Electronic Supplementary Information

Polysaccharide Nano-vesicular Multidrug Carrier for Synergistic Killing of Cancer Cells

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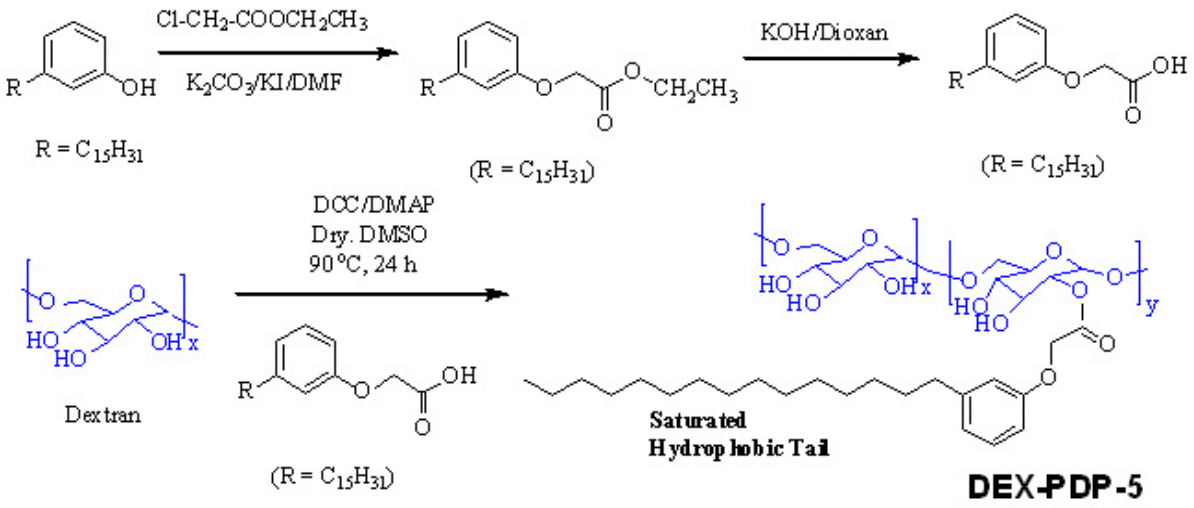

SS-1:Synthetic Scheme of DEX-PDP

Note: DEX-PDP-5 was synthesized by using previously published procedure (Ref. Pramod, P.S. *et al*. *Biomacromolecules*, **2012**, *13*, 3627-3640.) Dextran and carboxylic functionalized pentadecylphenol (0.5 equivalents to anhydro-glucose unit) was coupled via DCC/DMAP route to obtain DEX-PDP\ ^{1}H NMR, ^{13}C NMR and HSQC data were as similar to that of earlier report.

