Electronic Supplementary Material (ESI) for New Journal of Chemistry.

SUPPORTING INFORMATION

Drug encapsulation and release with a nonionic amphiphilic calix[4]pyrrole

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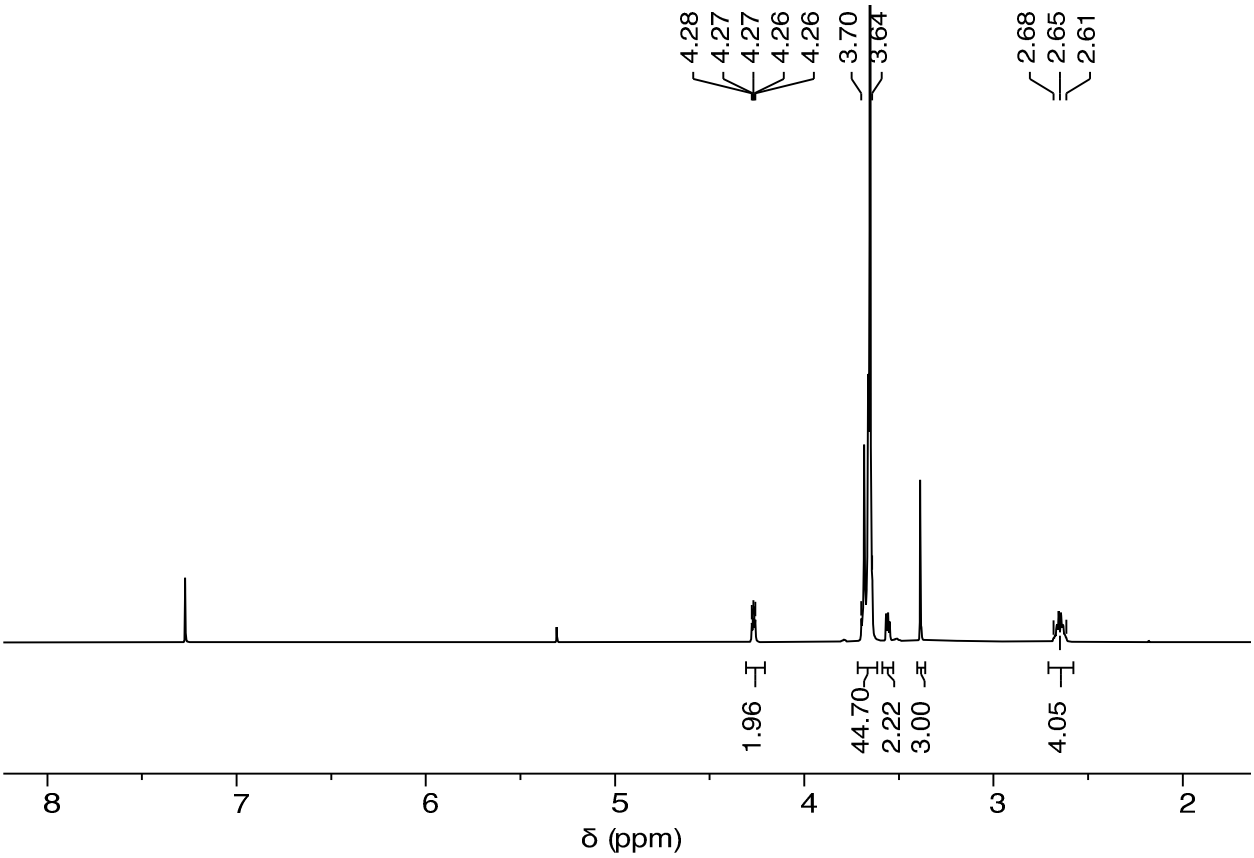


Fig S1. ^{1}H NMR (500 MHz) spectrum of mPEG-COOH recorded in $CDCl_3$.

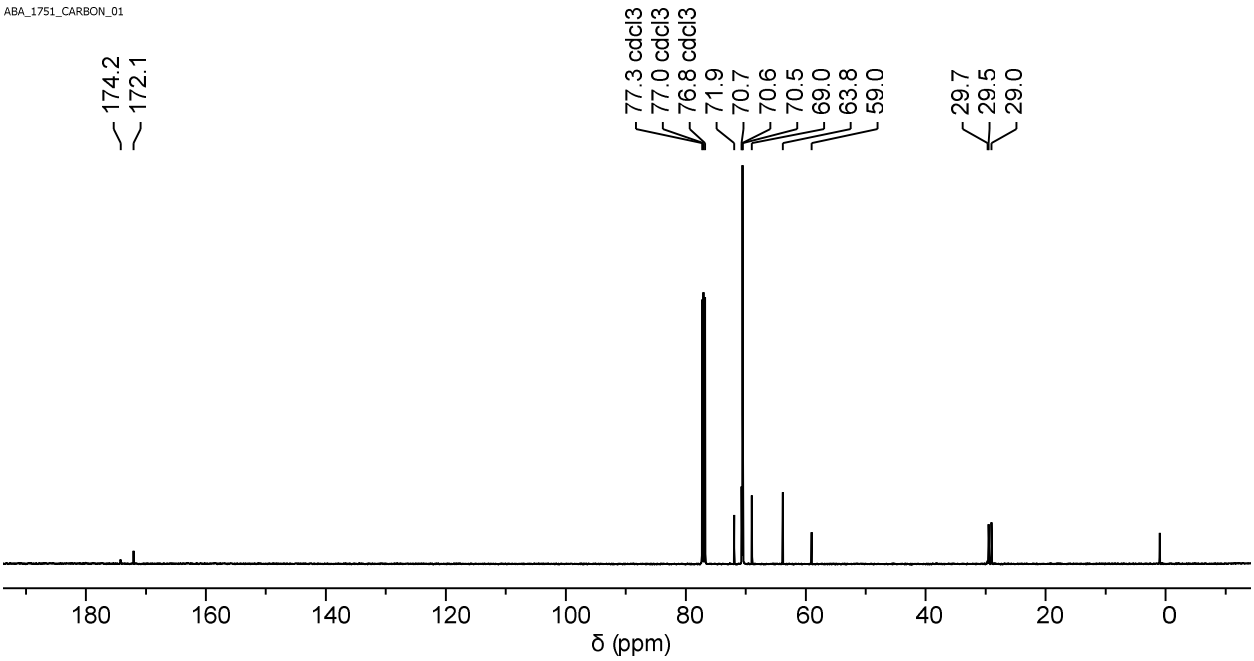


Fig S2. ^{13}C NMR (126 MHz) spectrum of mPEG-COOH recorded in $CDCl_3$.

