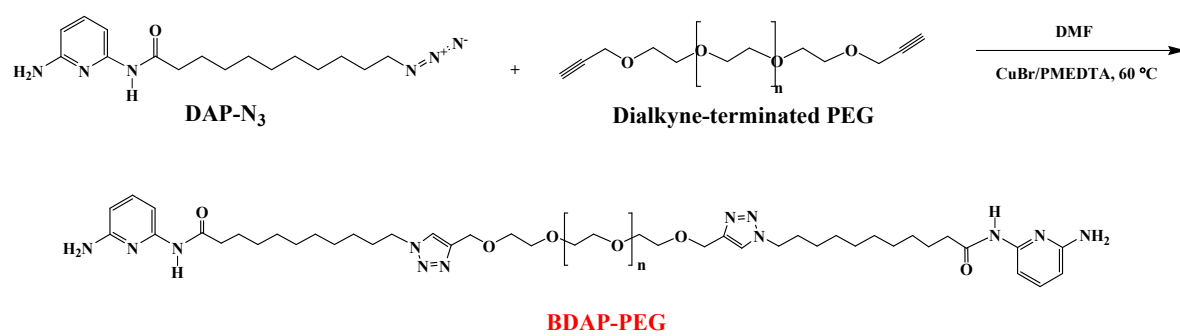


## Supporting Information

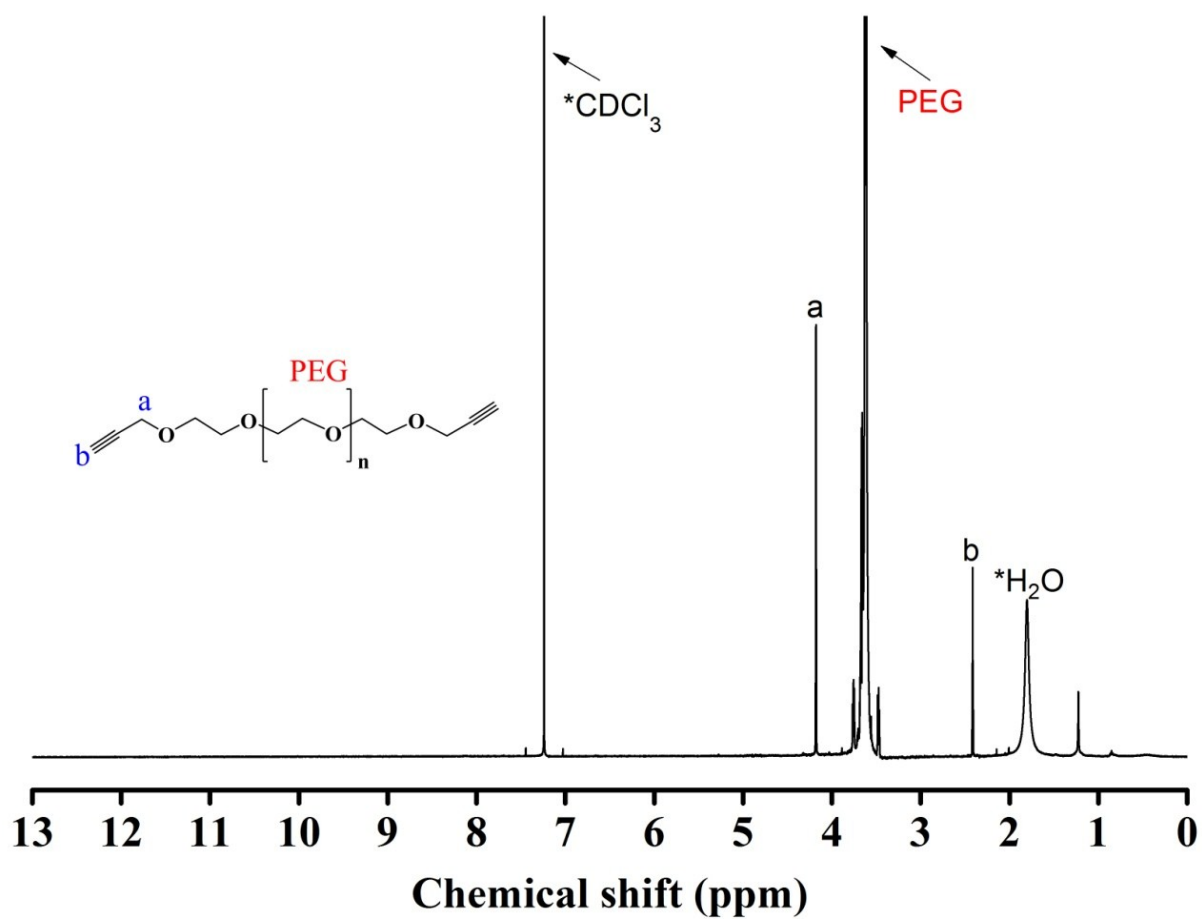
### ***Hydrogen-Bonded Supramolecular Micelle-Mediated Drug Delivery Enhances the Efficacy and Safety of Cancer Chemotherapy***

