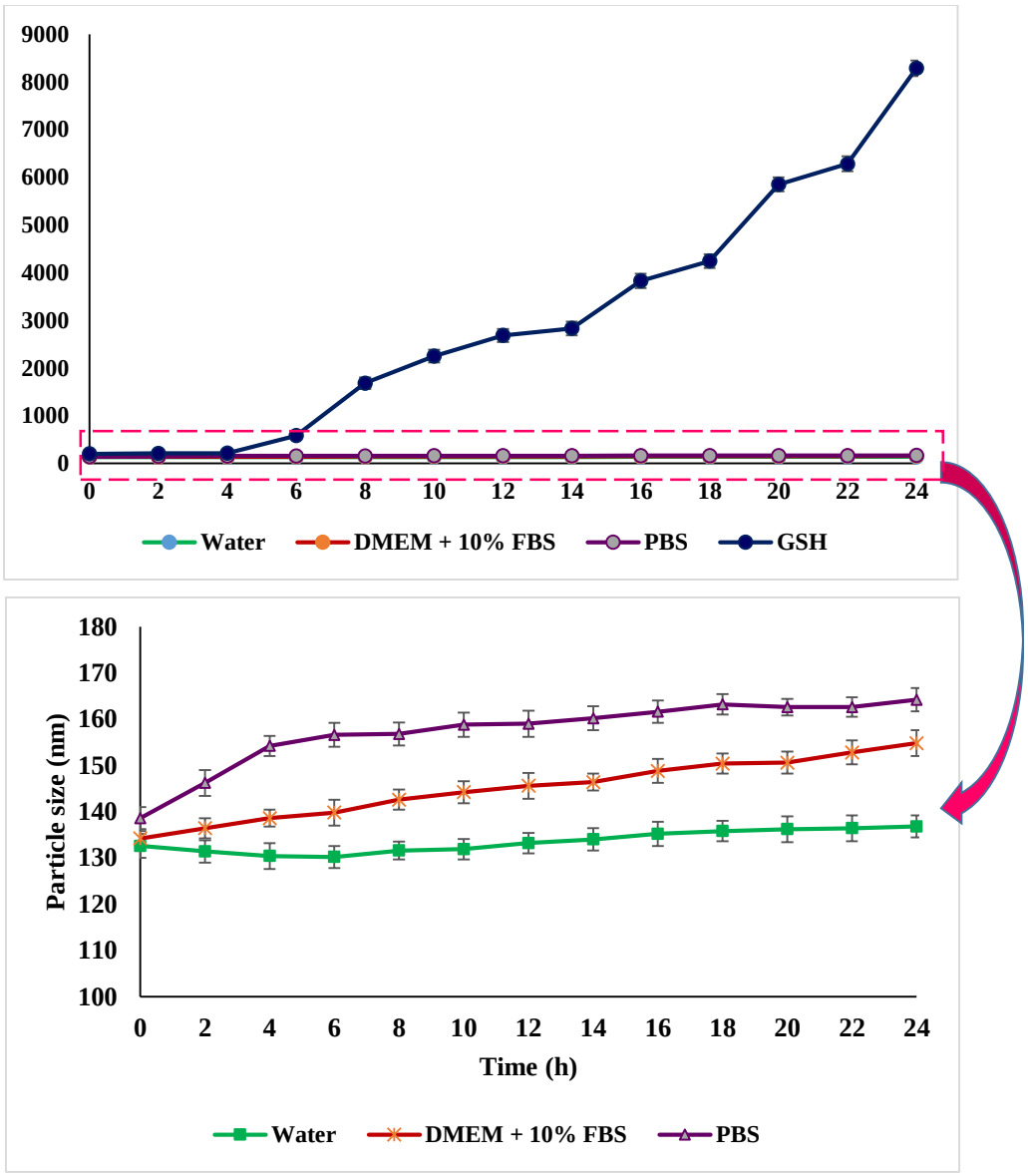


Figure S6. Colloidal stability of polymeric nanoparticles (MB-30-ss-FA-Her-Dox-NPs)

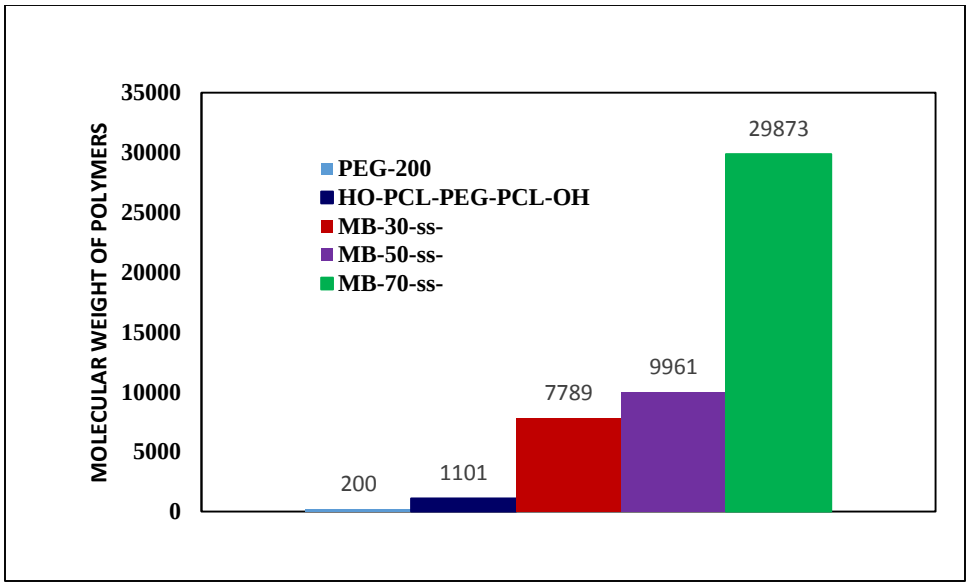


Figure S7. Comparison of molecular weights of PEG, triblock copolymer and multiblock copolymers

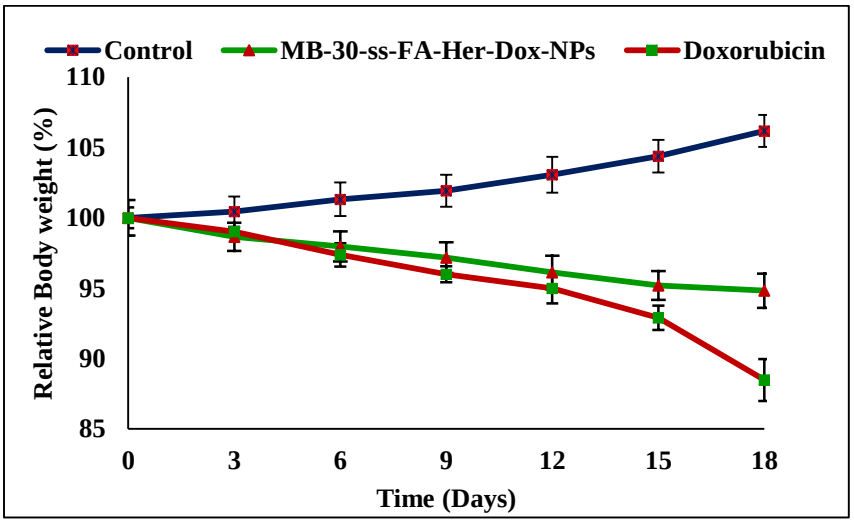


Figure S8. Relative body weight of EAT bearing Swiss albino mice during the treatment (mean ± SD, n=6)