

## Supporting Information

### Exploring the release mechanisms by disrupting the $\pi$ - $\pi$ stacking region from stable micelle

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## EXPERIMENTAL SECTION

**Calculation of polymerization degree.** The degree of polymerization (DP) of BOOPMA, HBMA and PEGMA in the copolymer from  $^1\text{H}$  NMR can be obtained by calculating the ratio of peak area. The hydrogen proton peak of  $-\text{C}(\text{CH}_3)\text{-Br}$  in the structure of copolymer was used as a calibrator ( $I_{\text{EBriB}} = 1$ ) to integrate all the other characteristic peaks. The molecular weight of the polymer from  $^1\text{H}$  NMR was calculated as in Equation S1.

$$M_{\text{polymer}} = \frac{3I_{\text{BOOPMA}}}{2I_{\text{EBriB}}} \times 262 + \frac{3I_{\text{HBMA}}}{I_{\text{EBriB}}} \times 158 + \frac{3I_{\text{PEGMA}}}{2I_{\text{EBriB}}} \times 475 + 195 \text{ \#S1}$$

Similarly, the theoretical degree of polymerization (DP) of BOOPMA, HBMA and PEGMA in the copolymer from GPC can be calculated as in Equation S2. The fit closest to the GPC measured molecular weight will be used.

$$M_{\text{polymer}} = DP_{\text{BOOPMA}} \times 262 + DP_{\text{HBMA}} \times 158 + DP_{\text{PEGMA}} \times 475 + 195 \text{ \#S2}$$

**Storage stability of micelles.** The long-term storage stability of polymeric micelles (PHB, PHB-ADH and PHB-EDE) were investigated at the concentration of 1 mg/mL under 4 °C for 6 weeks. At each week, 2 mL of the micelles was withdrawn for DLS characterization.