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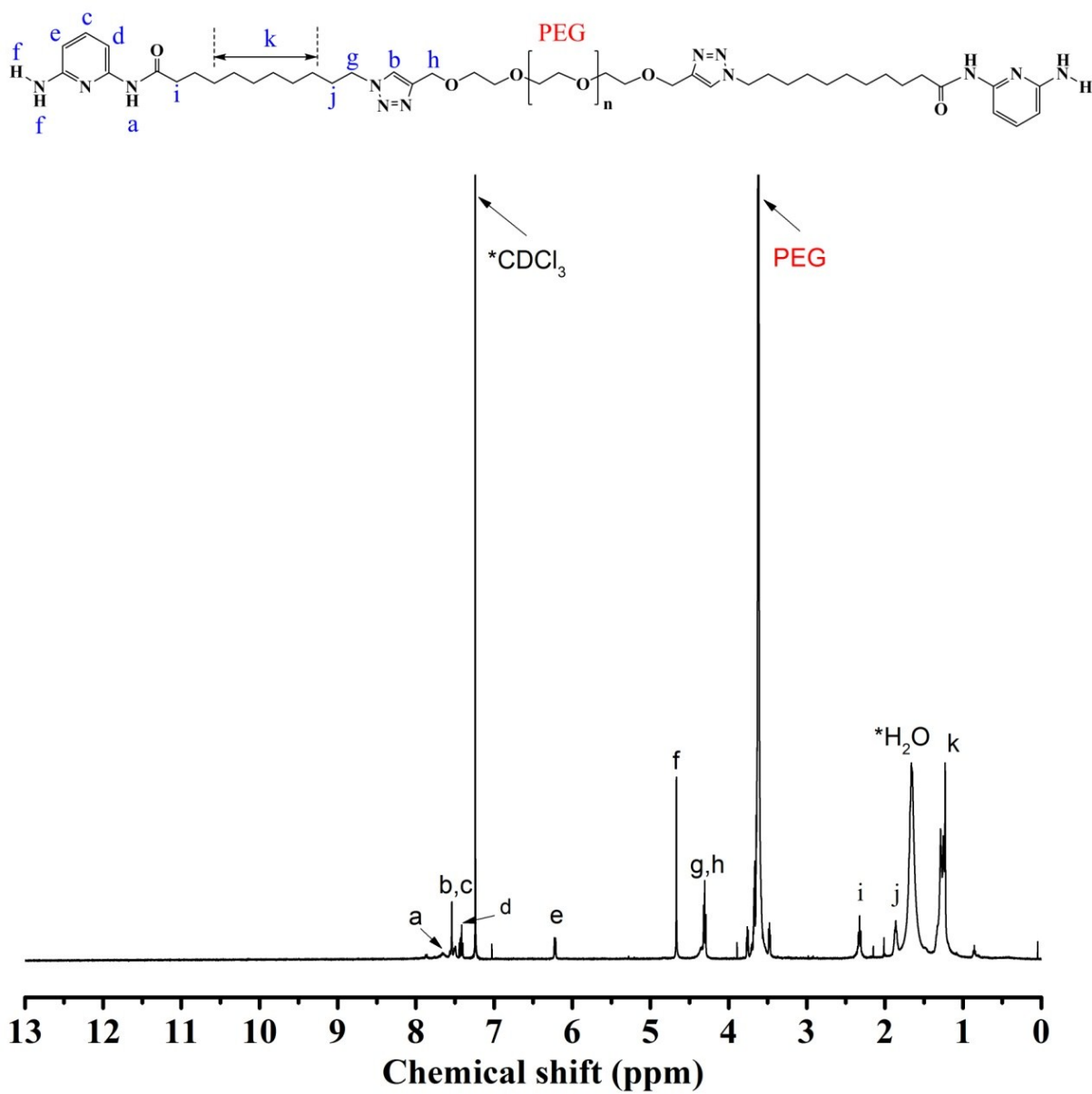
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**Scheme S1:** Synthetic routes for BDAP-PEG.



**Fig. S1:** 500 MHz  $^1\text{H}$  NMR spectrum of dipropargyl PEG in deuterated chloroform ( $\text{CDCl}_3$ ) at 25  $^\circ\text{C}$ .



**Fig. S2:** 500 MHz  $^1\text{H}$  NMR spectrum of BDAP-PEG in  $\text{CDCl}_3$  at 25 °C.

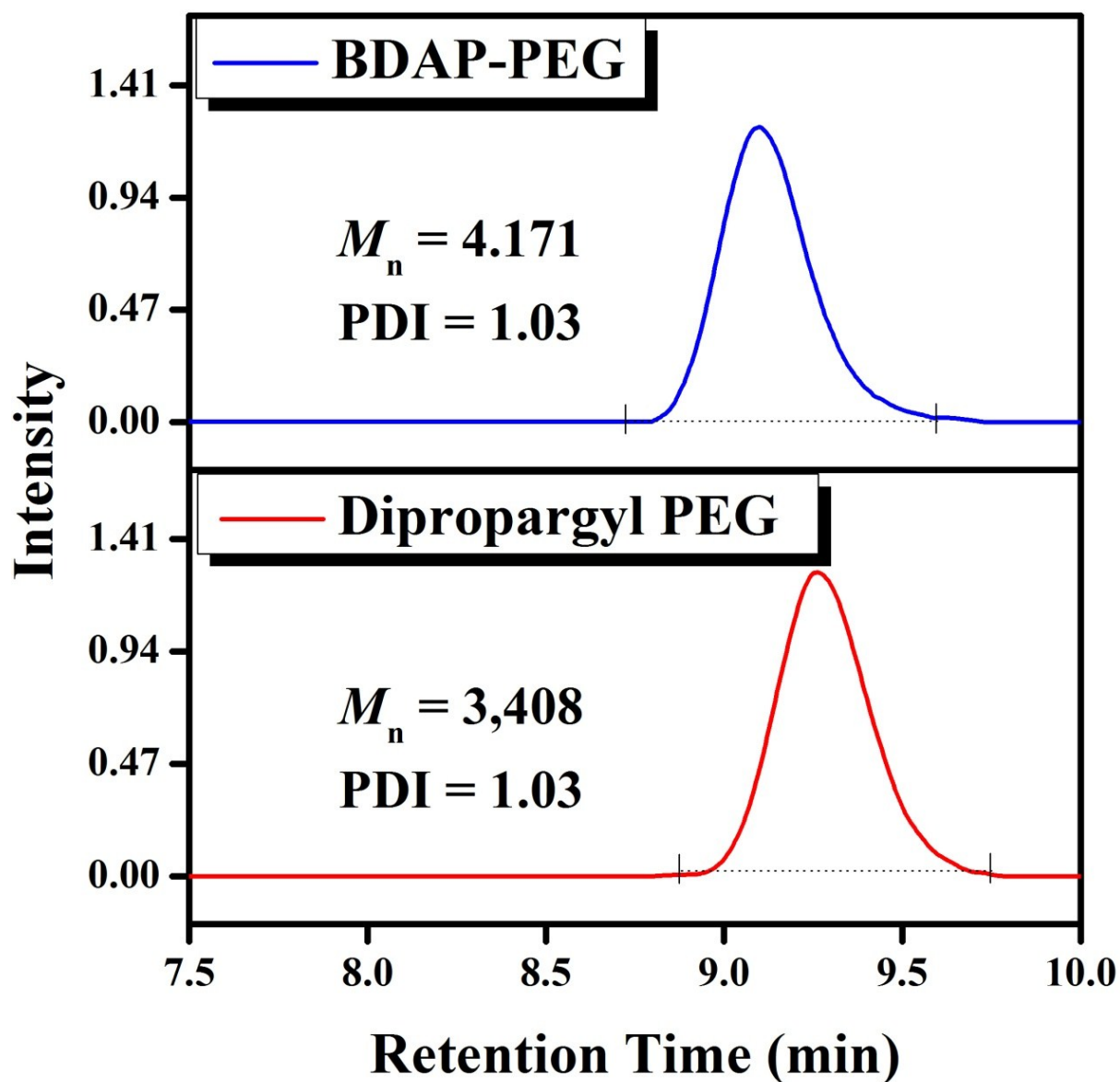


Fig. S3: GPC traces of dipropargyl PEG and BDAP-PEG with DMF eluent at 50 °C.