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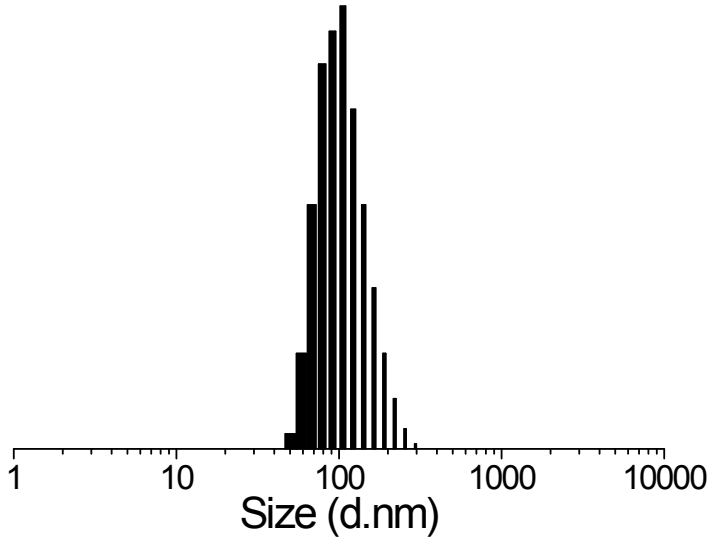
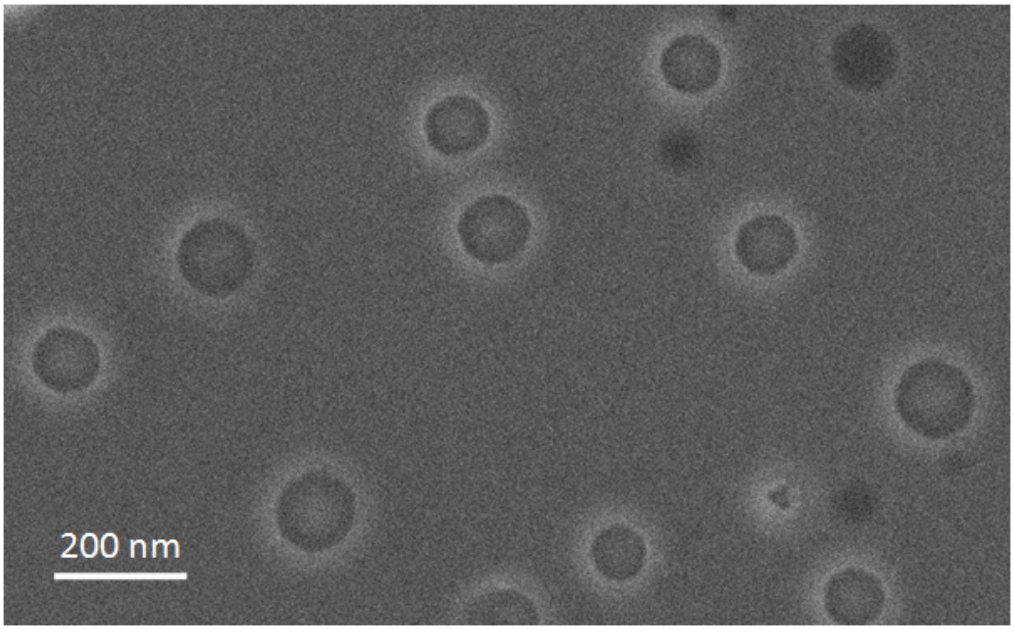


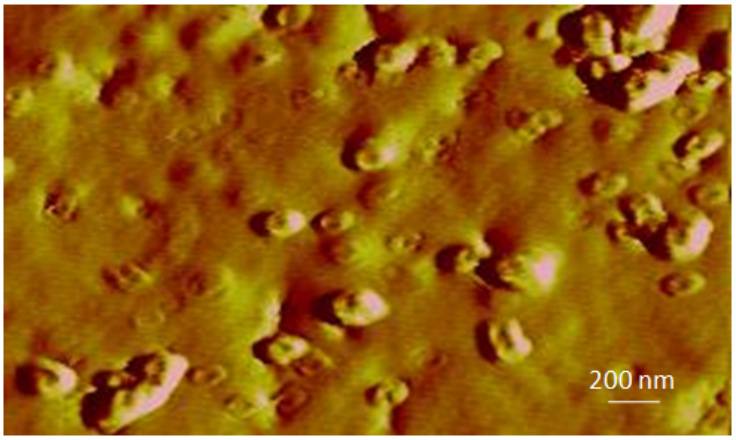
SF-1: *DLS size distribution of DEX-PDP*

Note: Dynamic light scattering (DLS) analysis of DEX-PDP was determined in PBS buffer showed mono modal distribution with average diameter of 120 nm. Thus hydrodynamic radus was calculated as 60 nm.



