

( Supplementary information )

**Enzyme/pH-Sensitive nanoparticles based on Poly ( $\beta$ -L-malic acid) for drug delivery with enhanced endocytosis**

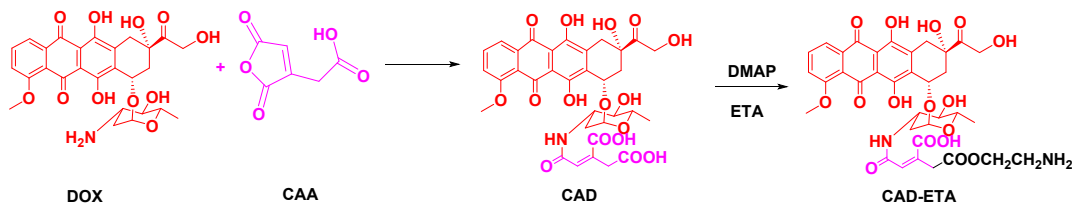
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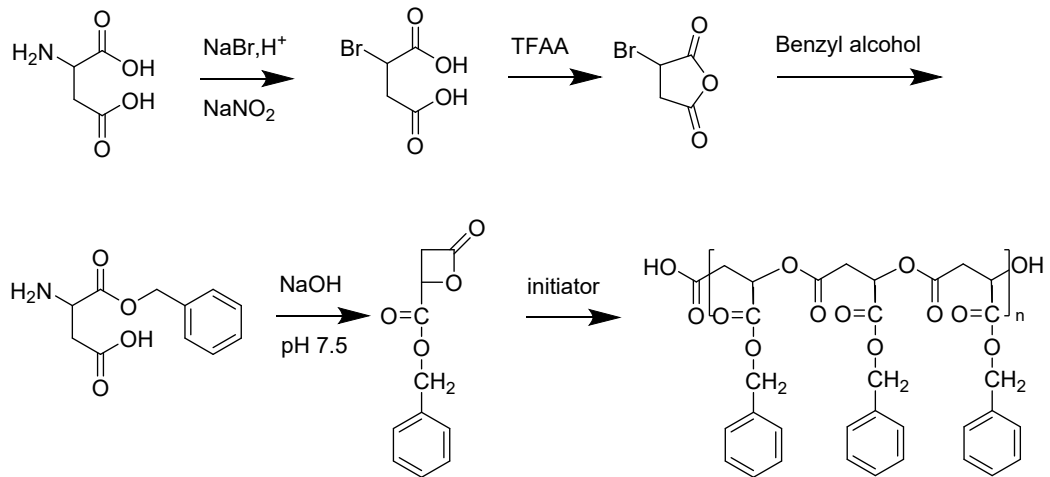
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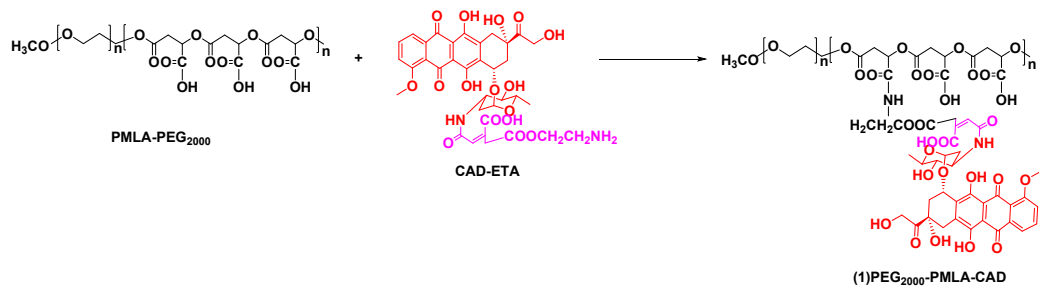
E-mail addresses: [spphgsy@126.com](mailto:spphgsy@126.com) (Songyan Guo), [hongwuxa@163.com](mailto:hongwuxa@163.com) (Hong Wu).