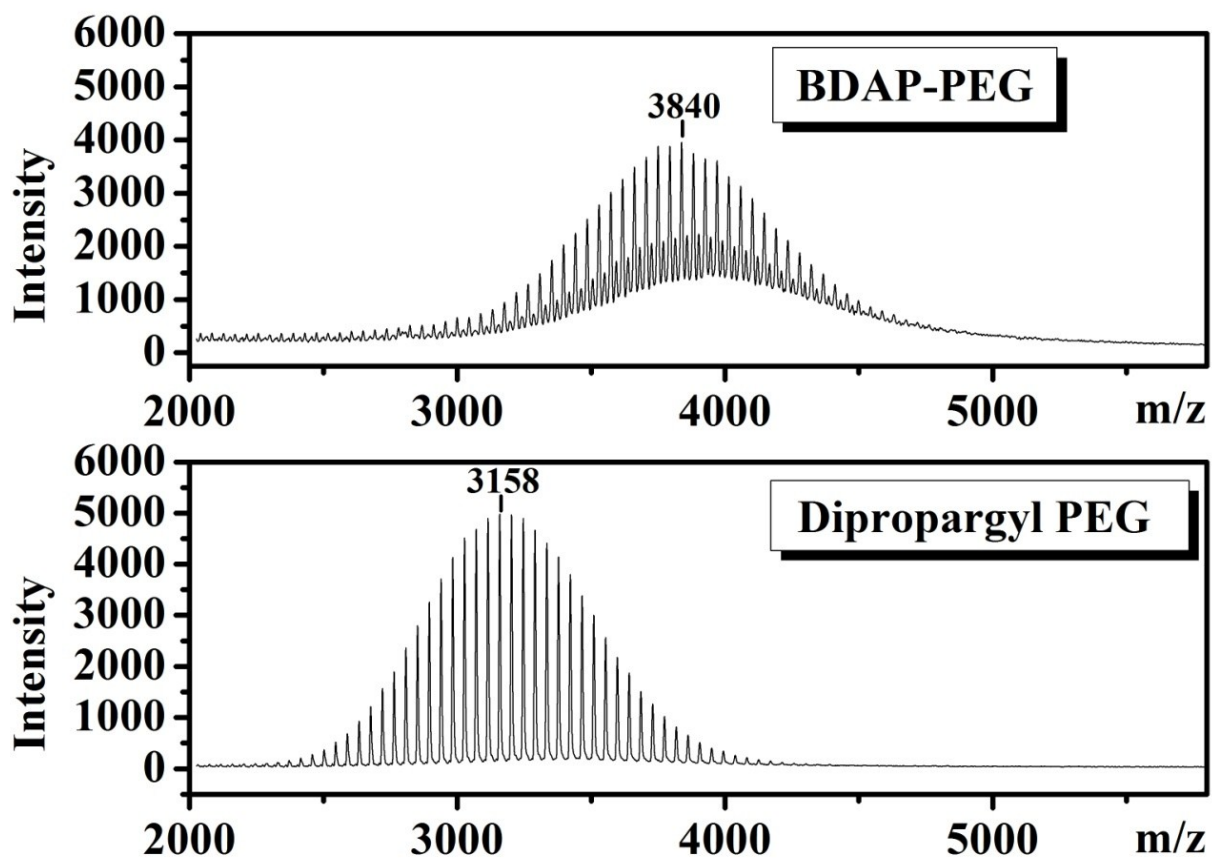


Fig. S4: MALDI-TOF mass spectra of dipropargyl PEG and BDAP-PEG.

