

Synthesis and self-assembly of mPEG-palmitic acid and mPEG-stearic acid conjugates for pH-responsive delivery and release of anticancer therapeutics

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Section S1.1 Synthesis of mPEG-NH₂

mPEG-NH₂ was synthesized by dissolving 2.00 g of mPEG (1 mmol) in 30 mL of anhydrous DCM, triethylamine (4.94 mL, 17.6 mmol) was added. The reaction was allowed to continue overnight at room temperature after adding MsCl (0.7 mL, 4.41 mmol) dropwise under argon stream. The product was then precipitated with diethyl ether and vacuum-dried to get mPEG-mesylate. In an autoclave, the mesylated mPEG was mixed with 25 wt % ammonia aqueous solution and the reaction was continued at 120 °C for 10 h. First, DCM was used for solvent extraction. Next, brine solution (saturated sodium chloride solution) was used for back-extraction. In order to obtain m-PEG-NH₂, the product was precipitated using diethyl ether and vacuum-dried. Yield = 49%. M.pt. 52-55 °C; ¹H-NMR (CDCl₃, ppm): δ 3.7 (–CH₂CH₂–O–), 3.39 (–O–CH₃), (2.89 (–CH₂–NH₂), and 2.22 (–NH₂) (Figure S1).

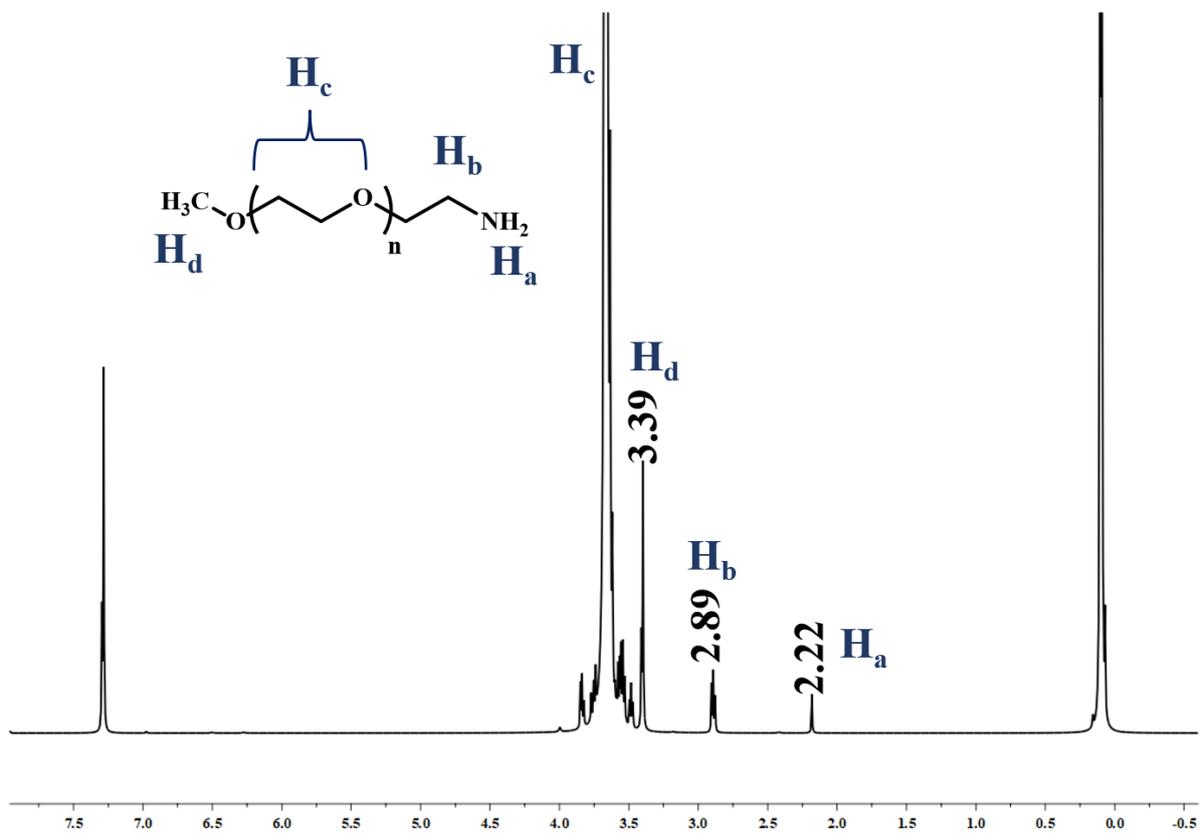


Figure S1. ¹H NMR spectrum of mPEG-NH₂

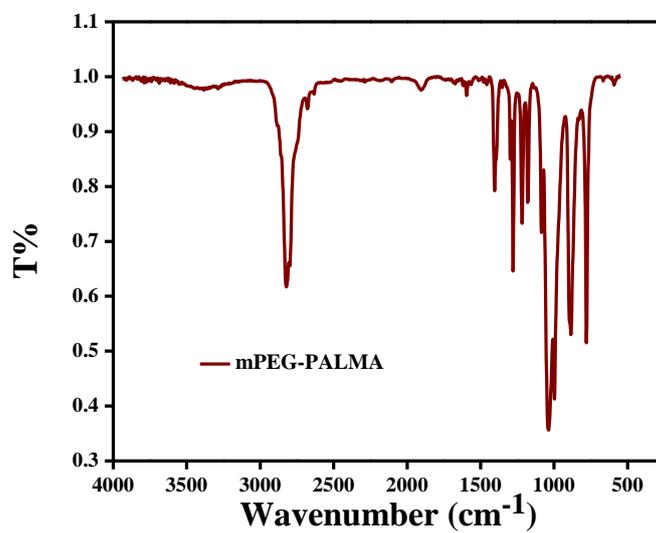


Figure S2. FTIR spectrum of mPEG-PALMA

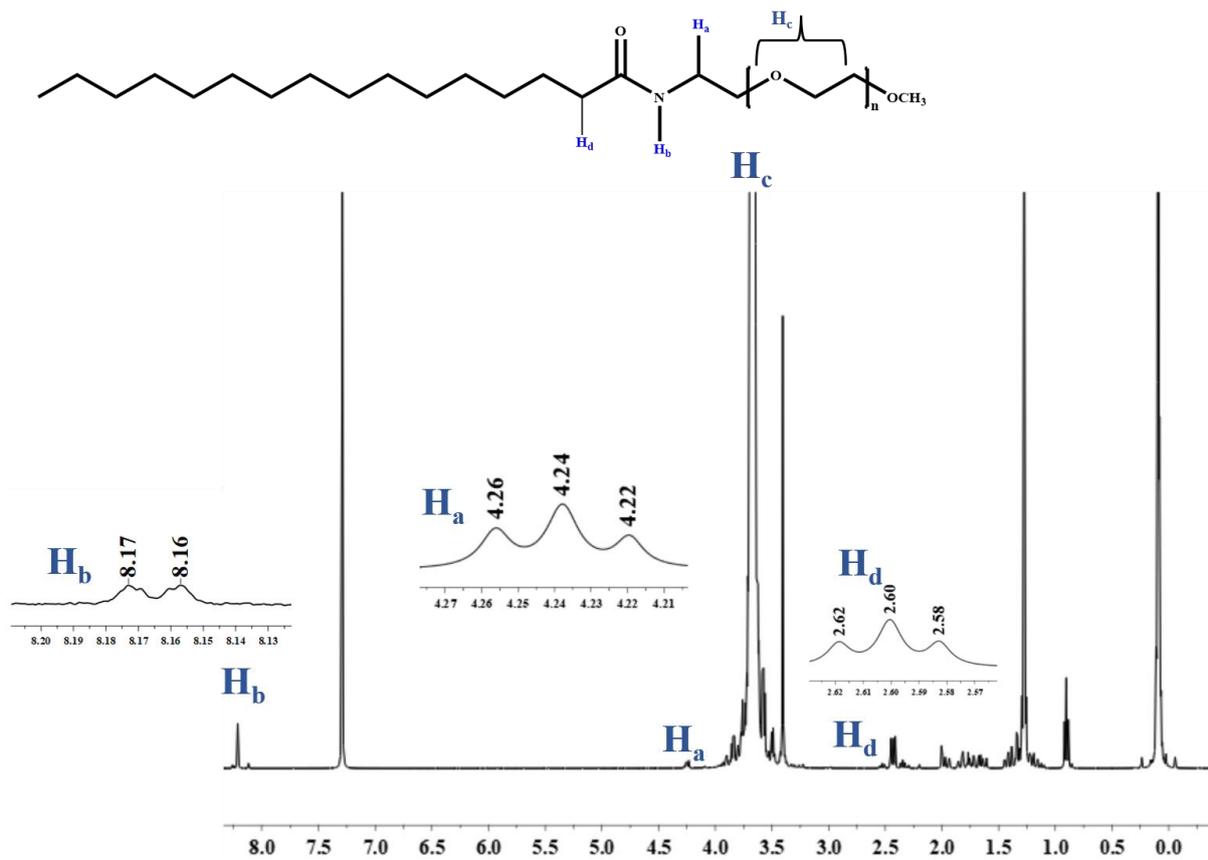


Figure S3. $^1\text{H-NMR}$ spectrum of mPEG-PALMA

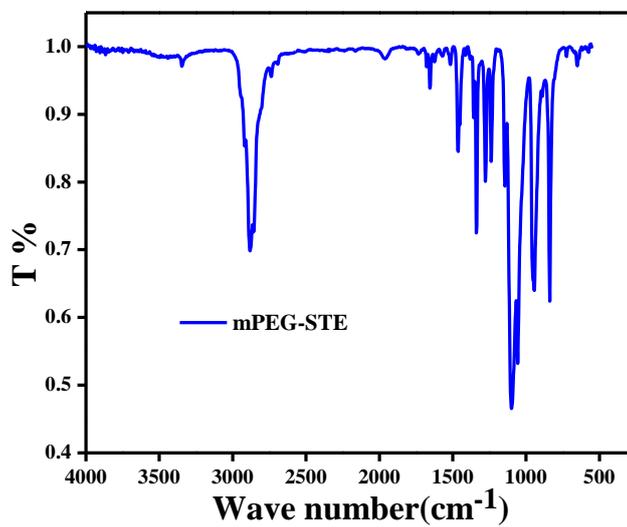


Figure S4. FTIR spectrum of mPEG-STE

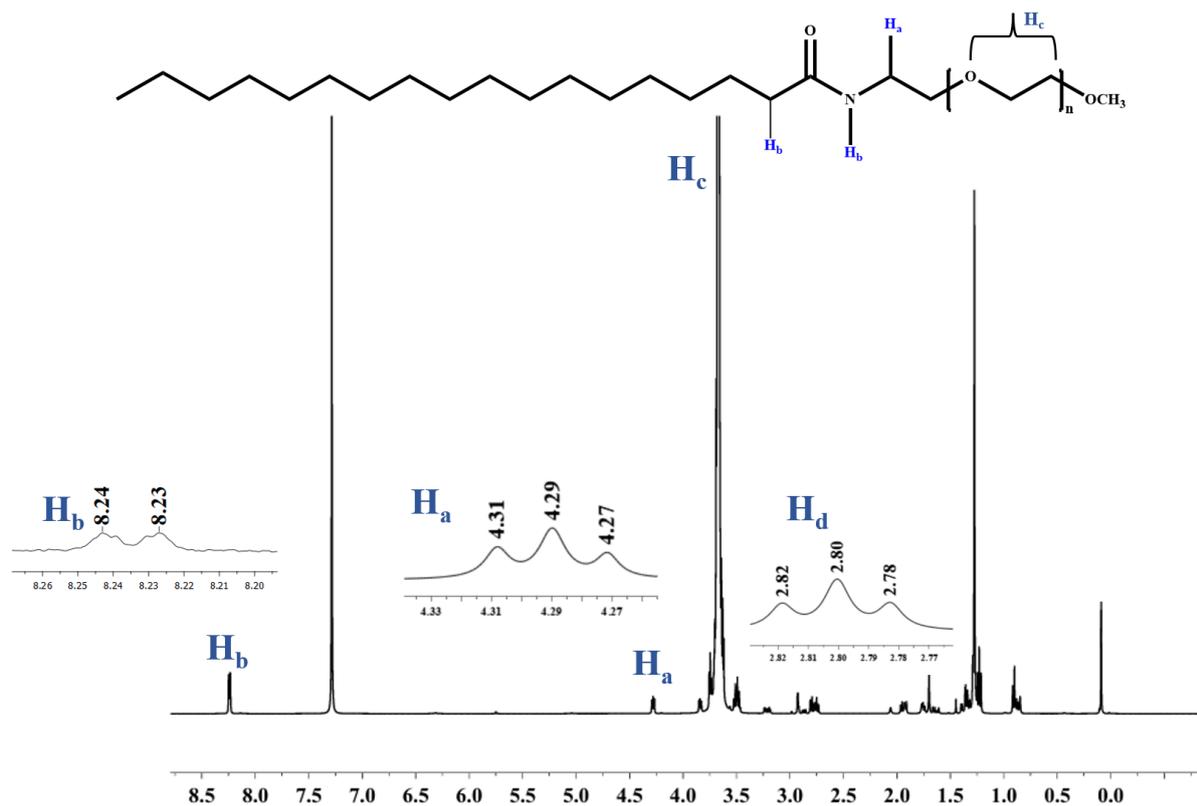