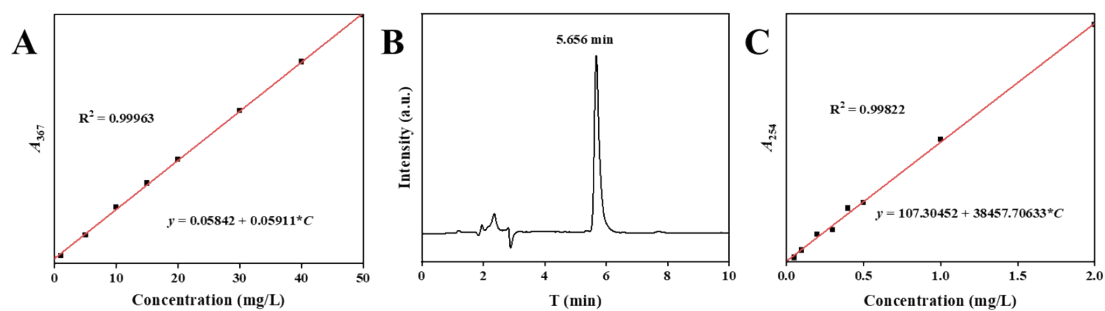
## DISCUSSION

### Physical stability of PHB based micelles.

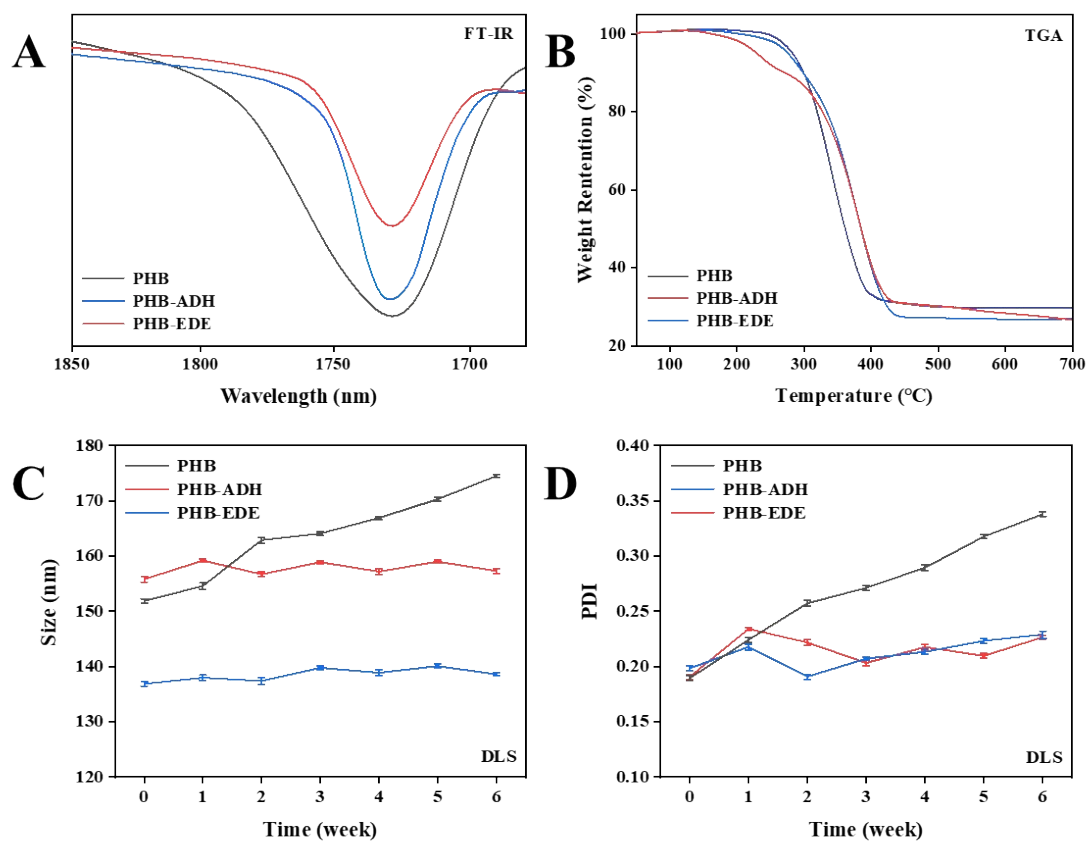
The  $\pi$ - $\pi$  stacking and crosslinking strategies were regarded as the most convenient approaches for enhancing the stability of micelles. To ensure the validity of these collaboration strategies, the physical stability of PHB based micelles was conducted. To begin with, the thermodynamic stability was represented by the DTA analysis (Figure S2B). It was obvious that the maximum degradation rate ( $T_{\text{d, max}}$ ) of PHB based micelles grew higher ( $T_{\text{d, max}} = 342$  °C for PHB, 382 °C for PHB-ADH and 380 °C for PHB-EDE) with the involvement of the crosslinking strategy, which also proved that the stability performance had less relevance on the pH sensitivity of crosslinker. Afterward, the kinetic stability of PHB based micelles was demonstrated with the storage stability of PHB based micelles (Figure S2C, D). After incubation in 6 weeks, the PHB exhibited good stability with a slowly increased particle size distribution (from 151 nm to 174 nm) and polydispersity (from 0.19 to 0.34), which mainly attributed to the help of  $\pi$ - $\pi$  stacking strategy to avoid micelle disintegration. By further introducing the crosslinking strategy, PHB-ADH and PHB-EDE displayed better stability with

slight changes in particle size distribution (3.4 nm and 3.2 nm, respectively) and polydispersity (both 0.04), the aggregate and dissolution were also diminished. Therefore, the stability enhancing effect of the collaboration strategies was convinced.