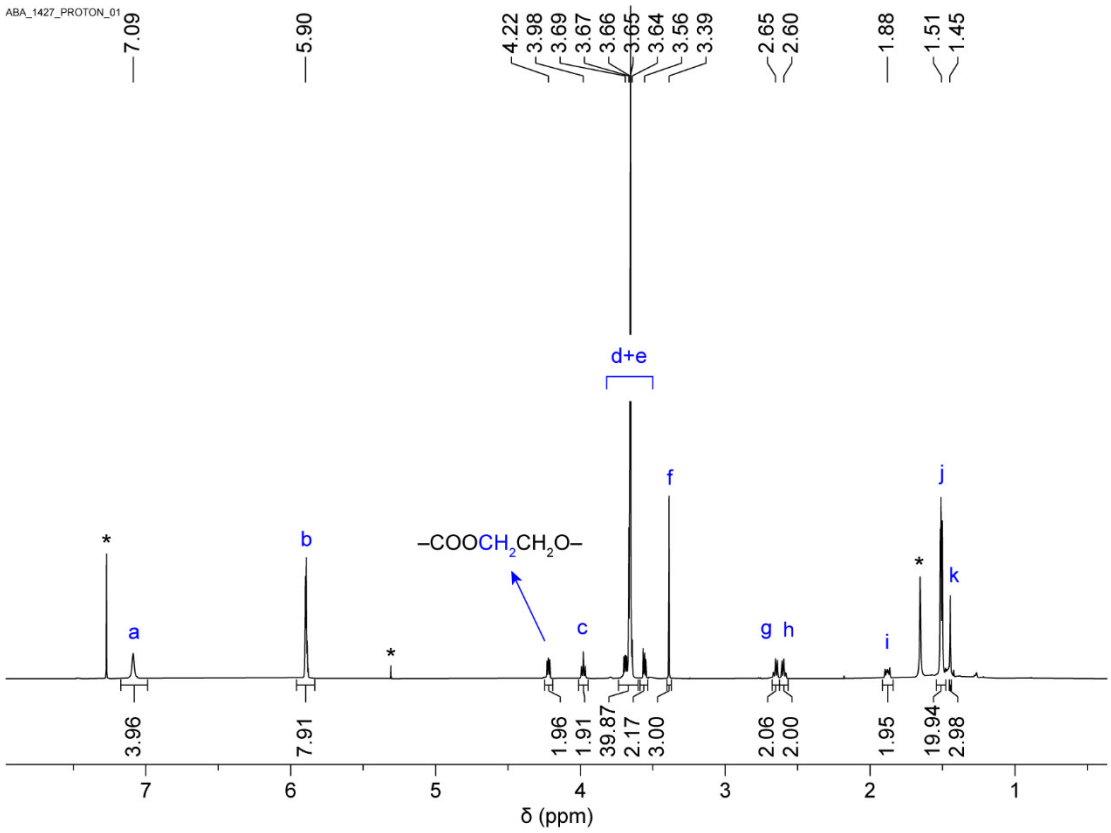


Fig S3. ^{1}H NMR (500 MHz) spectrum of **C4P-PEG** recorded in $CDCl_3$.

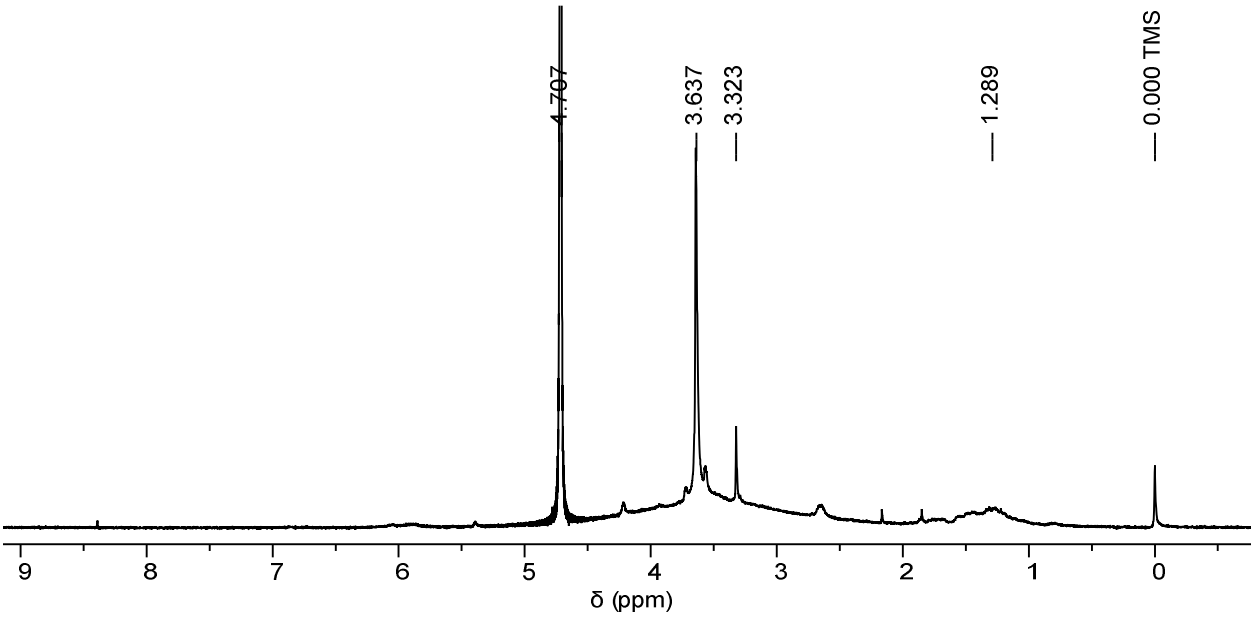


Fig S4. ^{1}H NMR (500 MHz) spectrum of **C4P-PEG** recorded in D_2O.

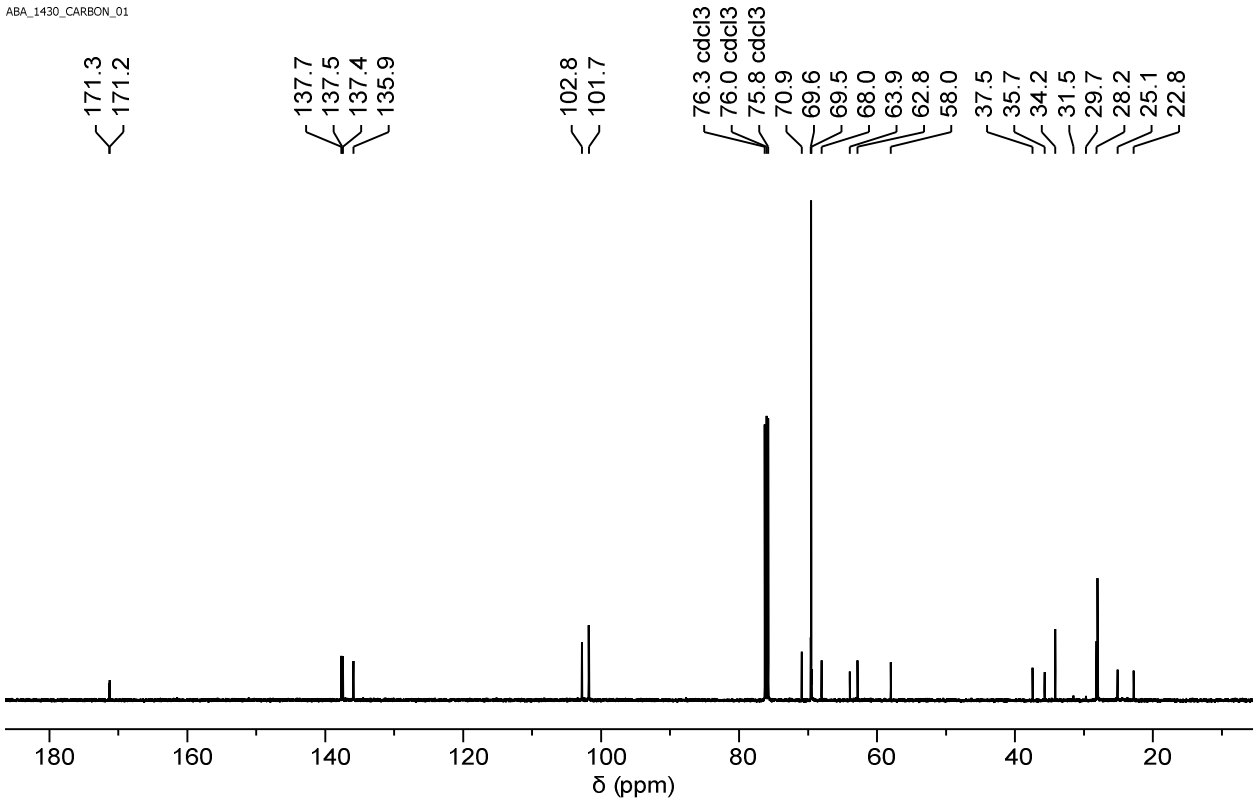


Fig S5. ^{13}C NMR (126 MHz) spectrum of **C4P-PEG** recorded in $CDCl_3$.