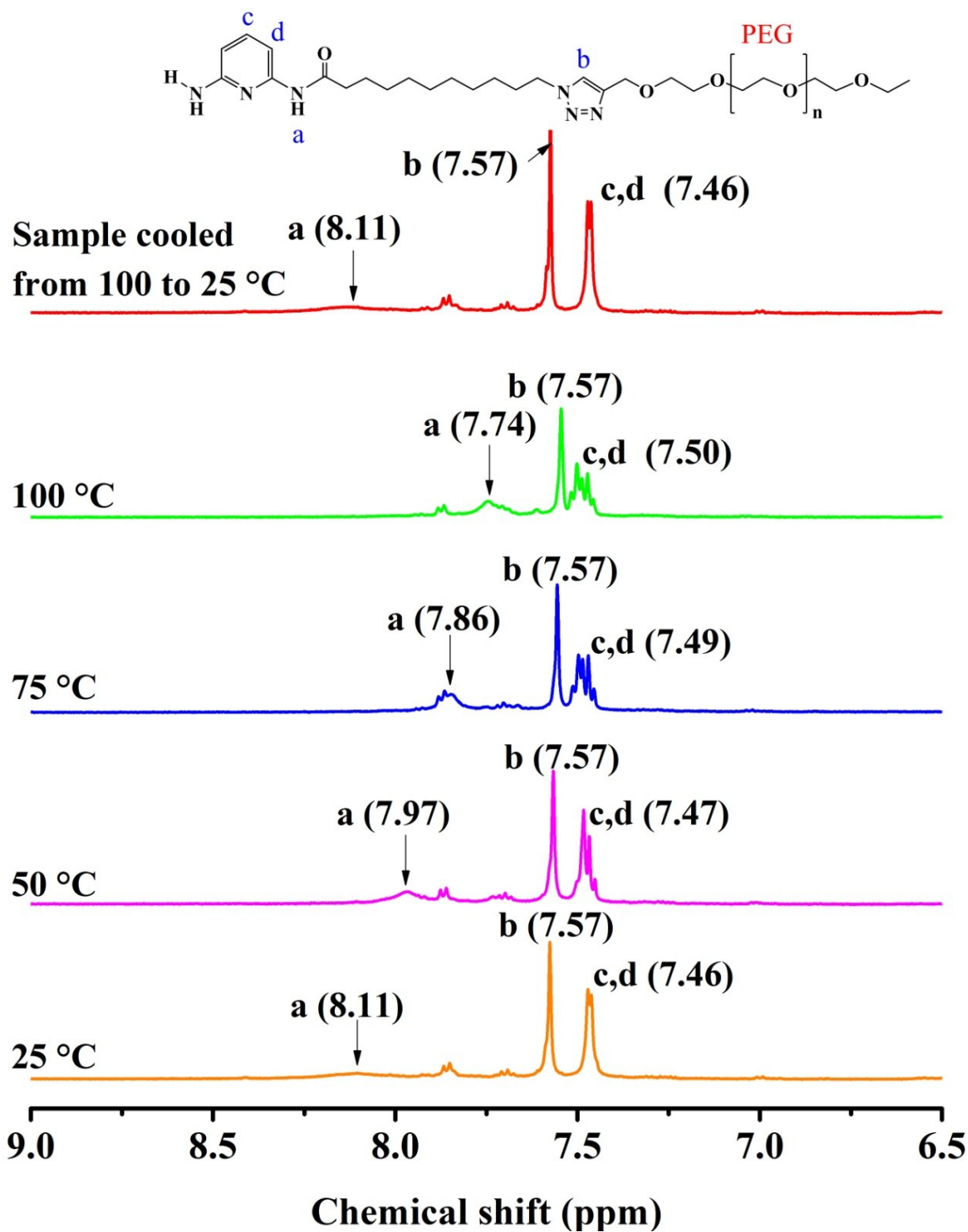
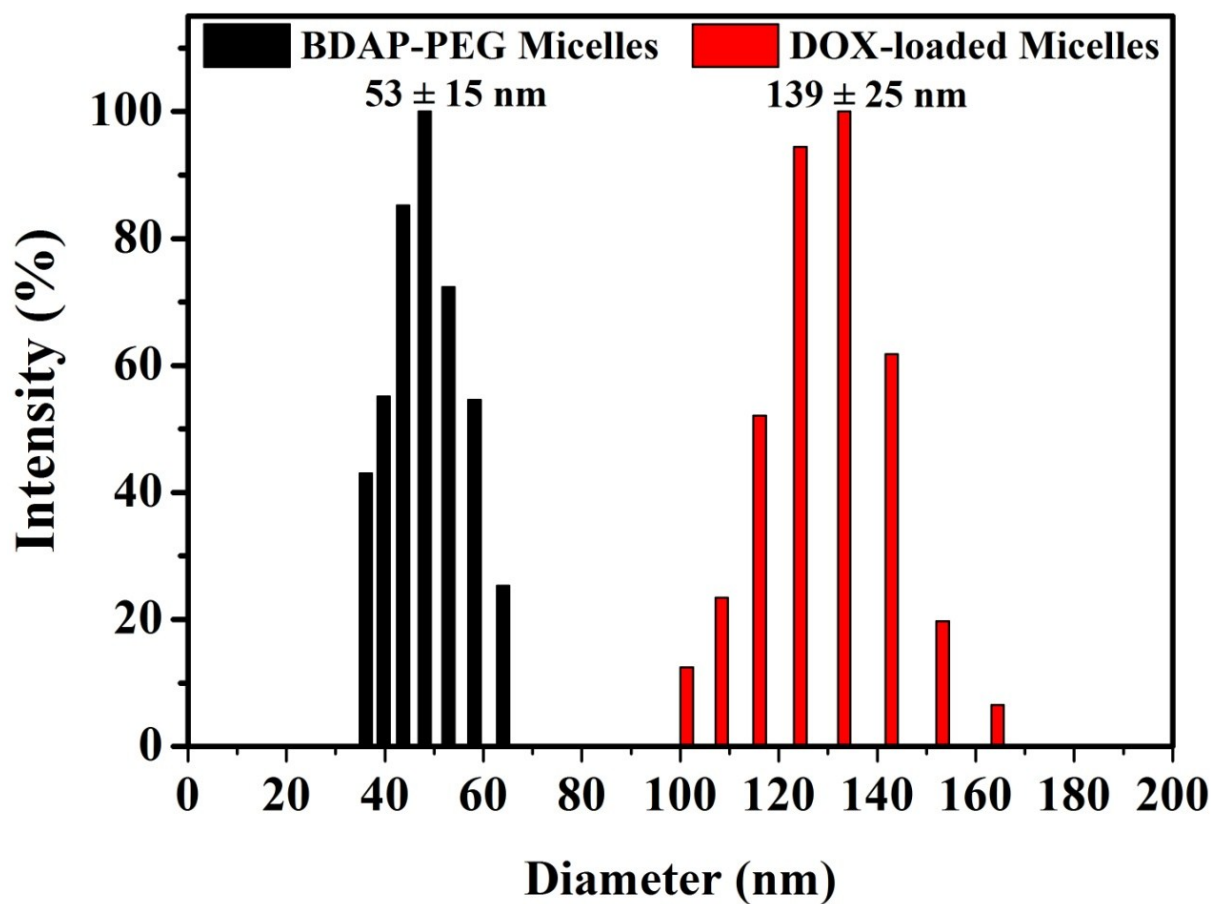
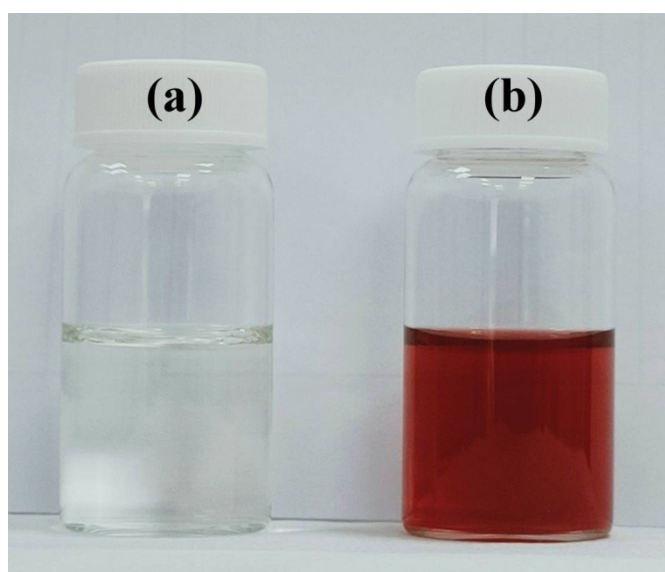


Fig. S5: 500 MHz  $^1\text{H}$  NMR spectra for BDAP-PEG in 1,1,2,2-tetrachloroethane- $d_2$  at various temperatures.