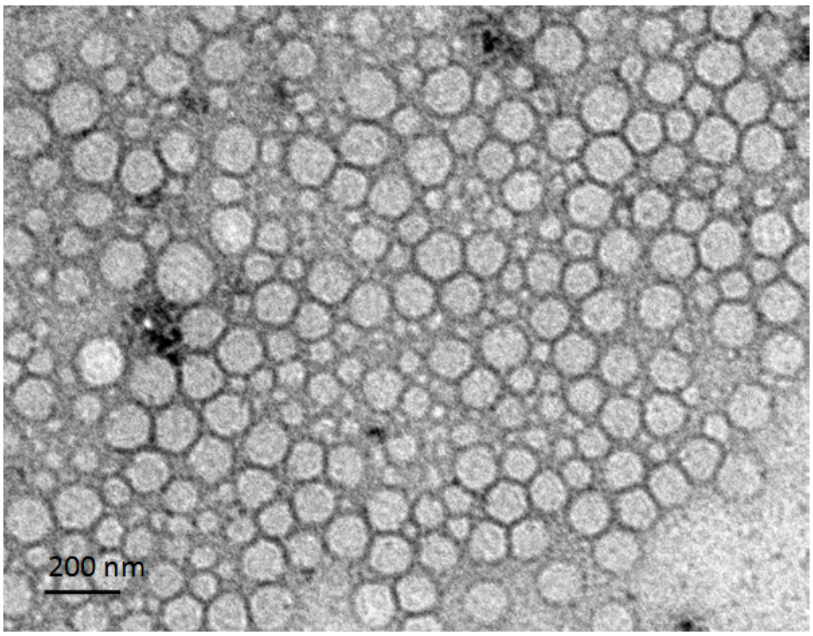
SF-2: *FE-SEM image of DEX-PDP*

Note : FE-SEM analysis of DEX-PDP was carried out by drop casting sample on silicon wafer and result revealed the formation of spherical hollow structure having a diameter of 110±10 nm. This morphology was similar to our earlier report.[37]



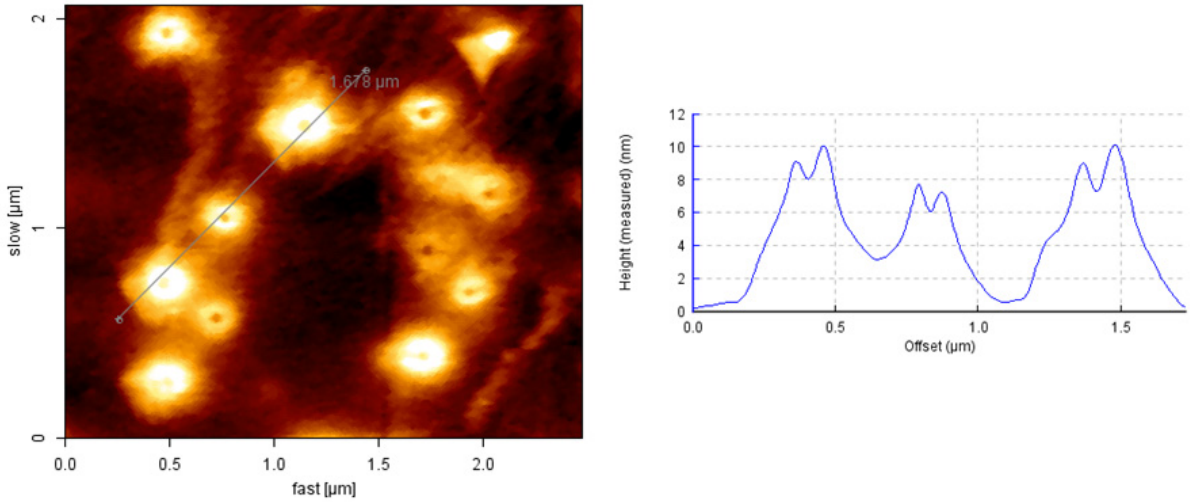
SF-3: *AFM image of DEX-PDP*

Note: Donut shaped structure obtained in AFM analysis provided more conclusive evidence for the vesicular structure formed form the DEX-PDP-5. This specialized geometry is attributed to the differential response imparted from the harder periphery and soft interior of vesicle. Shape and size were similar our earlier report.[37]



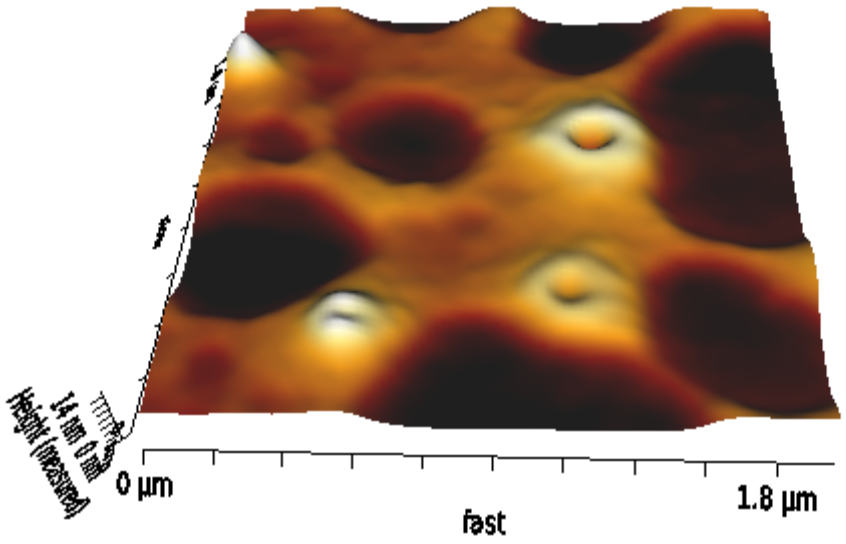
SF-4: *TEM image of DEX-PDP*

Note: TEM analysis of DEX-PDP-5 performed by drop-casting sample on formvar coated copper grid and the result showed hollow spherical object with molecularly thin hydrophobic membrane, further substantiated the vesicular geometry. This morphology was similar to our earlier report.[37]