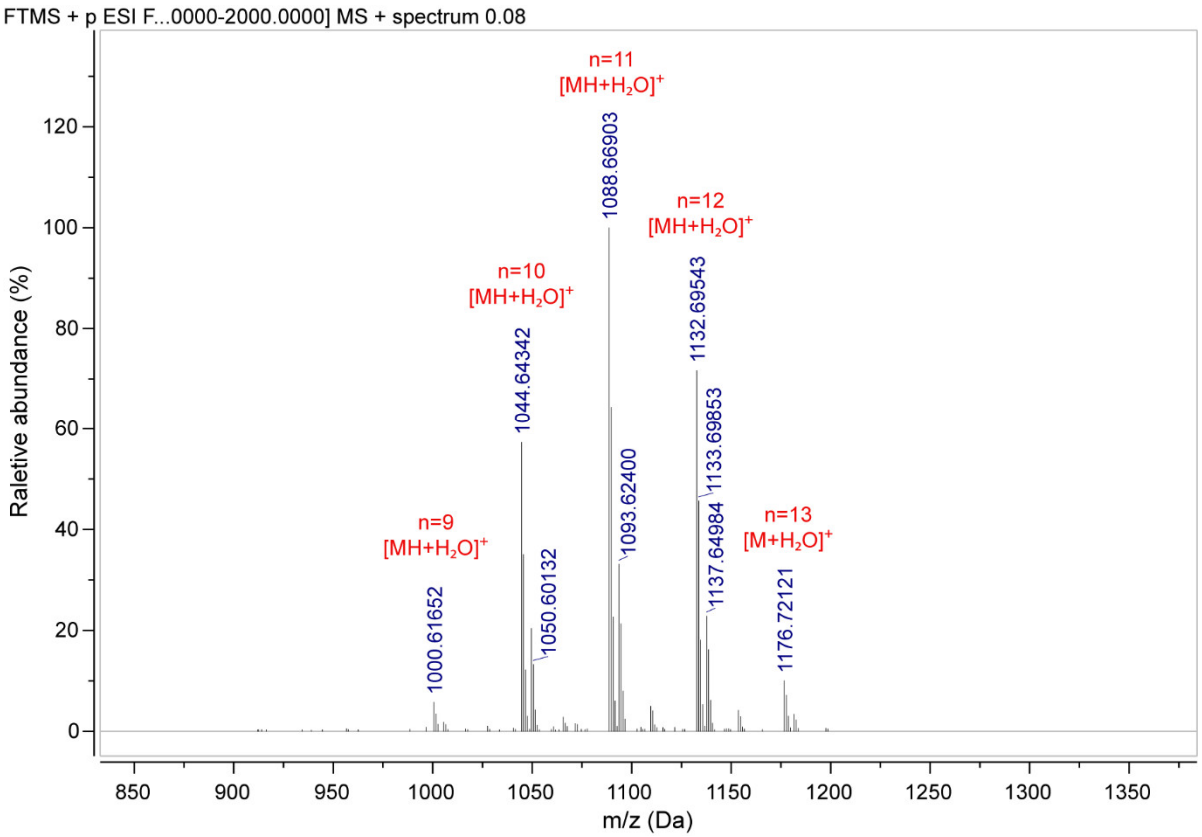


Fig S6. HR-ESIMS spectrum of **C4P-PEG**.

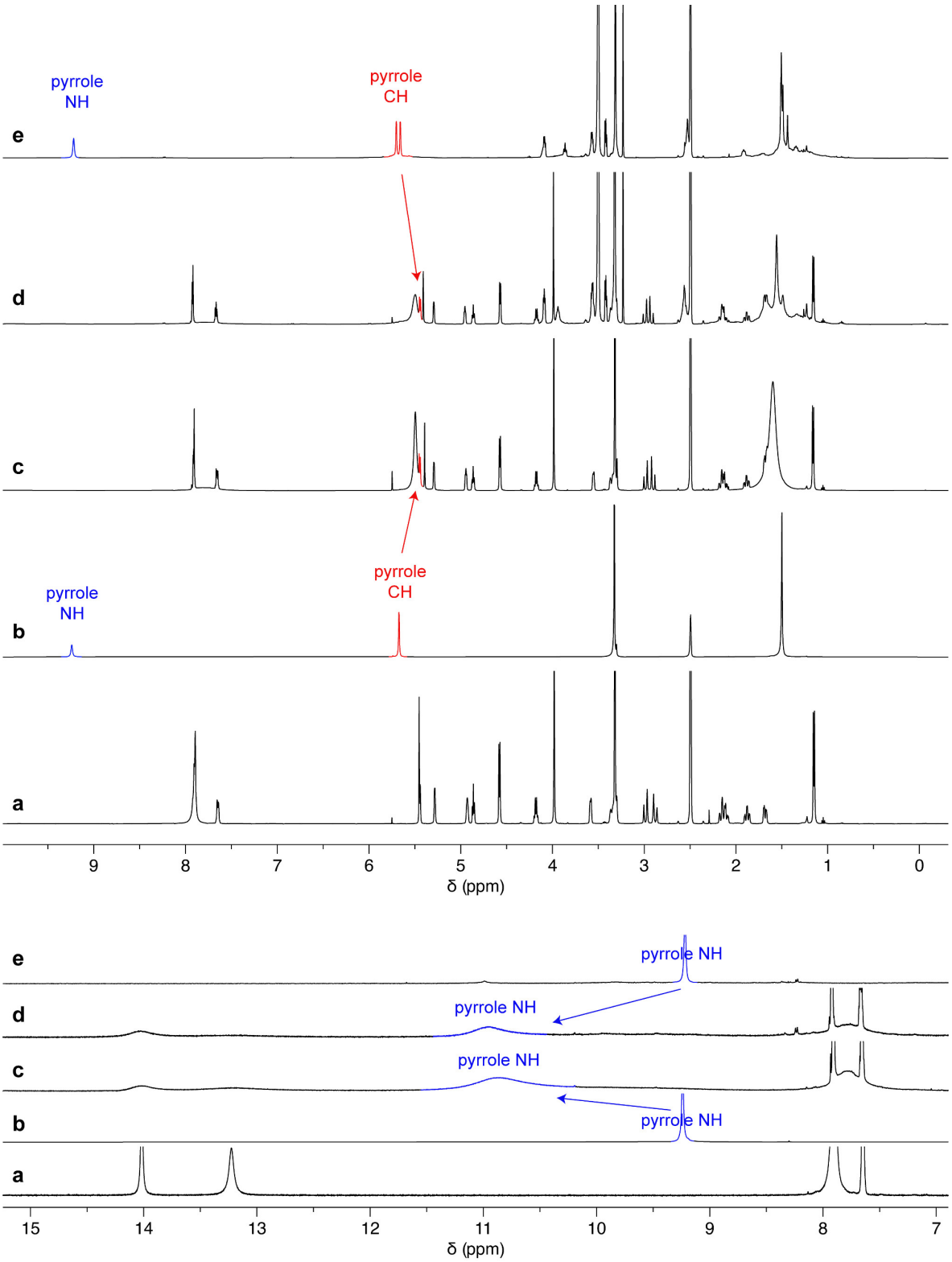


Fig S7. ^{1}H NMR spectra (500 MHz) of (a) DOX, (b) **C4P**, (c) **C4P** + DOX, (d) **C4P-PEG** + DOX, and (e) **C4P-PEG** recorded in DMSO-d_6.