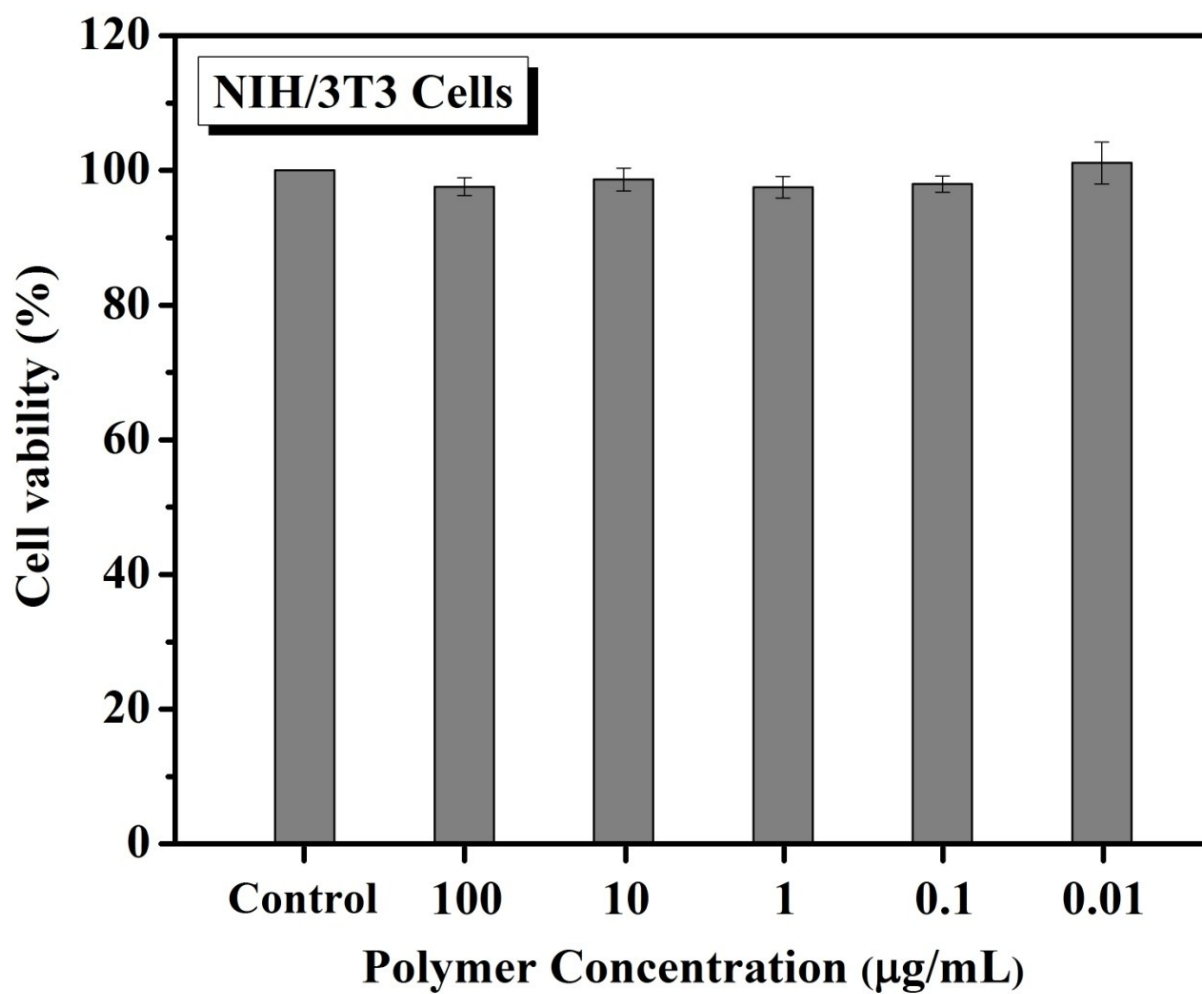


**Fig. S6:** Particle size distribution of blank and DOX-loaded BDAP-PEG micelles (DLC =  $17.60 \pm 1.5\%$ ) in water at 25 °C.