Figure S5. ¹H-NMR spectrum of mPEG-STE

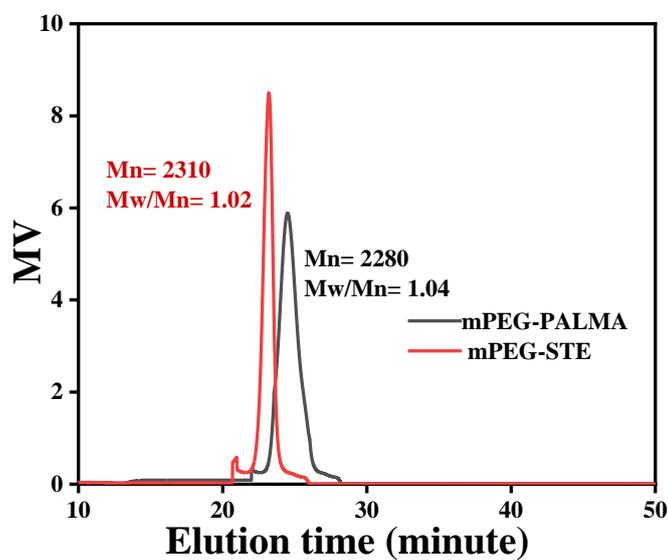


Figure S6. GPC analysis of mPEG-PALMA and mPEG-STE

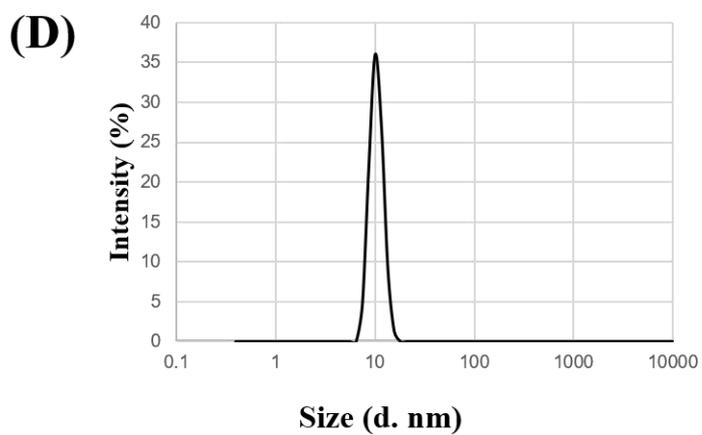
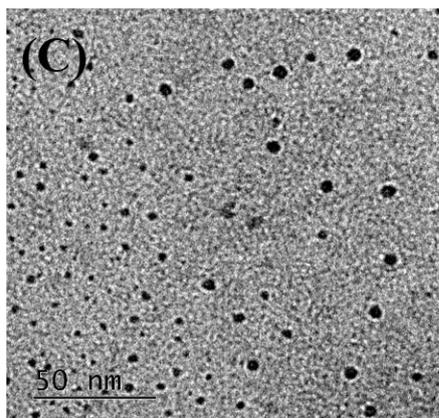
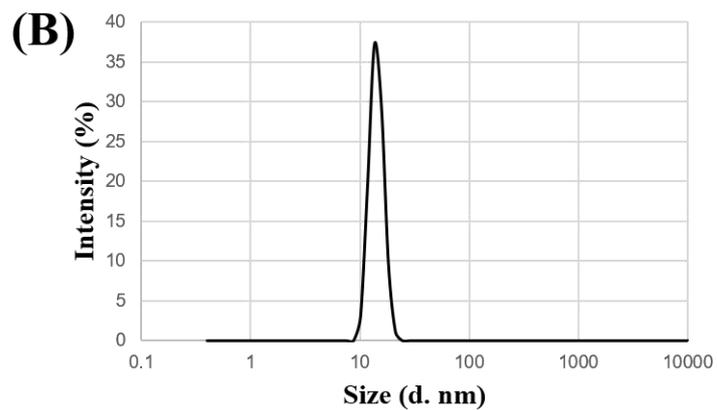
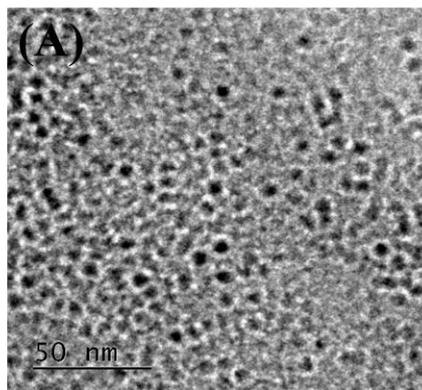


Figure S7. (A) TEM picture of mPEG-STE micelle, (B) DLS particle size distribution of mPEG-STE micelle, (C) TEM picture of PEG-STE micelle, (E) DLS particle size distribution of mPEG-PALMA micelle.