FTIR Spectra

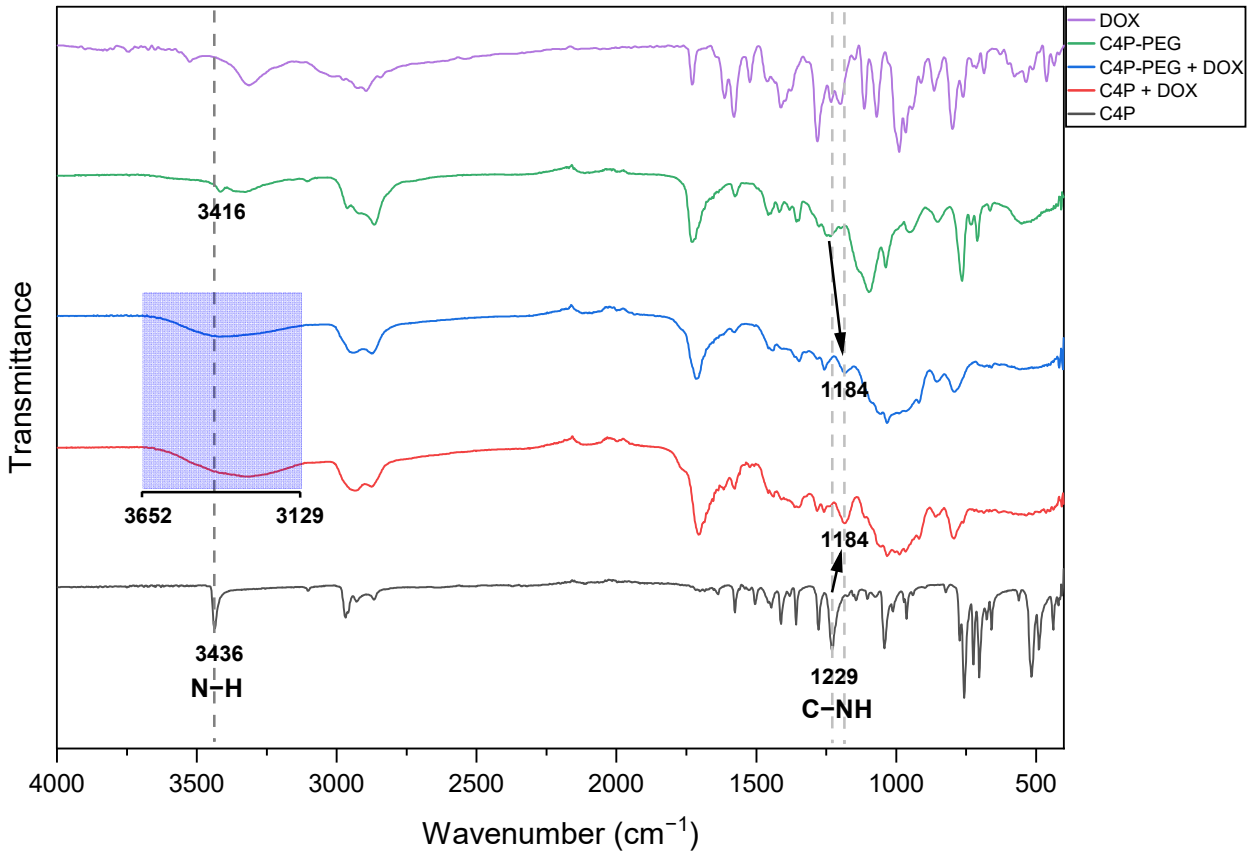


Fig S8. Stacked FTIR spectra of DOX, **C4P**, **C4P**+DOX, **C4P-PEG**, and **C4P-PEG**+DOX.

UV-Vis Spectra

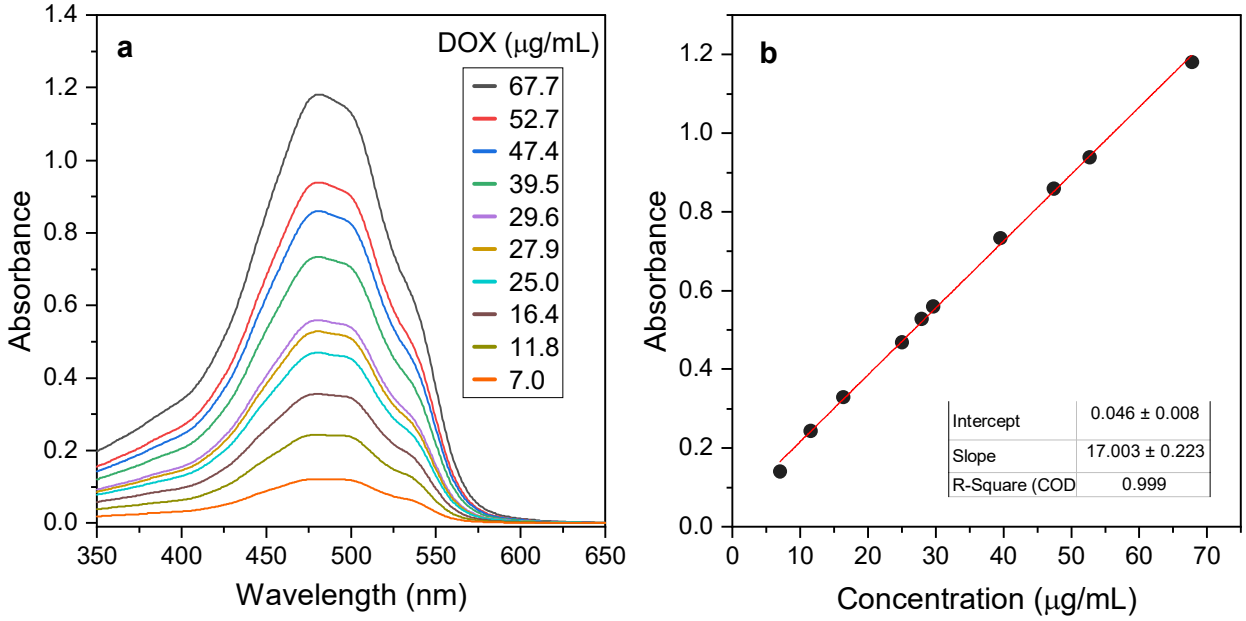


Fig S9. (a) UV-vis spectra of DOX in DMSO at varying concentrations and (b) the corresponding calibration curve generated from the absorbance values at 593 nm.