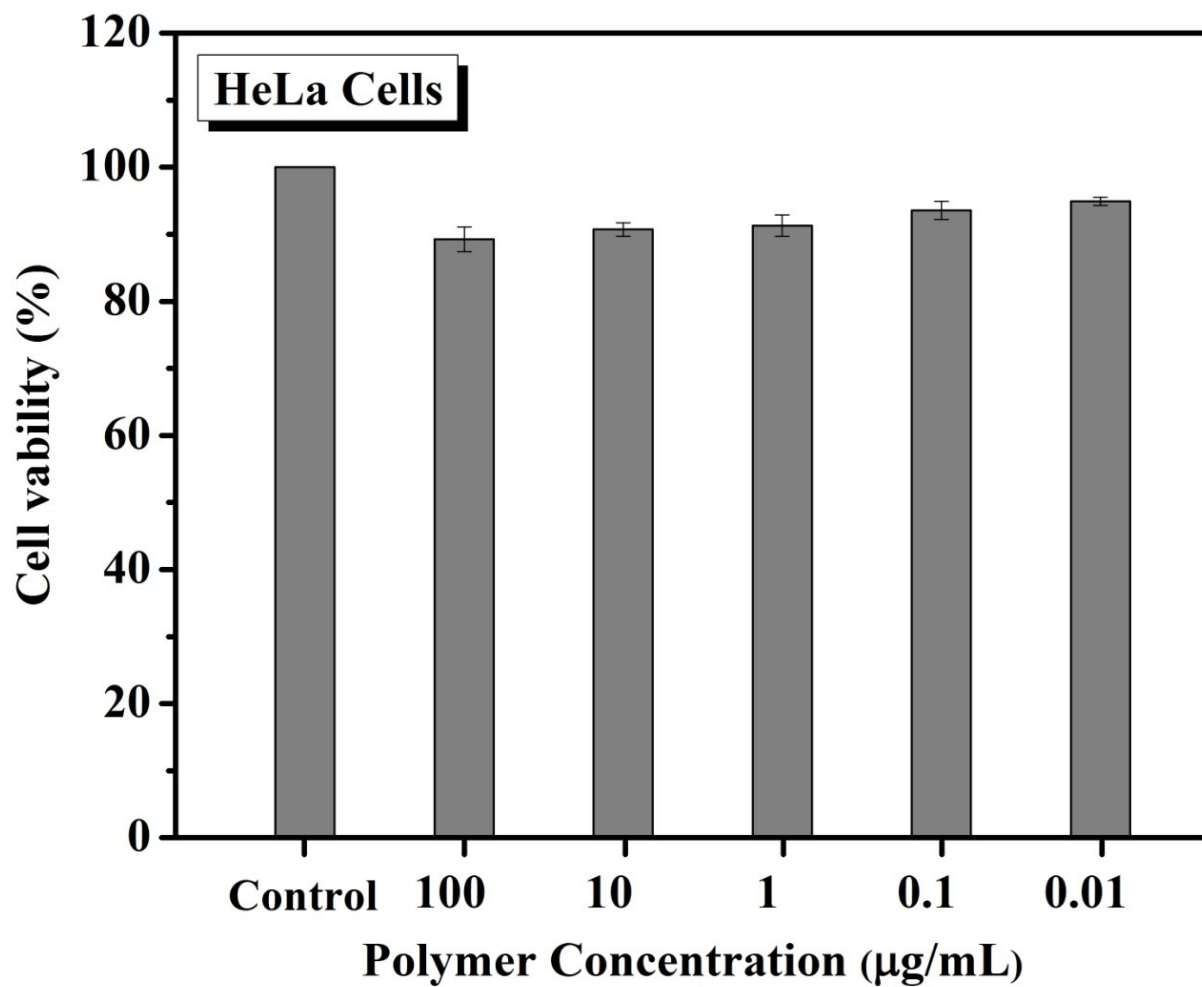


**Figure S7:** Digital photos for (a) blank and (b) DOX-loaded BDAP-PEG micelles in aqueous solution.



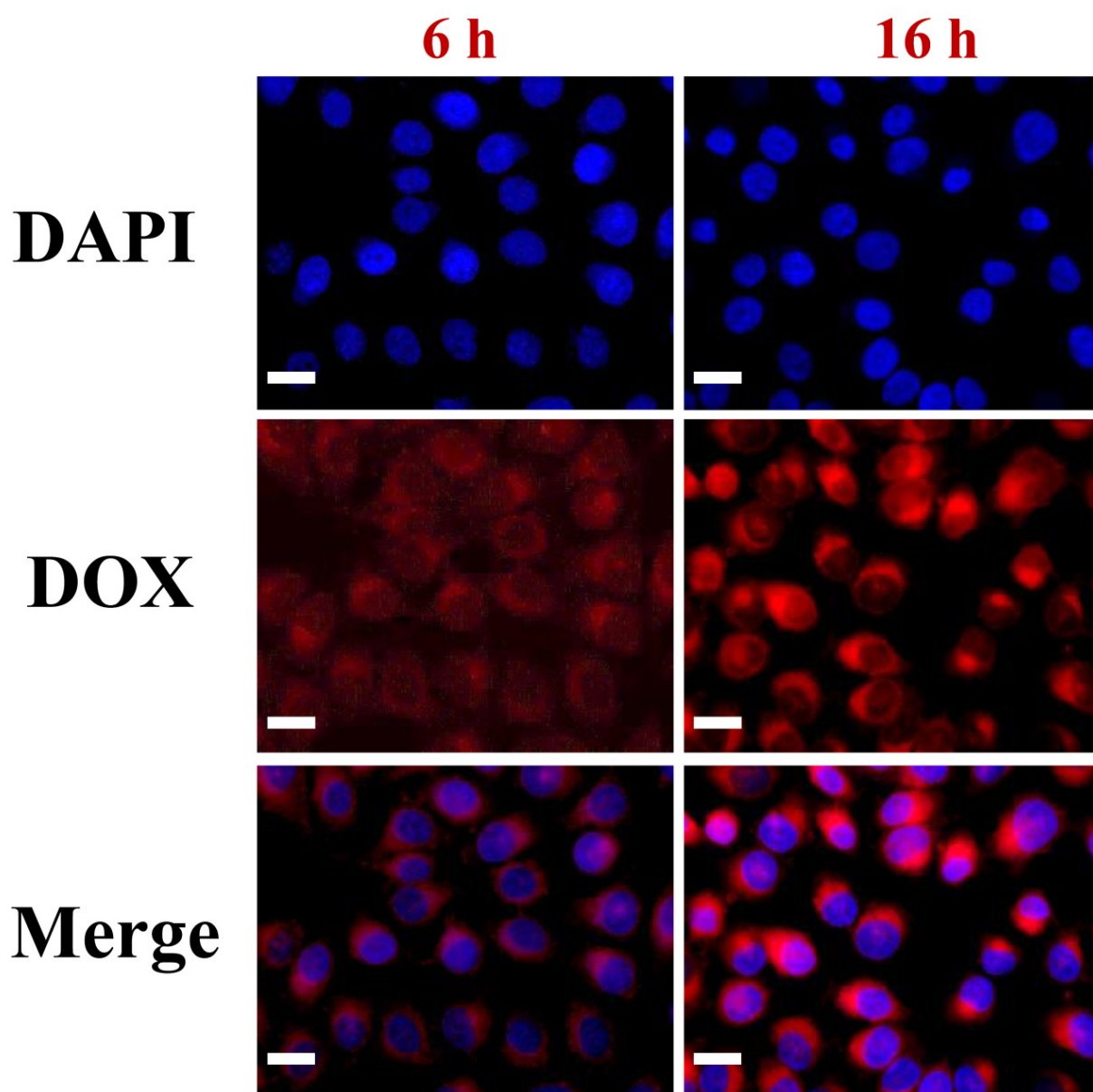


**Fig. S8:** *In vitro* cytotoxicity assay of BDAP-PEG micelles towards NIH/3T3 cells at 24 h.

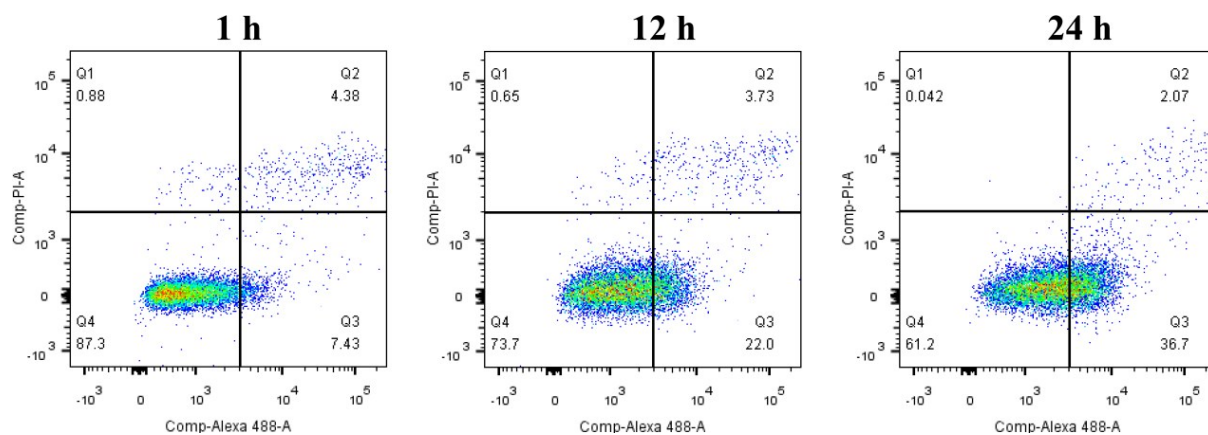


**Fig. S9:** *In vitro* cytotoxicity of BDAP-PEG micelles towards HeLa cells at 24 h.

## BDAP-PEG ( pH 7.4 )

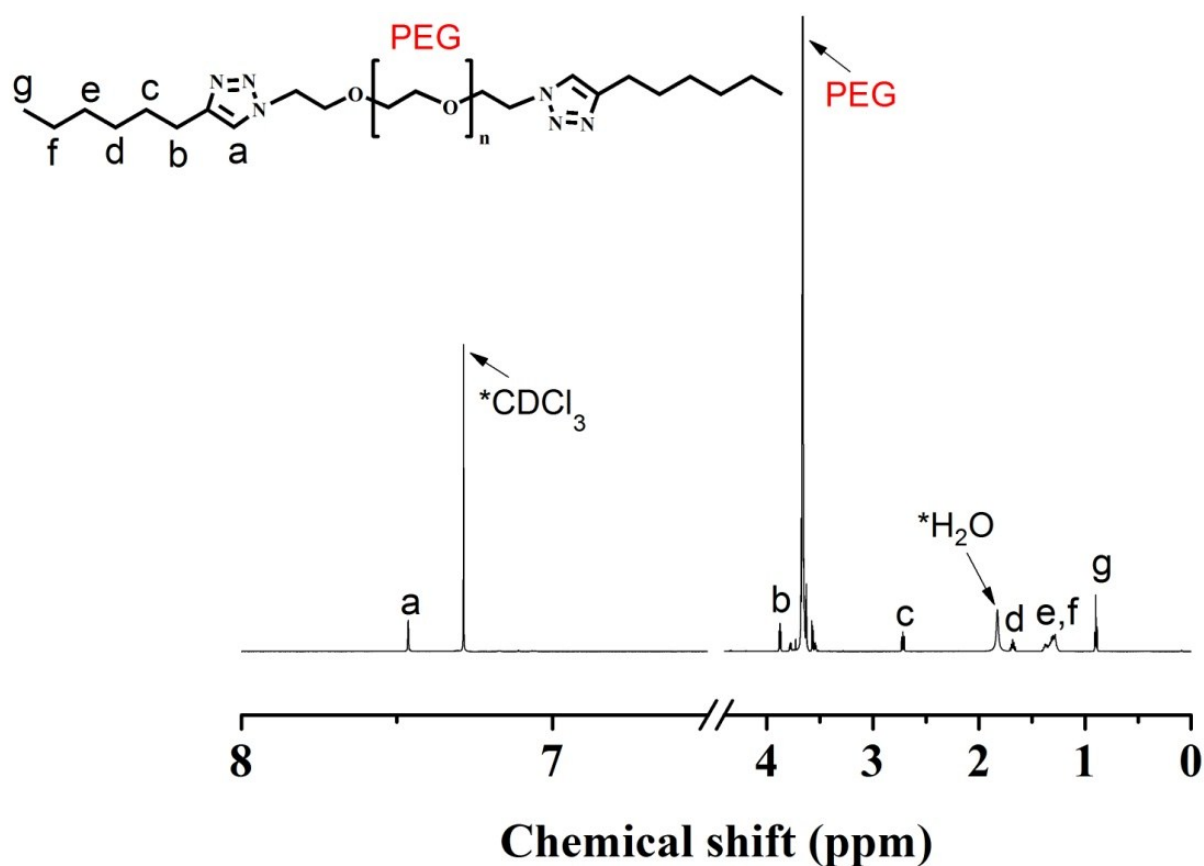


**Fig. S10:** CLSM images of HeLa cells incubated with DOX-loaded BDAP-PEG micelles (DLC =  $17.60 \pm 1.5\%$ ) for 6 h or 16 h at pH 7.4 and 37 °C. Micrographs of DOX-loaded micelles stained with the nuclear stain DAPI (top panel; blue), characteristic DOX fluorescence (middle panel; red) and merged images (lower panel). Scale bars are 20  $\mu\text{m}$  for all images.