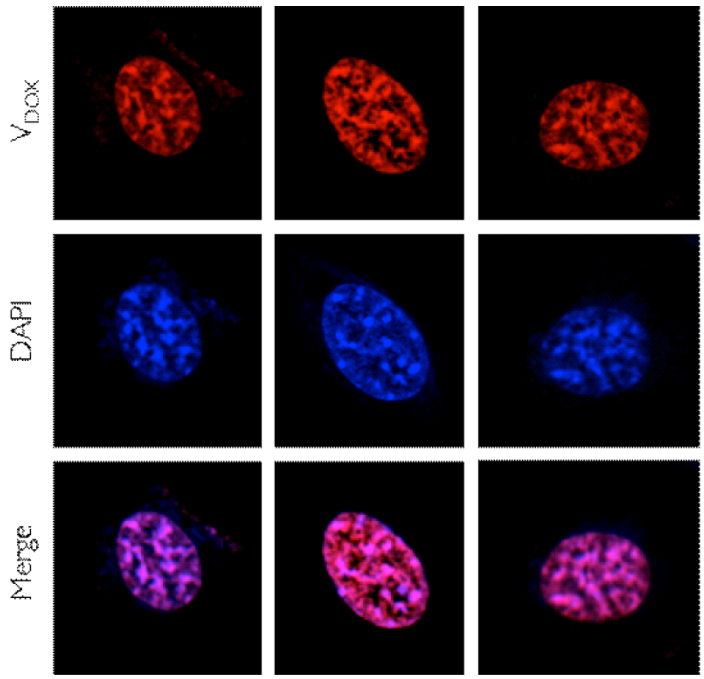


SF-5: *AFM image of* $V_{DOX+CPT}$

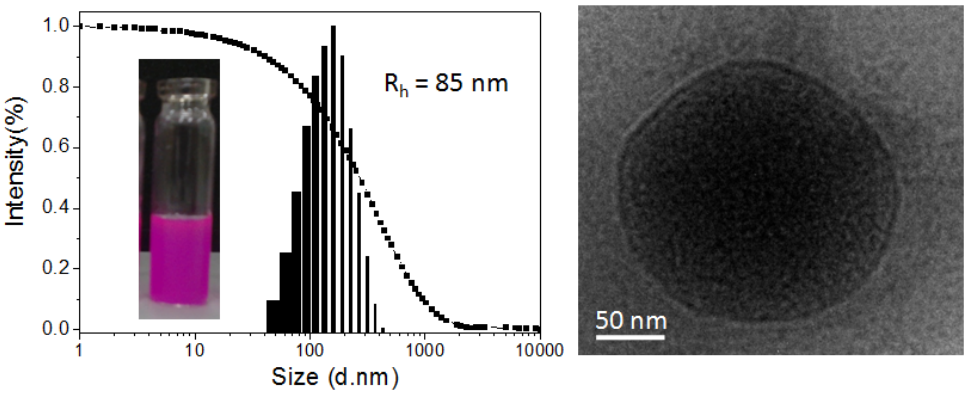
Note: AFM analysis of DOX and CPT dual loaded (both 1:4 and 4:1) system was performed using tapping mode. For this purpose sample was drop casted on a freshly cleaved mica surface and air dried. The vesicular structure obtained in imaging was further proved by the cross sectional analysis. The surface profile exhibited higher periphery and lower centre having a diameter of 200 ±20 nm and height of 10±3 nm.