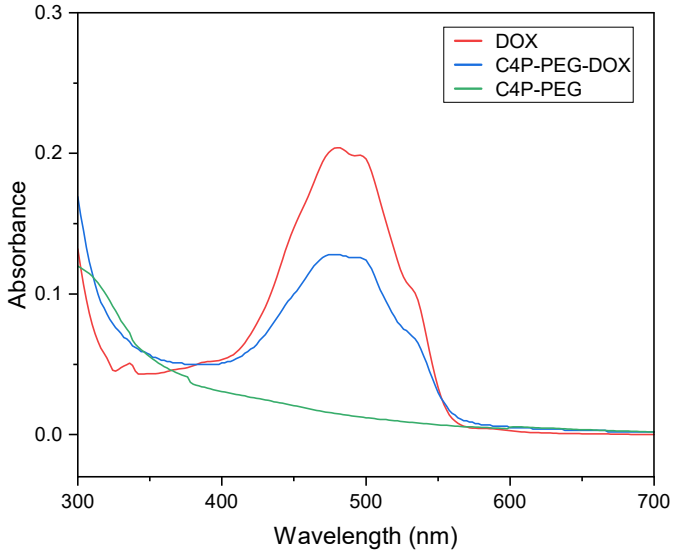


Fig S10. UV-vis spectra of **C4P-PEG**, DOX (before drug loading) and **C4P-PEG-DOX** (after drug loading).

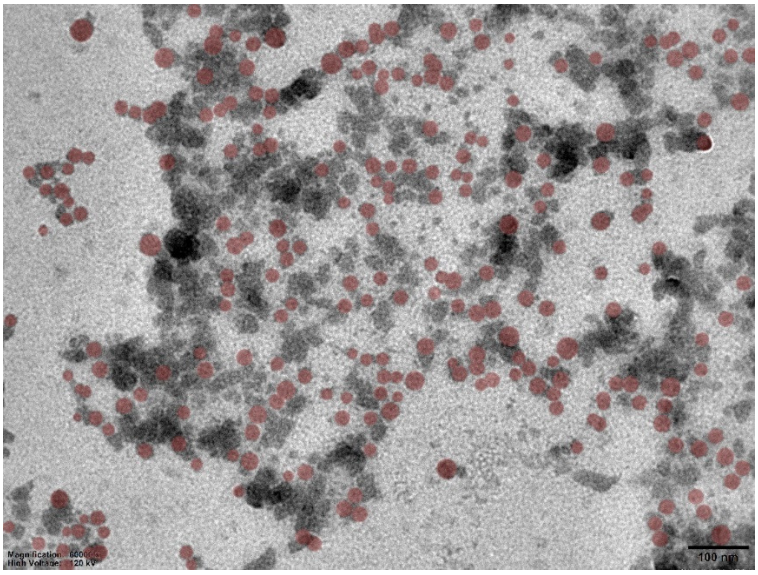


Fig S11. TEM image of **C4P-PEG** showing the selected aggregates (252 points) for the calculation of size distribution.

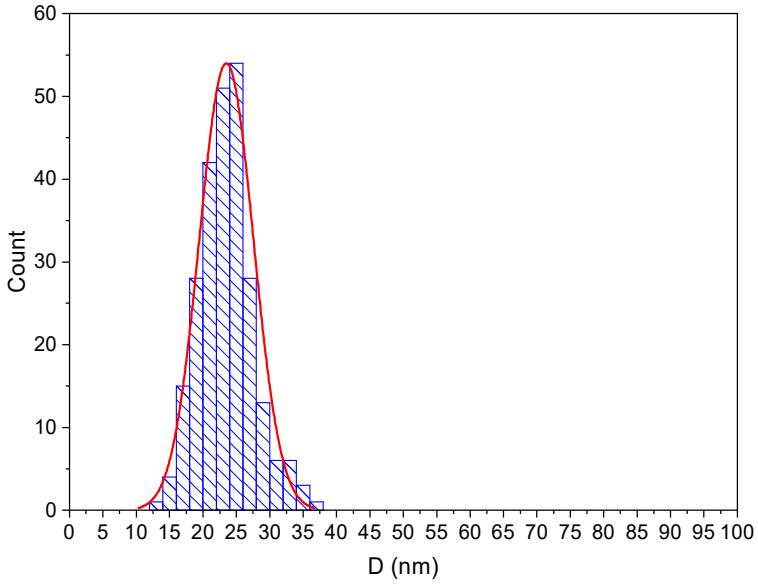


Fig S12. Size distribution of **C4P-PEG** based on the data obtained from Fig. S11.

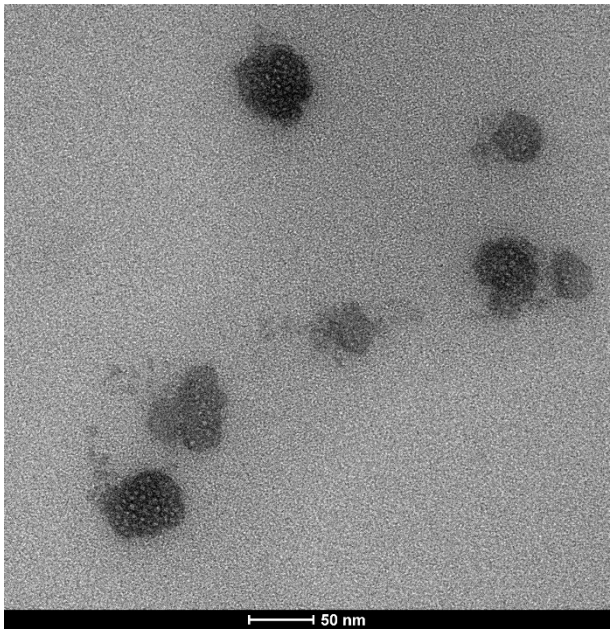


Fig S13. TEM image of **C4P-PEG-DOX**.

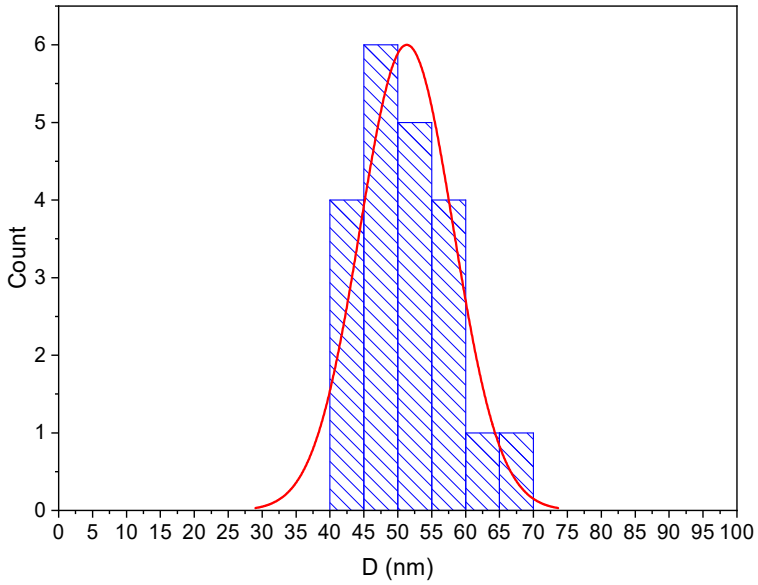


Fig S14. Size distribution of **C4P-PEG-DOX** based on the data obtained from Fig. S13.