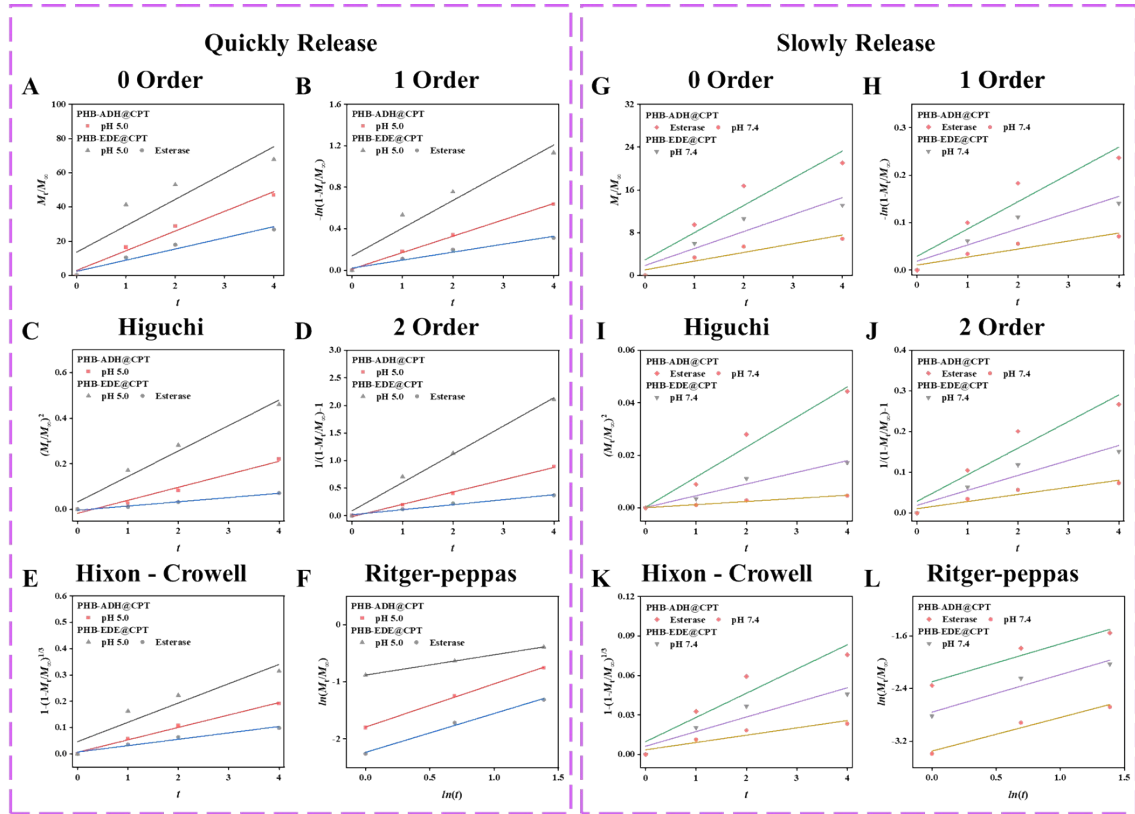
## Figure



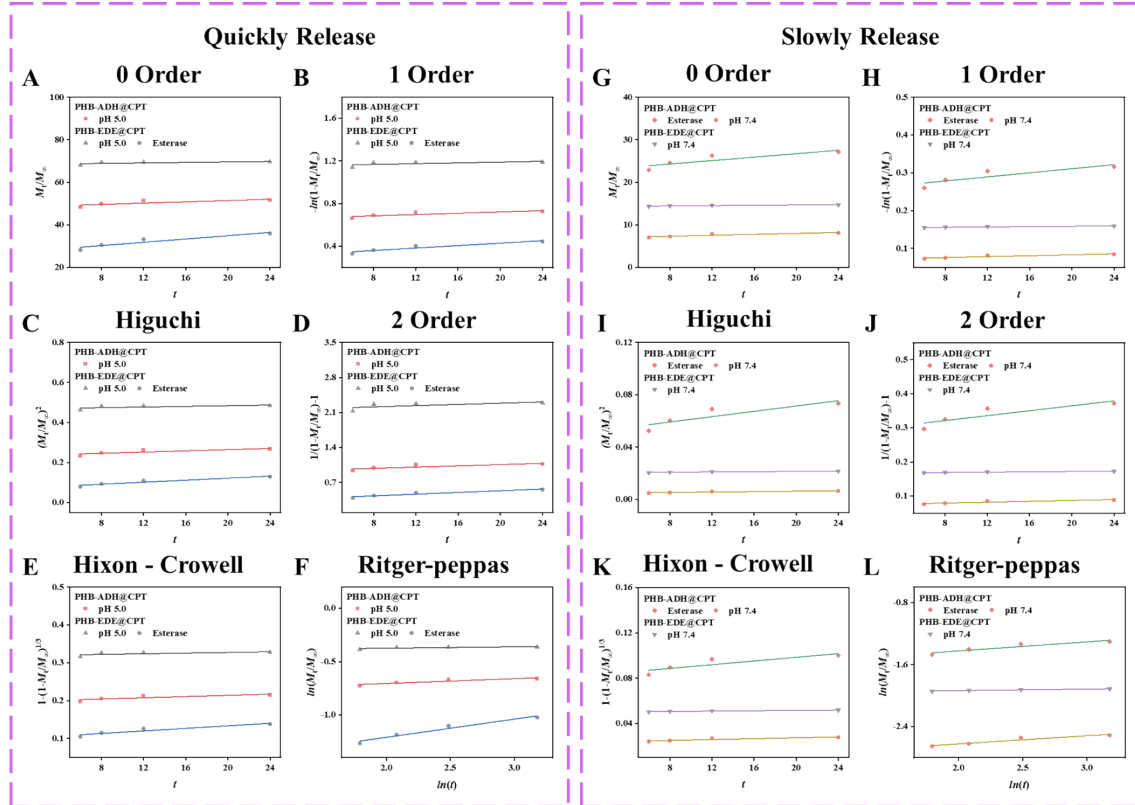
**Figure S1** (A) The standard concentration curve of CPT in DMSO. (B) HPLC trace of CPT in water. (C) The standard concentration curve of CPT in water.



**Figure S2** (A) Localized FT-IR spectra (ketone group) of PHB based micelles. (B) Thermal weight loss curves of PHB based micelles. (C) Size distribution and (D) polydispersity index of PHB based micelles for storage stability.



**Figure S3** Early drug release fitting curves with different kinds of mathematical models in 0 – 4 h. (A-F) quickly releasing situations: PHB-ADH@CPT in pH = 5.0, PHB-EDE@CPT in pH = 5.0 and PHB-EDE@CPT in 60 units/mL PLE, (G-L) slowly releasing situations: PHB-ADH@CPT in pH = 7.4, PHB-EDE@CPT in pH = 7.4 and PHB-ADH@CPT in 60 units/mL PLE.