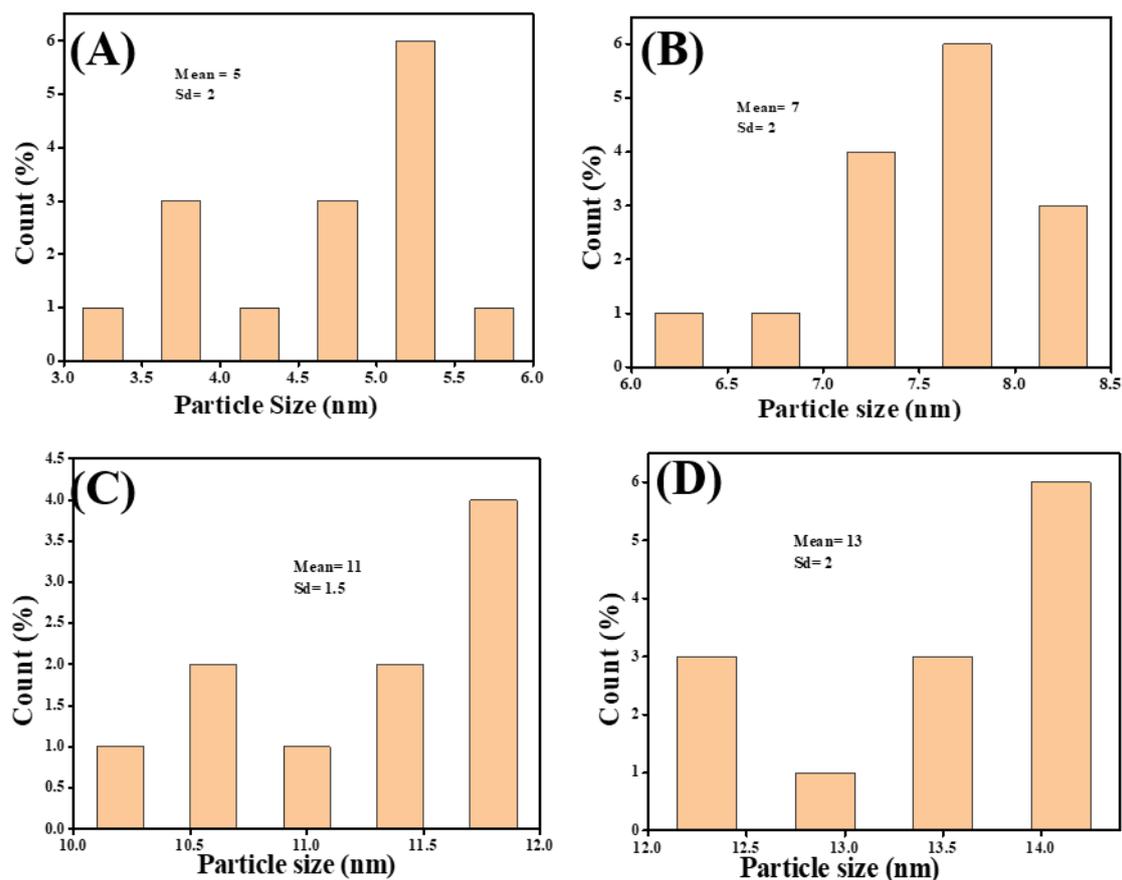


Figure S8. TEM histograms of (A) mPEG-PALMA micelle, (B) Doxorubicin loaded mPEG-PALMA, (C) mPEG-STE micelle and (D) Doxorubicin loaded mPEG-STE micelle.