**Fig. S11:** Quantification of apoptosis by Annexin-V/PI double staining and flow cytometry. Dot plot diagrams of HeLa cells incubated with DOX-loaded BDAP-PEG (DLC =  $17.60 \pm 1.5\%$ ) for 1, 12 or 24 h at pH 6.5 and 37 °C.

In order to provide more detailed material properties, CMC and DLS measurements were employed to characterize the self-assembly behavior of difunctional hexyl-terminated PEG (BC6-PEG, Fig. S12) in water. Fig. S13 shows that aqueous BC6-PEG solution with a broad range of concentrations between 1 and  $10^{-5}$  mg/mL did not exhibit a CMC transition. However, BDAP-PEG exhibited a clear CMC at 0.005 mg/mL, suggesting that the DAP moieties within BDAP-PEG significantly affected the amphiphilicity and molecular motion of the PEG backbone in water. DLS revealed that BC6-PEG did not exhibit micellar aggregates, whereas BDAP-PEG exhibited a mean hydrodynamic diameter of  $53 \pm 15$  nm (Fig. S14), indicating introduction of DAP groups into the PEG chain ends facilitated the formation of nanosized micelles.



**Figure S12:** <sup>1</sup>H NMR spectrum of BC6-PEG in CDCl<sub>3</sub>.

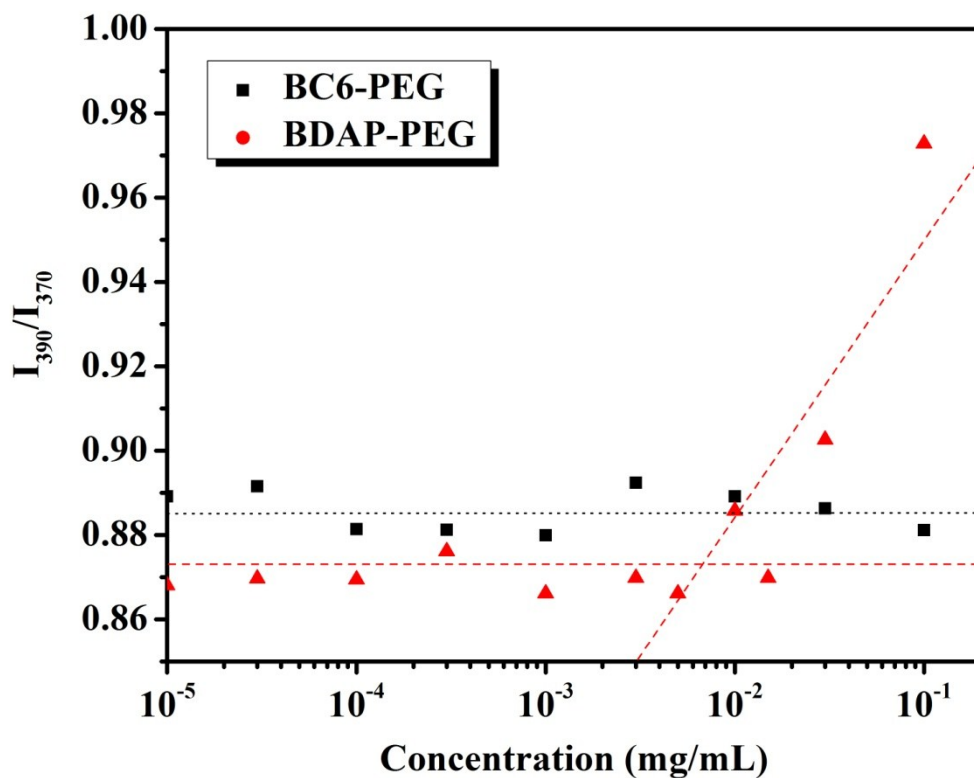


Figure S13: CMC determination for BC6-PEG and BDAP-PEG.

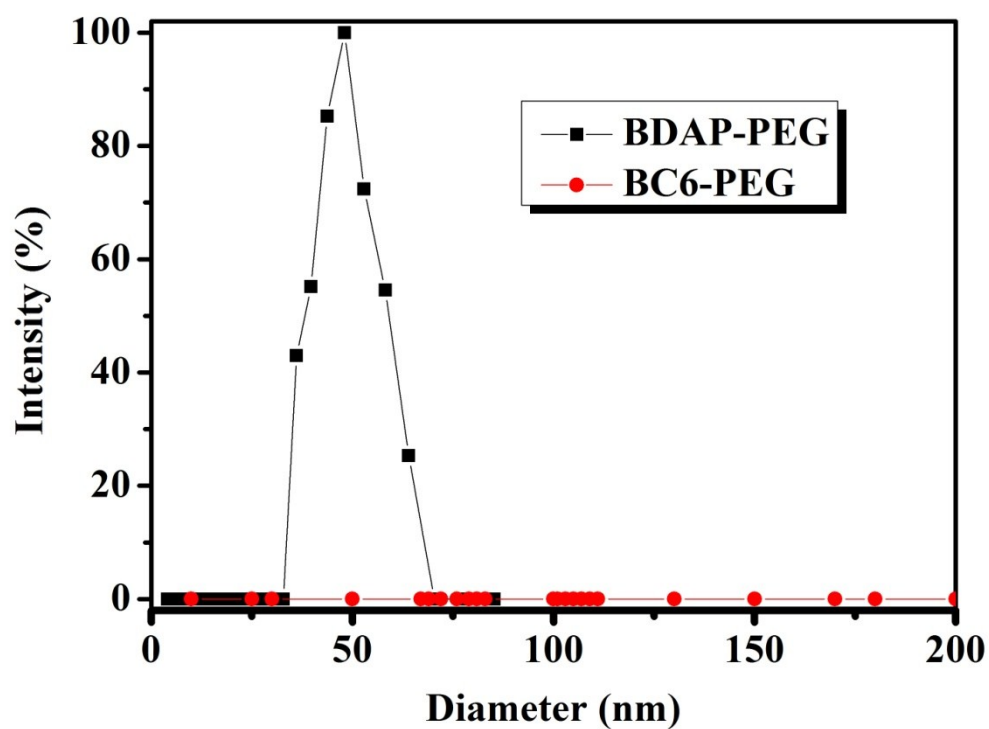


Figure S14: DLS analyses of 1.0 mg/mL solutions of BC6-PEG and BDAP-PEG in aqueous solution.