Binding Constant Determination and NOESY Analysis

To determine the stoichiometry and binding constant between calix[4]pyrrole core of **C4P-PEG** and DOX·HCl (through Cl^- binding), ^1H NMR titrations were performed in DMSO-*d6* solutions which had a constant concentration of **C4P-PEG** (6.28 mM) and varying concentrations of DOX·HCl (Fig S16). By a non-linear curve-fitting method, the association constant between **C4P-PEG** and Cl^- anion of DOX·HCl was determined to be $1.55 \times 10^3 \pm 148\ M^{-1}$ by monitoring the pyrrole-CH protons of **C4P-PEG** (Fig. S15 and Fig. S16). The complexation stoichiometry was found to be 1:1 as shown in Fig. S17.

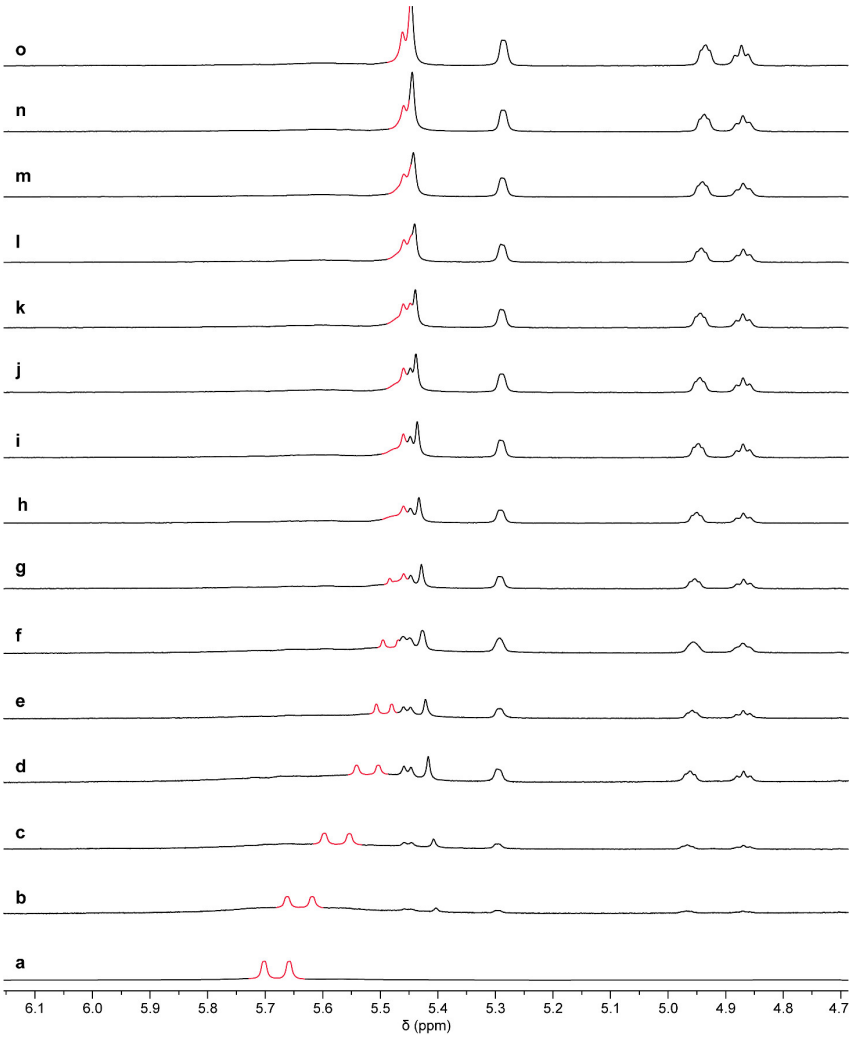
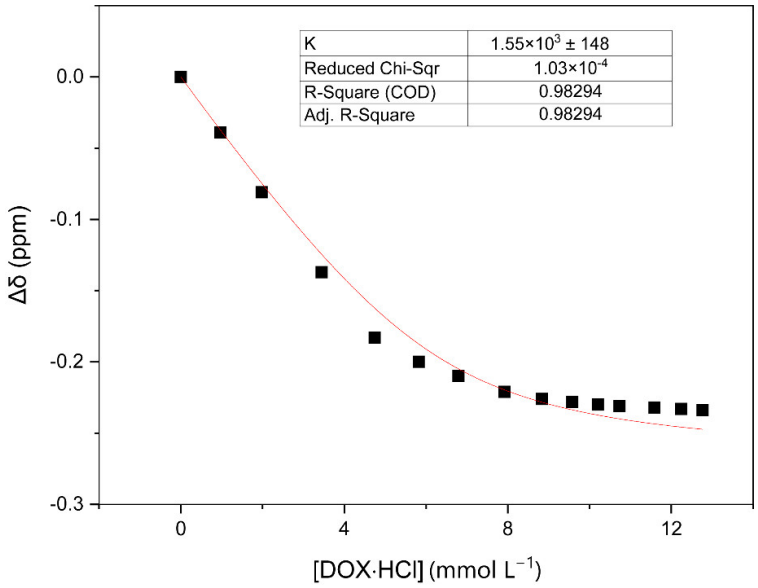


Fig S15. Partial ^1H NMR spectra (500 MHz, DMSO-*d6*, 25 °C) of **C4P-PEG** (6.28 mM) upon addition of DOX·HCl at 0.00, 0.98, 1.98, 3.45, 4.75, 5.82, 6.79, 7.92, 8.83, 9.58, 10.20, 10.74, 11.59, 12.24, 12.76 mM concentrations from bottom to top.



$$\Delta\delta = \Delta\delta_{max}\frac{[1+K([H]_0+[G])]-\sqrt{[1+K([H]_0+[G])]^2-4K^2[H]_0[G]}}{2K[H]_0}$$

Fig S16. Chemical shift changes of pyrrole CH protons (initially at 5.68 ppm) belonging to **C4P-PEG** (6.28 mM) upon incremental addition of DOX·HCl. The red solid line was obtained from a non-linear curve fitting using the equation provided under the figure.

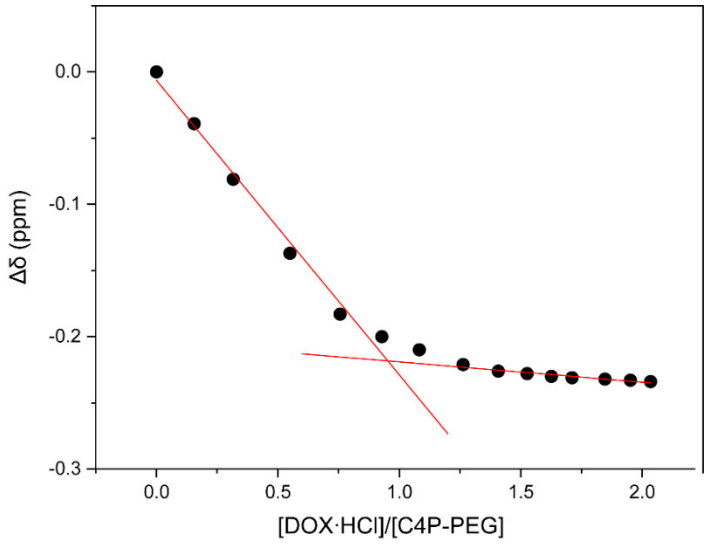


Fig S17. Molar ratio plot for the interaction of **C4P-PEG** with DOX·HCl, indicating a 1:1 stoichiometry.