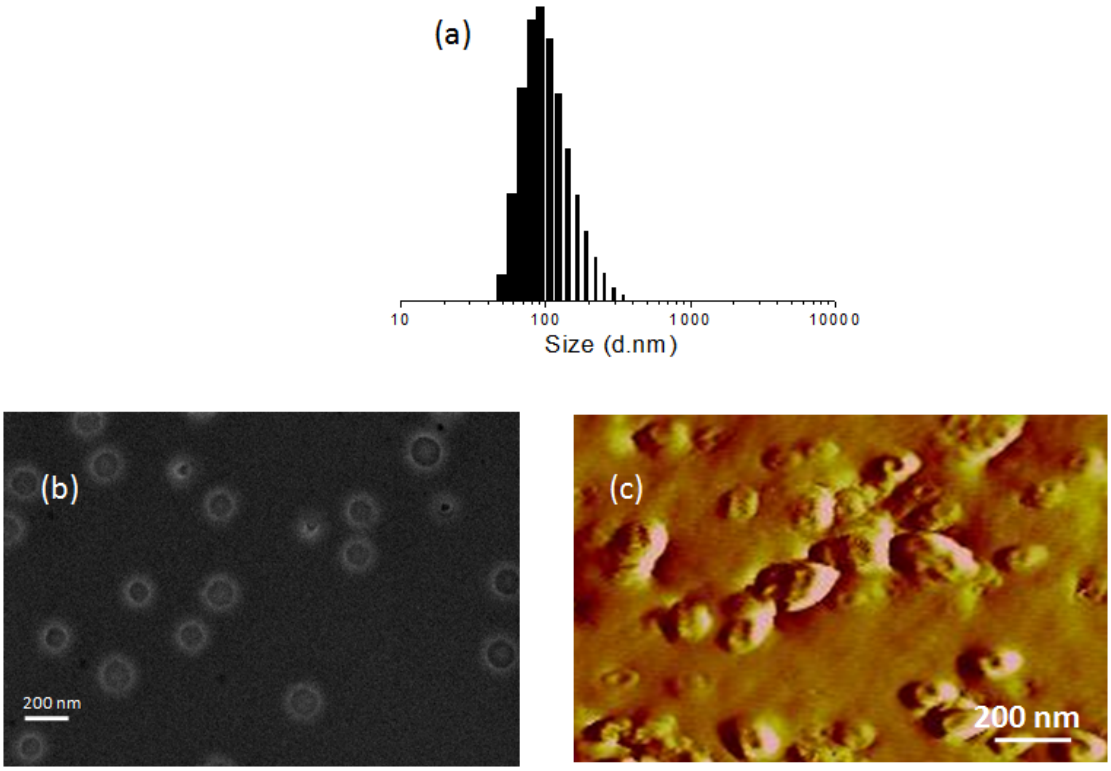
SF-6: *AFM image of* V_{DOX}



SF-7 Nuclear Localization and overlap between DOX from V_{DOX} and DAPI staining

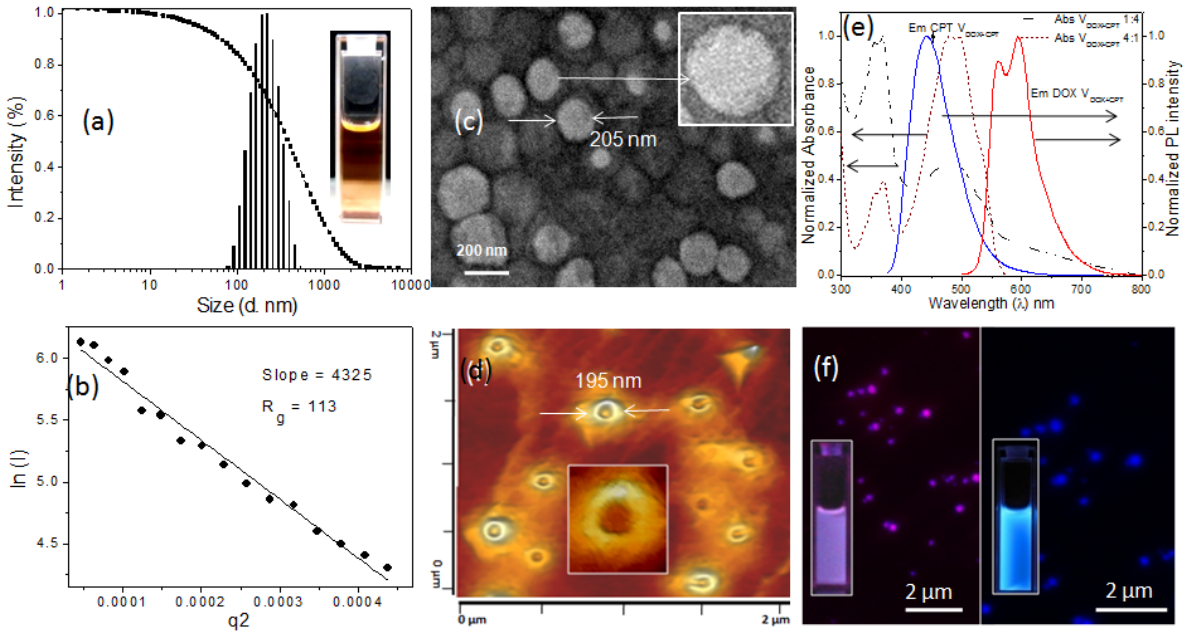


SF-8 : *DLS histogram (a), HR-TEM image (b) of V_{RHO}. Vial inset in (a) showed Rhodamine loaded vesicle solution.*

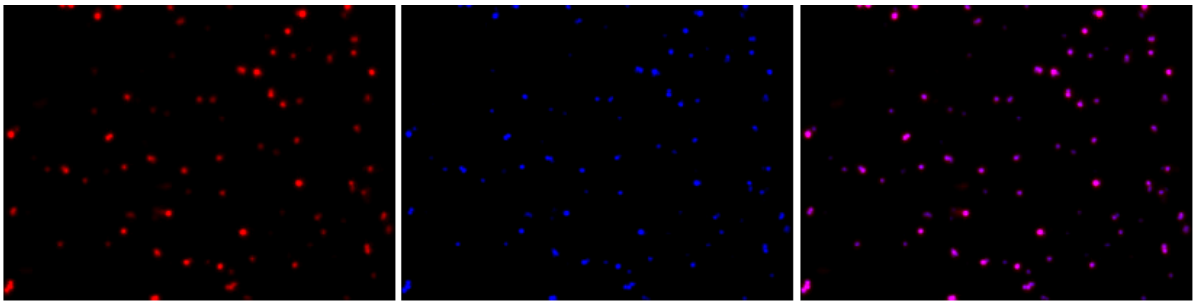


SF-9: *DLS histogram (a), FE-SEM image (b) and AFM image (c) of* V_{CPT}

Note: The retention of vesicle structure of CPT loaded DEX-PDP-5 was proved by DLS, FE-SEM and AFM analysis. Hydrodynamic radius (R_h) was calculated from DLS as 60 nm. The FE-SEM (Hollow spheres)and AFM investigations (concavity in the structure) further corroborates the vesicle structure.