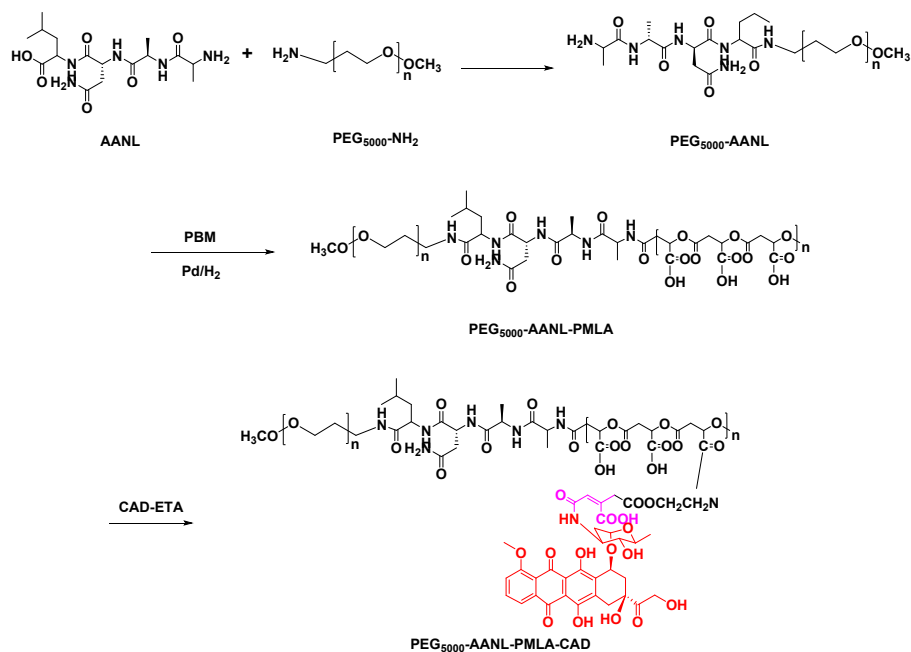
**Scheme. S1** Synthesized of CAD and CAD-ETA