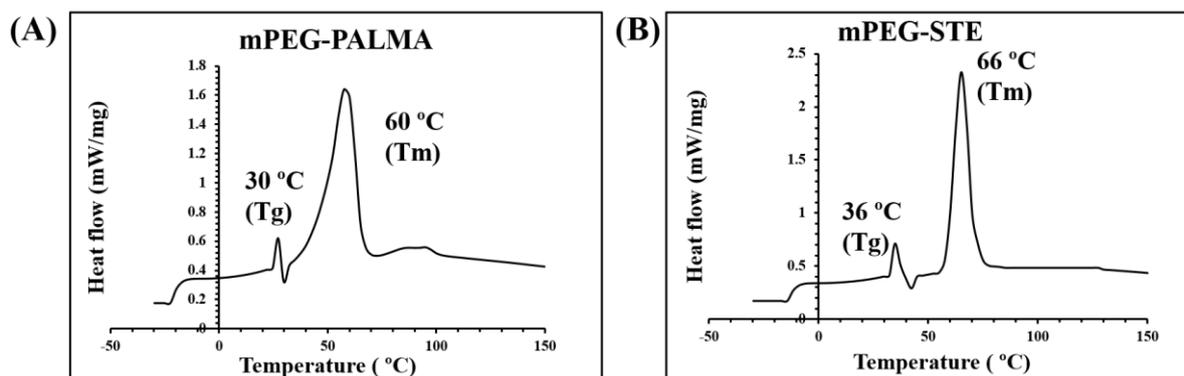
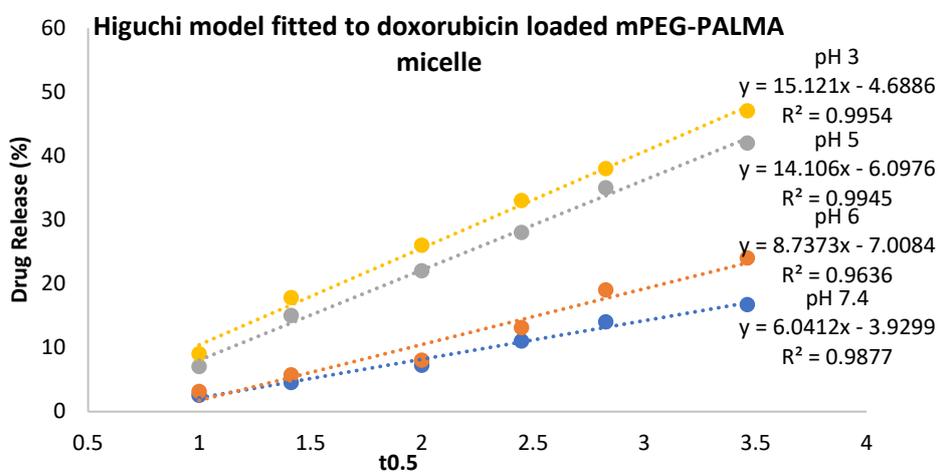


Figure S9. DSC plots of (A) empty mPEG-PALMA micelle and (B) empty mPEG-STE micelle.

(A)



(B)

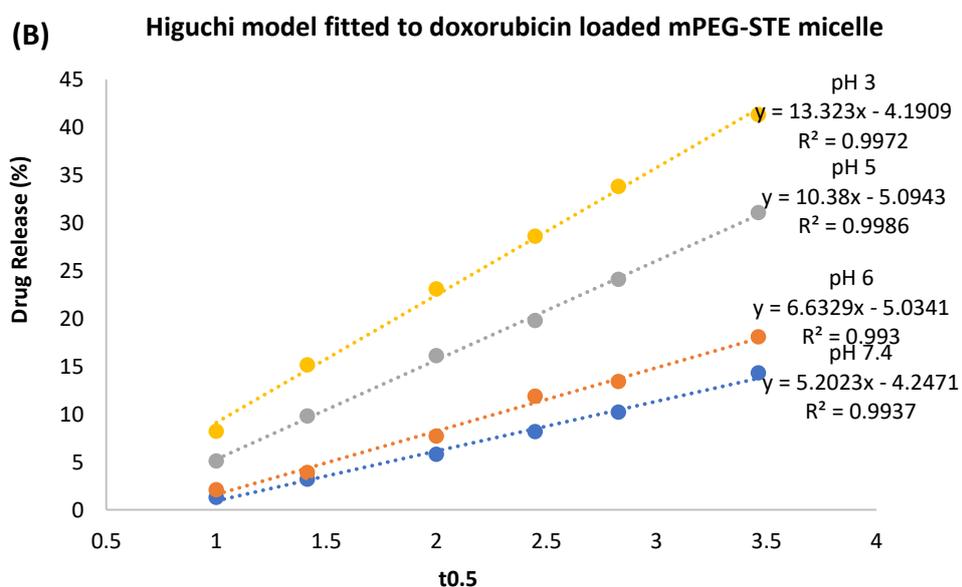


Figure S10. Plots of cumulative drug release percentage versus $t_{0.5}$ and fitting parameters for doxorubicin release from doxorubicin loaded micelle in PBS buffer at pH 3, pH 5, pH 6 and pH 7.4. (A) for mPEG-PALMA (B) mPEG-STE micelle.