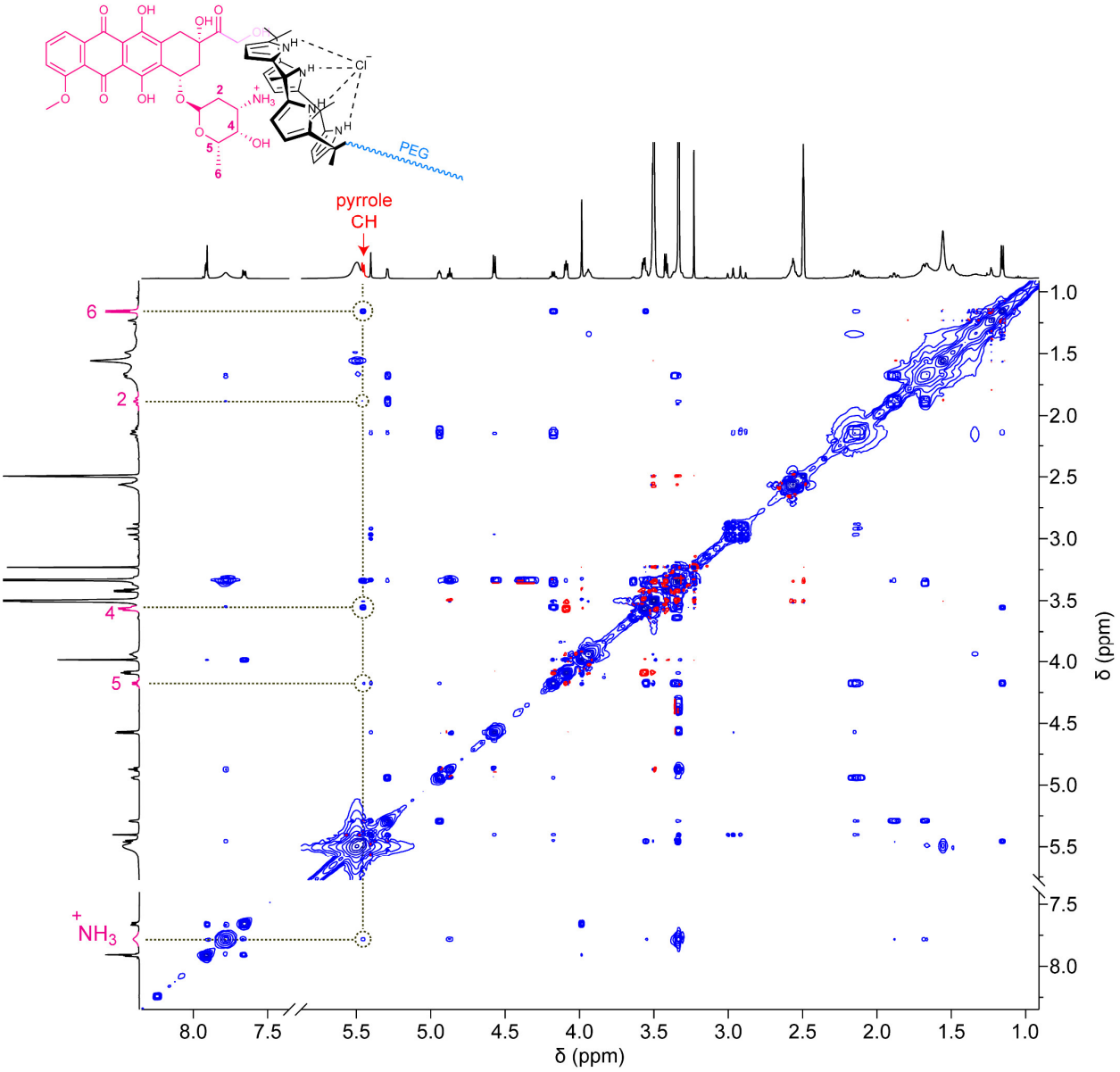


Fig S18. NOESY NMR spectrum of **C4P-PEG** + DOX·HCl (1:1) recorded in DMSO-*d6* containing 1.5% (wt) H_2O. This spectrum shows the concurrent complexation of **C4P** core of **C4P-PEG** with $–NH_3^+$ unit of DOX·HCl (see Fig S7 for peak shift changes in the case of NH···$Cl^–$ interaction) through cation–π interaction.

DLS and Zeta Potential Measurements

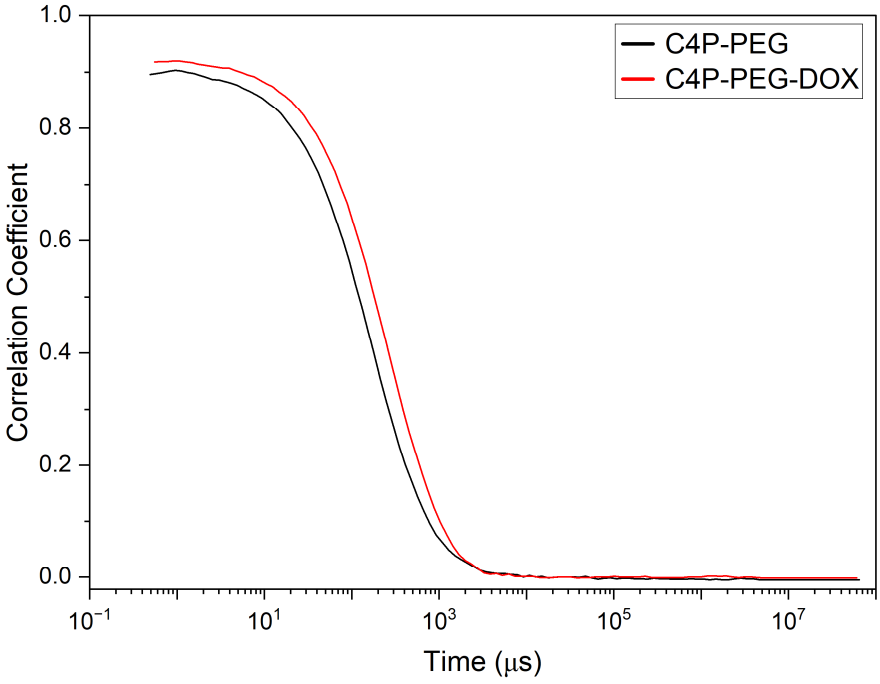


Fig S19. Correlation coefficient plots for **C4P-PEG** and **C4P-PEG-DOX** during DLS measurements.