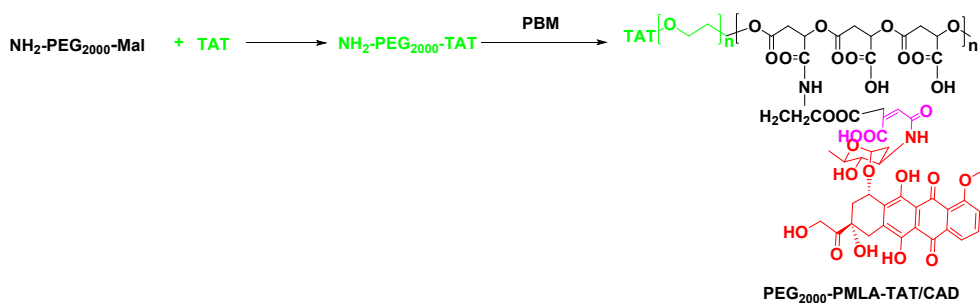
**Scheme. S2** Synthesized of PBM



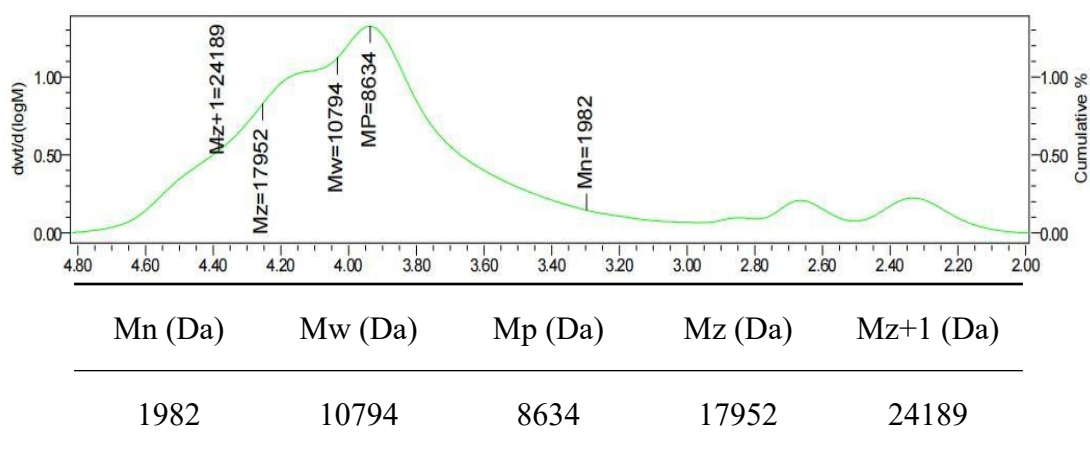
**Scheme. S3** Synthesized of PPC



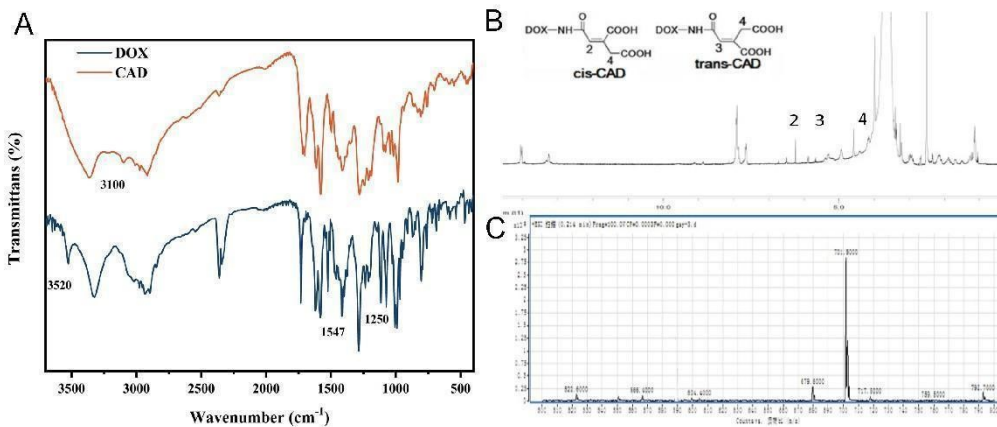
**Scheme. S4** Synthesized of PAPC



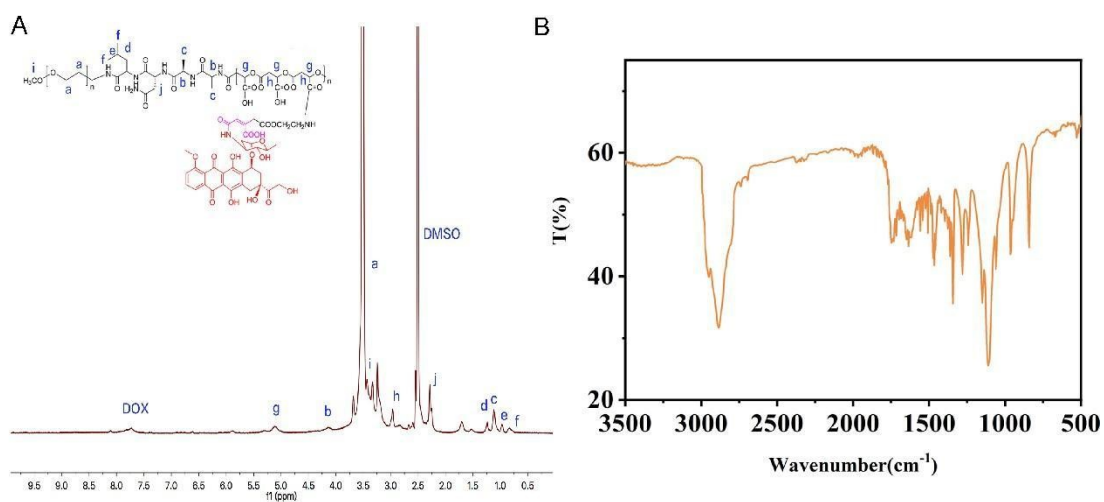
**Scheme. S5** Synthesized of PPTC



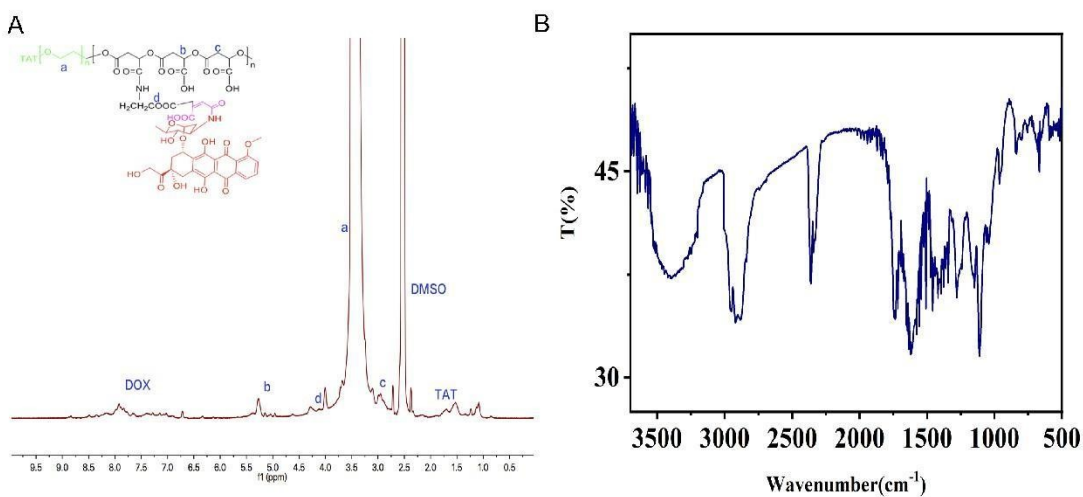
**Fig. S1** The GPC chromatography of PMLA.