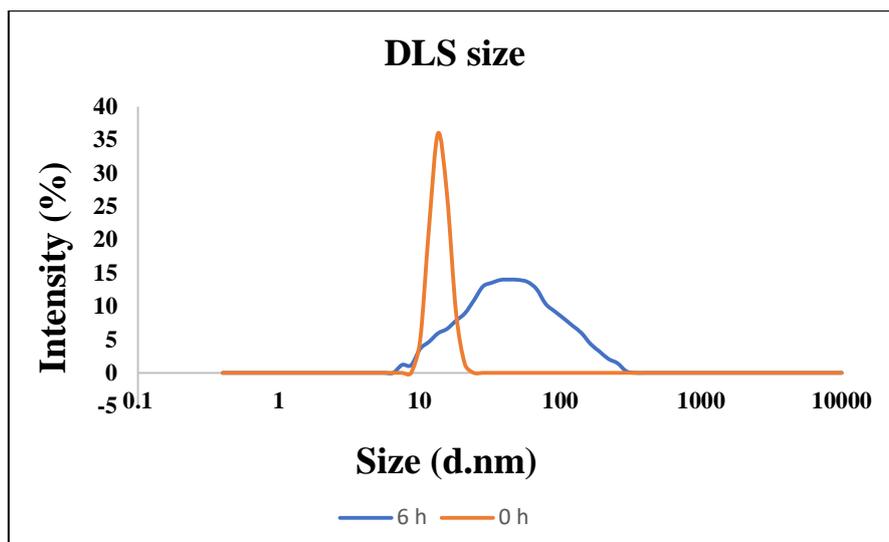


Figure S11. Changes in DLS particle size distribution of doxorubicin loaded mPEG-STE micelle at pH 5 (Orange: at time $t=0$ h and blue: at time $t=6$ h)

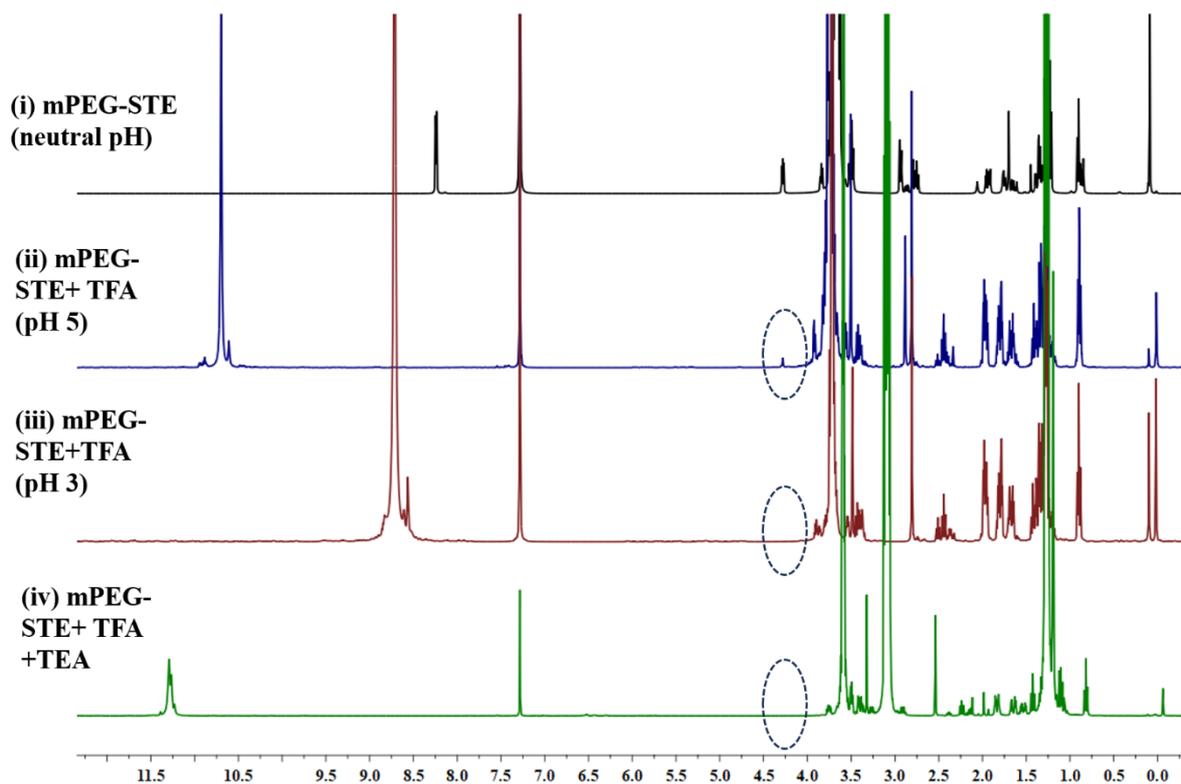


Figure S12. Comparison ^1H NMR of mPEG-STE (i) at neutral pH, (ii) at pH 5, (iii) at pH 3 (with addition of trifluoroacetic acid(TFA)) and (iv) after addition of triethylamine (TEA).