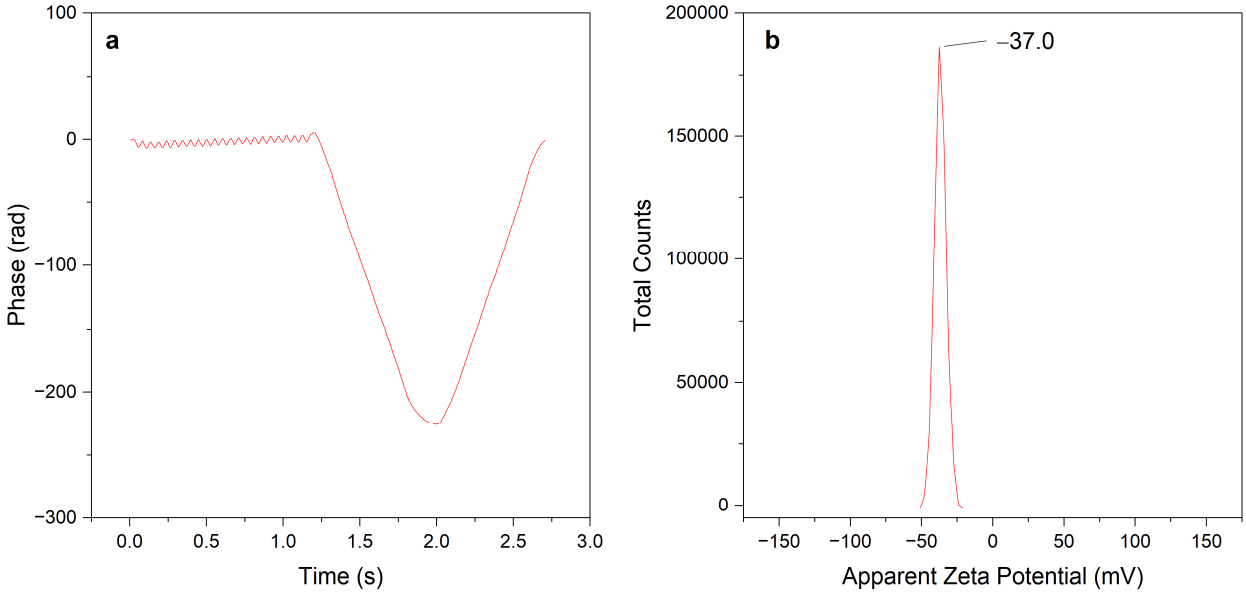


Fig S20. (a) Phase plot and (b) zeta potential distribution of **C4P-PEG**.

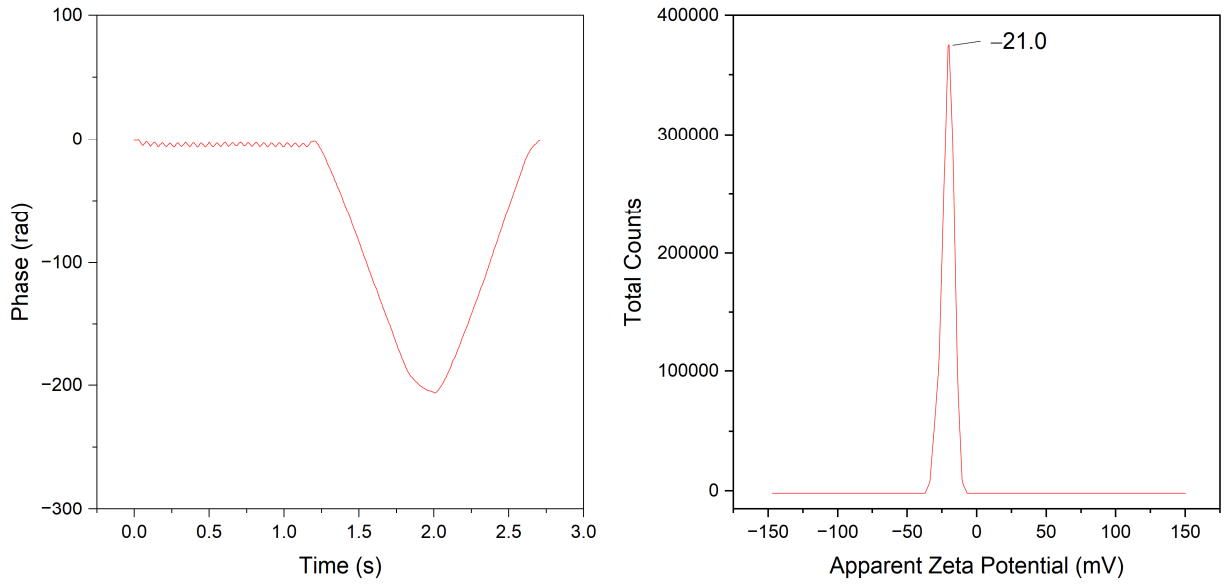


Fig S21. (a) Phase plot and (b) zeta potential distribution of **C4P-PEG-DOX**.

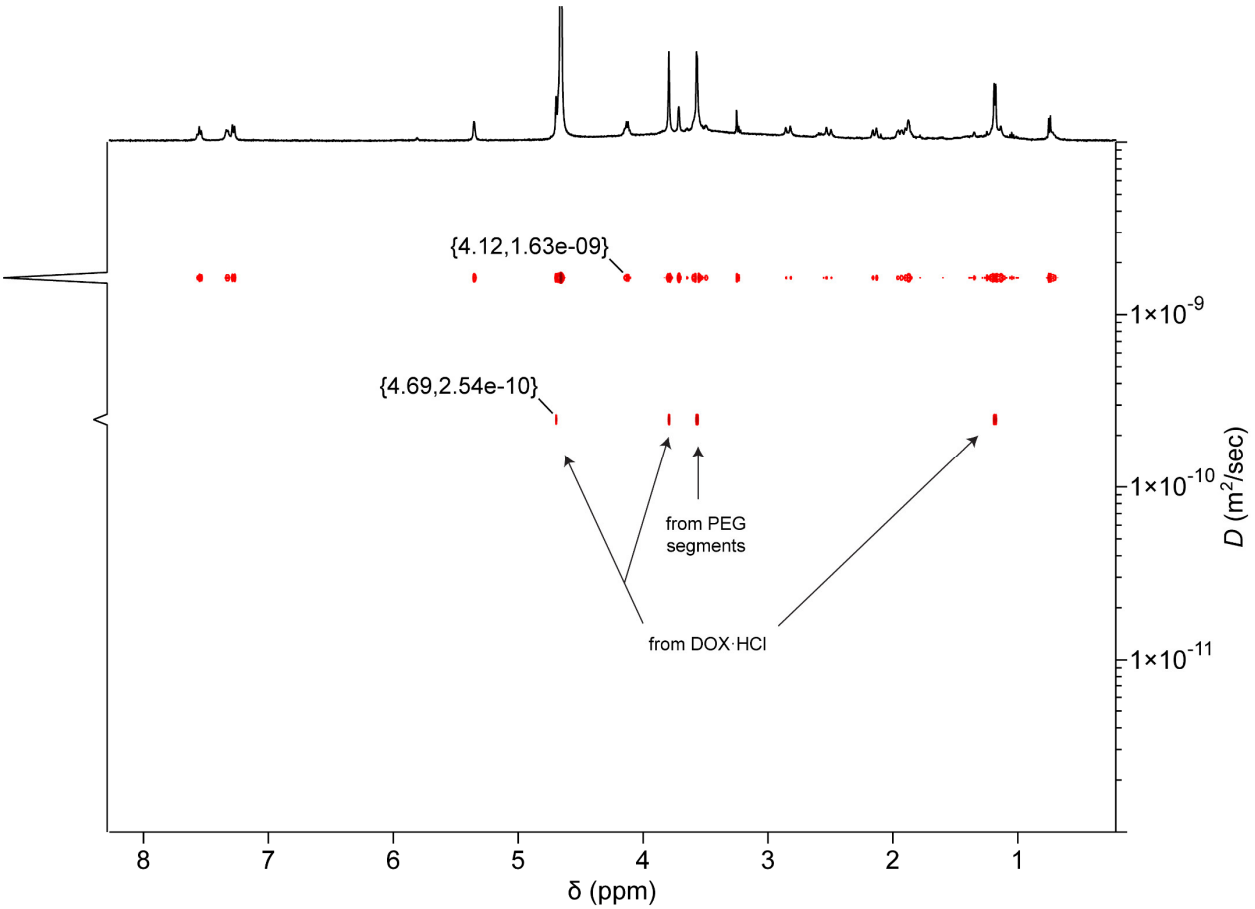


Fig S22. DOSY NMR spectrum of **C4P-PEG** + DOX·HCl (1:1) recorded in D_2O (2.69 mM, 25 °C), showing the free (big trace) and encapsulated (small trace) DOX·HCl moieties.