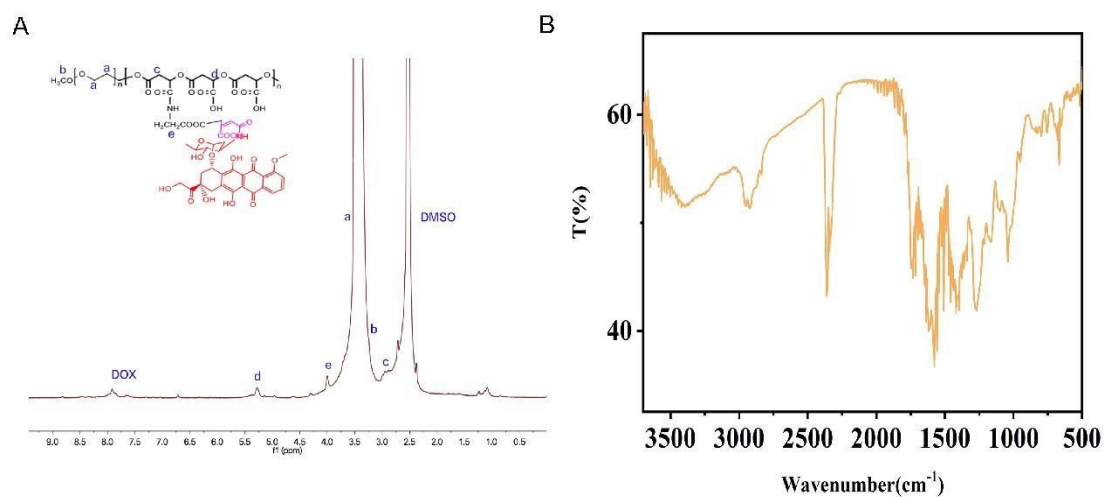
**Fig. S2** FTIR (A), <sup>1</sup>H NMR (400 MHz) (B) and MS(C) spectrum of CAD



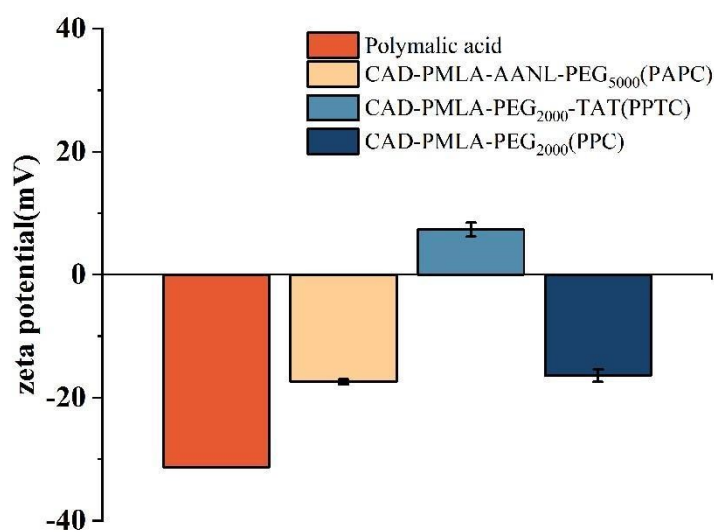
**Fig. S3** <sup>1</sup>H-NMR (400 MHz) (A) and FTIR(B) spectrum of PEG-AANL-PMLA-CAD(PAPC)



**Fig. S4**  $^1\text{H-NMR}$  (400 MHz) (A) and FTIR (B) spectrum of TAT-PEG-PMLA-CAD (PPTC)



**Fig. S5**  $^1\text{H-NMR}$  (400 MHz) (A) and FTIR(B) spectrum of PEG-PMLA-CAD(PPC)



**Fig. S6** The zeta potential of different DOX-loaded nanomaterials

**Table. S1** Summary of size, Zeta-potential, PDI, and DOX drug content of EP-NPs, P-NPs, E-NPs and C-NPs.

Nanoparticles	Size	PDI*	Zeta-potential	DOX content
	(nm)		(mV)	
EP-NPs	129.7±3.5	0.19	-17.63±1.06	25.3
P-NPs	116.9±2.6	0.12	-16.89±0.63	24.2
E-NPs	143.1±3.2	0.19	-16.65±1.51	21.6
C-NPs	132.0±4.2	0.17	-15.89±1.15	24.1

\*PDI: Polydispersity Index.

**Table. S2** Summary of IC<sub>50</sub> value of Free DOX, EP-NPs, P-NPs, E-NPs and C-NPs against MDA-MB-231 cells and L929.

	MDA-MB-231 (µg/mL)		L929 (µg/mL)	
	IC <sub>50</sub> (pH 7.4)	IC <sub>50</sub> (pH 6.3)	IC <sub>50</sub> (pH 7.4)	IC <sub>50</sub> (pH 6.3)
Free-DOX	0.92	0.96	1.22	1.31
EP-NPs	27.52	1.08	31.22	9.12
P-NPs	27.43	4.03	33.54	9.97
E-NPs	27.99	17.24	36.21	10.16
C-NPs	29.15	19.13	34.11	16.22