**Figure S4** Lately drug release fitting curves of Early drug release fitting curves with different kinds of mathematical models in 8 – 24 h. (A-F) quickly releasing situations: PHB-ADH@CPT in pH = 5.0, PHB-EDE@CPT in pH = 5.0 and PHB-EDE@CPT in 60 units/mL PLE, (G-L) slowly releasing situations: PHB-ADH@CPT in pH = 7.4, PHB-EDE@CPT in pH = 7.4 and PHB-ADH@CPT in 60 units/mL PLE.

## Table

**Table S1** Drug loading capacity and entrapment efficiency of PHB based micelles

Entry	LC (%)	EE (%)
PHB@CPT	1.12	3.36
PHB-ADH@CPT	5.72	17.17
PHB-EDE@CPT	5.84	17.52

**Table S2** Different mathematical model equations of drug release

Models	Equations
0 Order	$M_t/M_\infty = kt$

Higuchi	$(M_t/M_\infty)^2 = k^2 t$
1 Order	$-\ln(1 - M_t/M_\infty) = kt$
2 Order	$1/(1 - M_t/M_\infty) - 1 = kt$
Hixon - Crowell	$1 - (1 - M_t/M_\infty)^{1/3} = kt$
Ritger-Peppas	$\ln(M_t/M_\infty) = n \ln(t) + \ln(k)$
Logistic	$\ln(M_\infty/M_t - 1) = -at + \ln(b)$

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