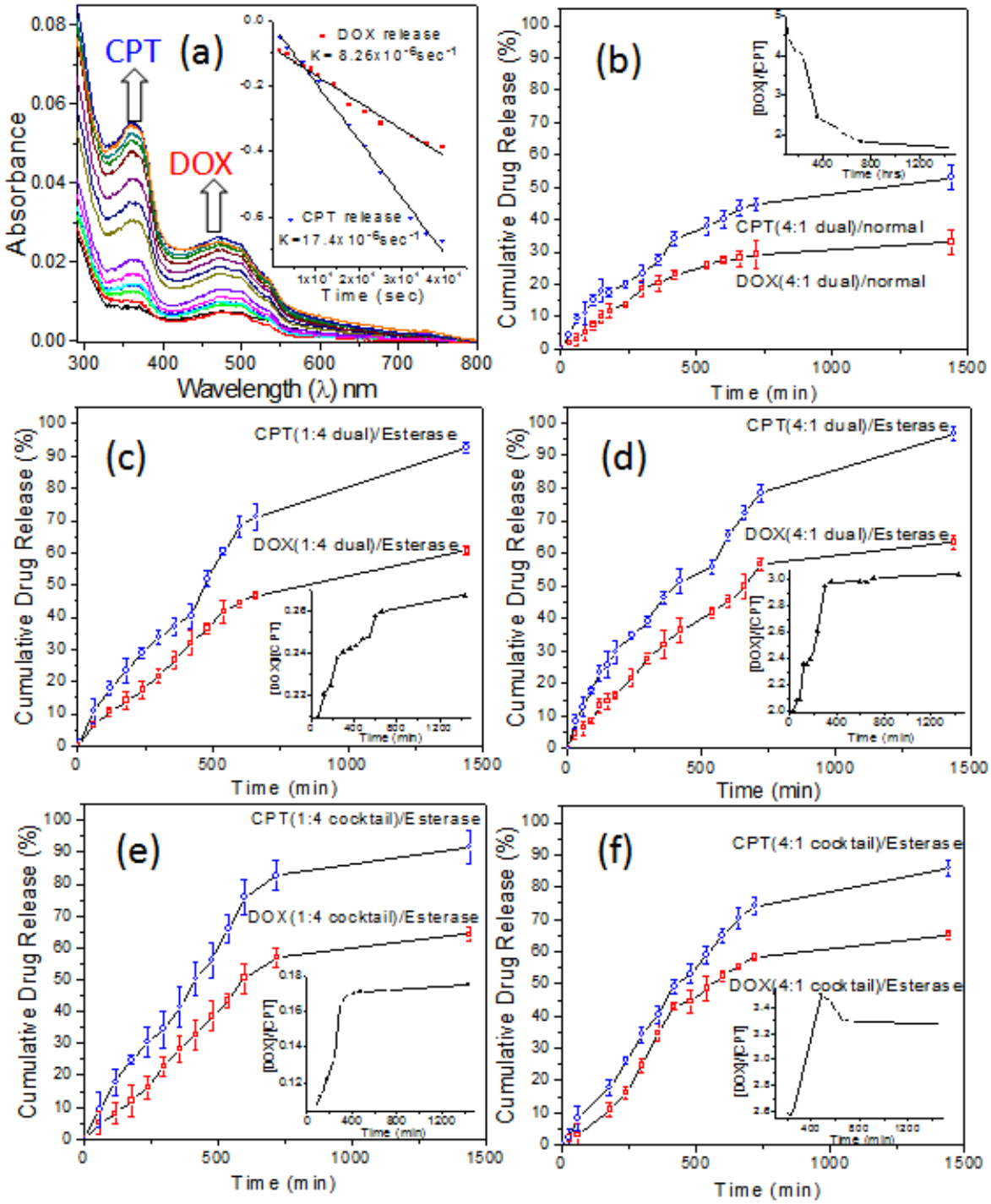


SF-10: *DLS histogram (a), SLS data (b,) HR-TEM image (c), AFM image (d), and absorbance and emission plot (e) of* $V_{DOX+CPT}$. *(f) Fluorescent micrographs of* $V_{DOX+CPT}$ *(pink) and* V_{CPT} *(blue). Insert in (c) and (d) shows magnified HR-TEM and AFM image of* $V_{DOX+CPT,}$ *The vials insert in (f) show the color of* $V_{DOX+CPT}$ *(pink) and* V_{CPT} *(blue) in PBS under hand held UV lamp.*