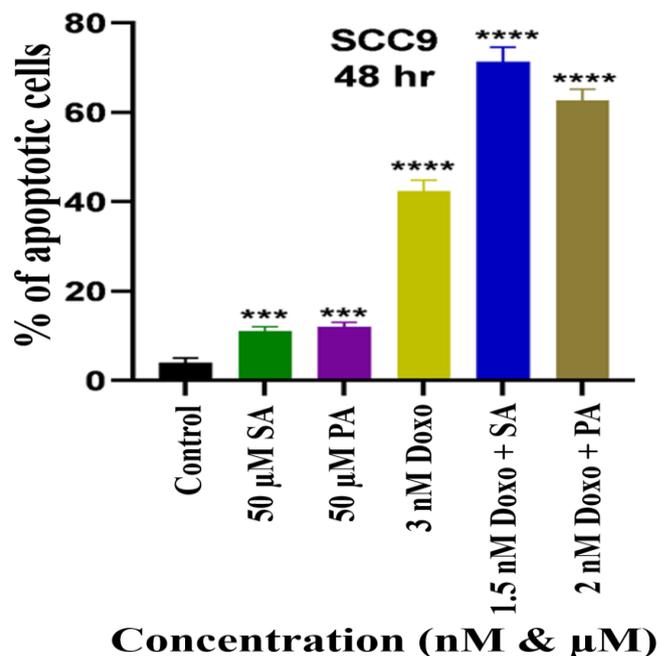


Figure S13. Bar graph showing the quantitative analysis of apoptotic cells in SCC9 cells after 48 hr of treatment, data are expressed as the mean (n = 3) ± standard deviation (SD), *p < 0.05, **p < 0.001, ***p < 0.0001

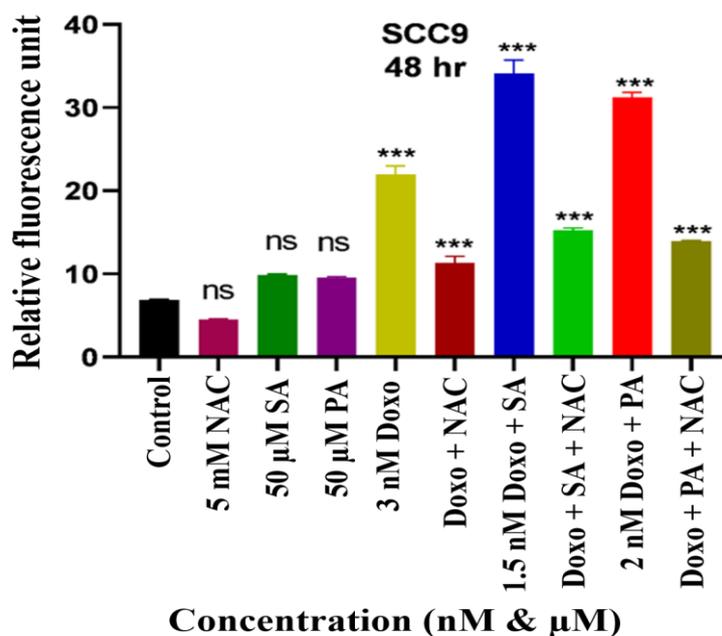


Figure S14. Graph depicting the quantitative analysis of fluorescence intensity emitted by treated SCC9 cells due to ROS accumulation. data are expressed as the mean (n = 3) ± standard deviation (SD), *p < 0.05, **p < 0.001, ***p < 0.0001.

Table S1. R² values for sigmoidal-Boltzmann curve fitted to CMC determination of mPEG-PALMA and mPEG-STE using curcumin and pyrene as a probe

Systems	R ² value using curcumin as a probe	R ² value using pyrene as a probe
mPEG-PALMA	0.99	0.99
mPEG-STE	0.99	0.99

Table S2. Comparison of CMCs of different polymeric micelle

Sl no.	Formulated micellar Systems	CMCs	References
1	mPEG– zein	5.5×10^{-2} g/L	1
2	PEG ₅₀₀₀ -PCL ₅₀₀₀	1.8 g/mL	2
3	PEG ₁₂₀₀₀ -PBLG ₈₄₀₀	2.7 g/mL	3
4	PEG ₁₂₀₀₀ -PBLA ₅₀₀₀	18 g/mL	4
5	MPEG ₂₀₀₀ -PVL ₅₅₀	176 g/mL	5

References

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