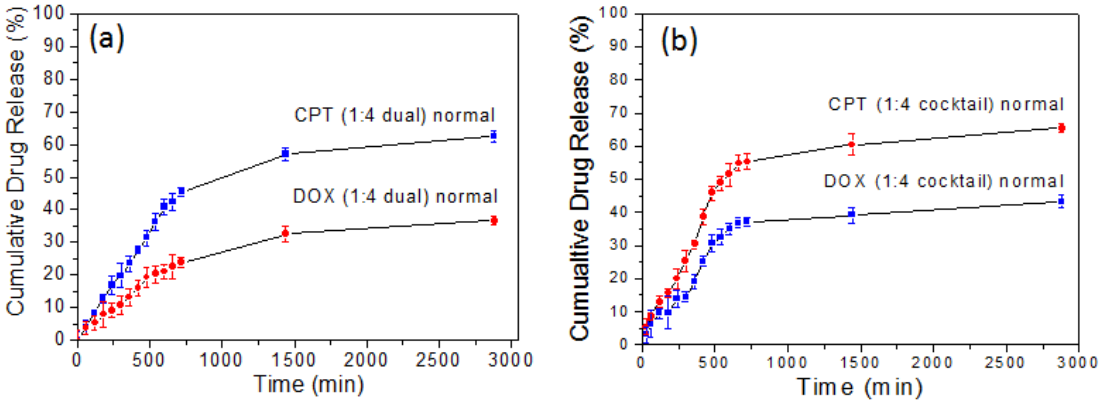


SF-11: *Fluorescent microscopic image of* $V_{DOX+CPT}$

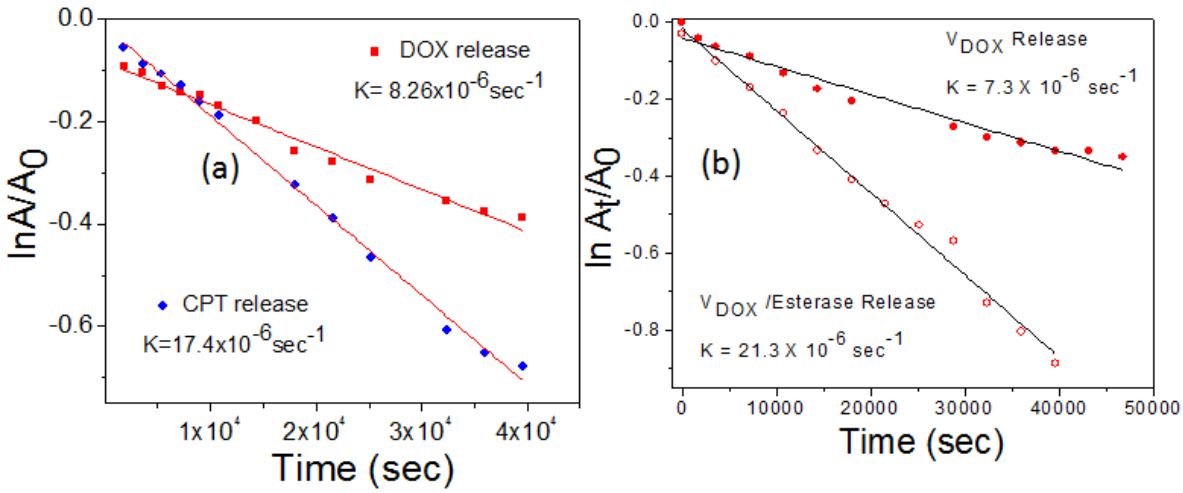
Note: The fluorescence microscopic images were taken multiple acquisition modes, where DEX-PDP-DOX-CPT system drop casted on a glass slide was observed through blue and red channels. The blue channel helped to make out the CPT content inside the vesicle and the red channel for DOX. The images acquired through blue as well as red channels from the same field were merged together and was appeared as pink coloured spot. This indicates that both blue and red molecules, ie. CPT and DOX were entrapped in the same position. This is characteristic feature of dual drug loaded system.



SF-12. (a) *Absorbance spectra of DOX and CPT released from* $V_{DOX+CPT}$*, (b) Cumulative drug release of* $V_{DOX+CPT}$ *(4:1) under normal physiological condition. Cumulative release of DOX and CPT in the presence of esterase enzyme for 1:4 dual drug loaded (c), 4:1 dual drug loaded (d), 1:4 cocktail (e) and 4:1 cocktail (f). Inset at (a) shows the ln At/Ao Vs time plot of* $V_{DOX+CPT}$ *(4:1). Inset at (b),(c),(d),(e) and (f) shows the corresponding mole ratio of DOX to CPT released at various time points.*



SF-13. *Cumulative drug release of DOX and CPT from 1:4 dual loaded and individual cocktail of vesicles under normal physiological conditions (pH 7.4 and 37 °C)*



SF-14: *ln A/Ao vs Time plot of DOX and CPT from $V_{DOX+CPT}$ 1:4(a) and DOX normal and DOX in the presence of esterase(b)*

Note: The release rate of DOX and CPT from the vesicles was described by using first order kinetics. The rate constant was determined from the slope of ln (A/A_0) vs Time plot, where A is amount of the drug retained after time 't' and A_0 is total initial amount of drug.

ST-1. Drug release kinetic parameters

Type of Loaded Vesicle	Release Profiles	
	Normal	Esterase
	k (μs^{-1})	k (μs^{-1})
V_{CPT}	15.3	43.4
V_{DOX}	7.3	21.3
$V_{DOX+CPT\ (4:1)}$	13.5 (CPT) 8.3 (DOX)	32.1 20.8
$V_{DOX+CPT\ (1:4)}$	12.9 (CPT) 6.3 (DOX)	30.7 20.3
$V_{DOX}+V_{CPT\ (4:1)}$	15.5 (CPT) 8.9 (DOX)	45.2 22.9
$V_{DOX}+V_{CPT\ (1:4)}$	14.9 (CPT) 8.4 (DOX)	44.1 21.8