SUPPORTING INFORMATION

Effects of "mature micelle" formation of Pluronic P123 on equilibrium between lactone and carboxylate forms of 10-hydrocamptothecin in water

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1. HPLC analysis of HCPT

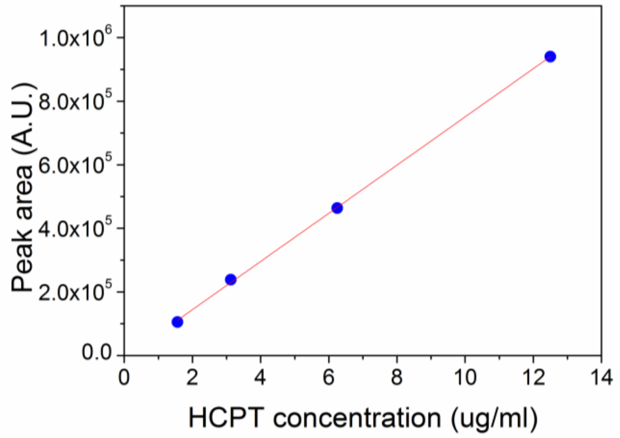

Fig. S1 Standard curve of the lactone form of 10-hydrocamptothecin (HCPT) in an acidic medium. The squared correlation coefficient R^2 outputted from the linear fit is 0.9995.

2. Normalized chromatograms of both ring-opening and ring-closing of HCPT after abrupt pH changes.

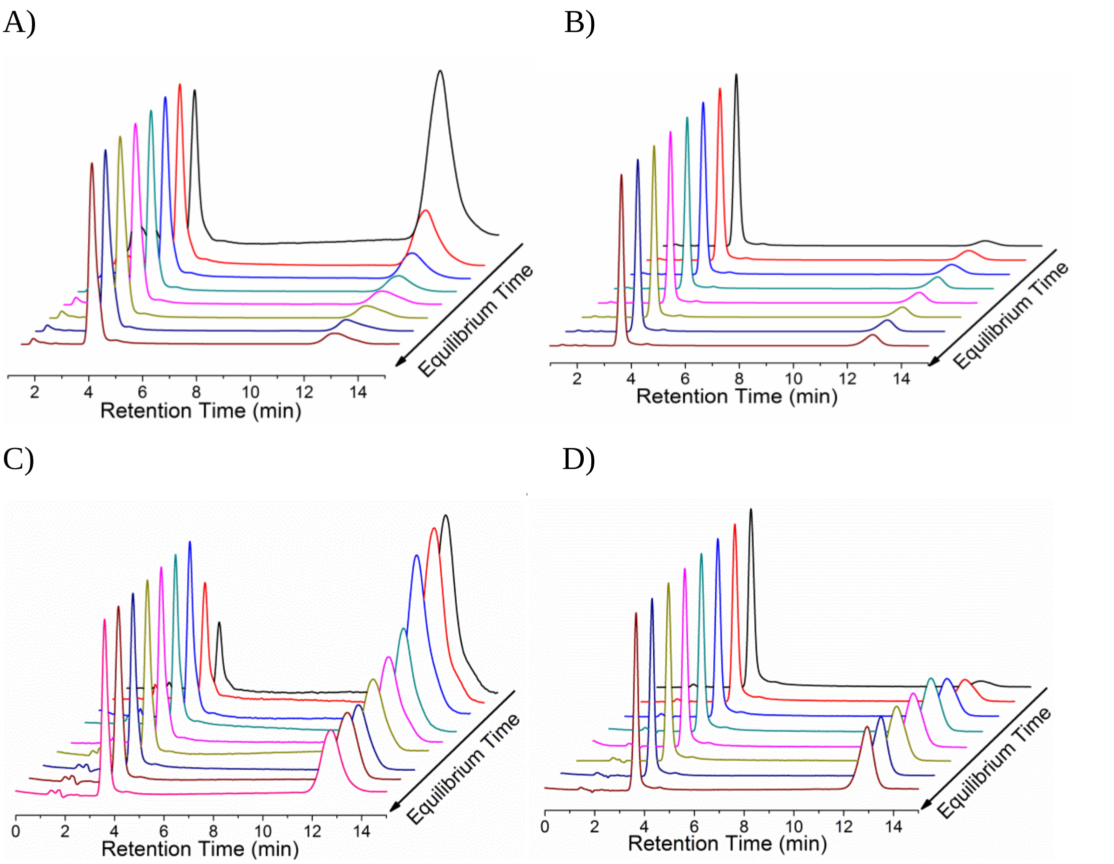

Fig. S2 HPLC profiles of HCPT. (A) Ring-opening in the phosphate buffer saline

(PBS) solution from pH < 4.0 to pH 7.4. The lines show data at 10 min, 30 min, 1 h, 2 h, 3 h, 4 h, 6 h and 8 h. (B) Ring-closing in PBS from pH > 9.0 to pH 7.4. The lines show data at 10 min, 30 min,1 h, 2 h, 3 h, 4 h, 5 h and 7 h. (C) Ring-opening in 10 wt% P123 from pH < 4.0 to pH 7.4. The lines show data at 10 min, 30 min,1 h, 2 h, 3 h, 4 h, 5 h, 7 h and 8 h. (D) Ring-closing in 10 wt% P123 from pH > 9.0 to pH 7.4. The lines show data at 10 min, 30 min,1 h, 2 h, 3 h, 4 h, 6 h and 8 h.

3. Micellization of 10 wt% P123 aqueous solution with temperature

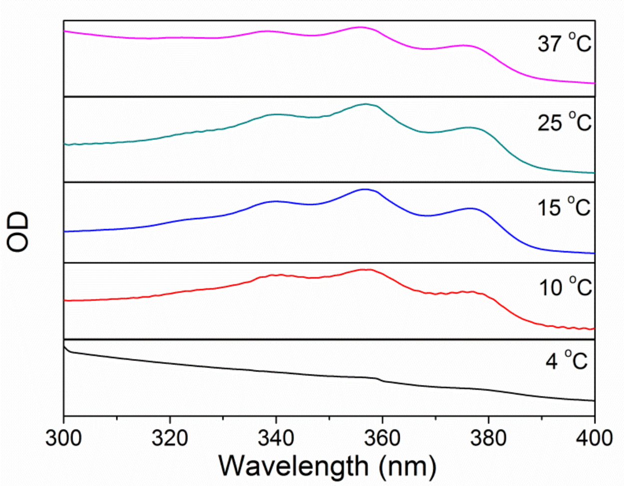

Fig. S3. UV-visible absorption spectra of the hydrophobic probe DPH in 10 wt% aqueous solutions of Pluronic block copolymer P123 (mainly EG_{20}-PG_{70}-EG_{20}) at indicated temperatures. The triple peaks indicate the formation of the block copolymer micelles in water.

Table S1. The *p* values of data in Fig. 6

10 wt% P123	4 ºC	10 ºC	15 ºC	25 ºC	37 ºC
4 ºC	/	0.58	0.015 *	0.005 **	0.0007 ***
10 ºC		/	0.0003 ***	0.00006 ***	0.004 **
15 ºC			/	0.001 ***	0.012 *
25 ºC				/	0.777

"*": Significant difference with $p < 0.05$;

"**": Significant difference with $p < 0.01$.

"***": Very significant difference with $p < 0.001$.

4. Gel permeation chromatography (GPC) of Pluronic P123

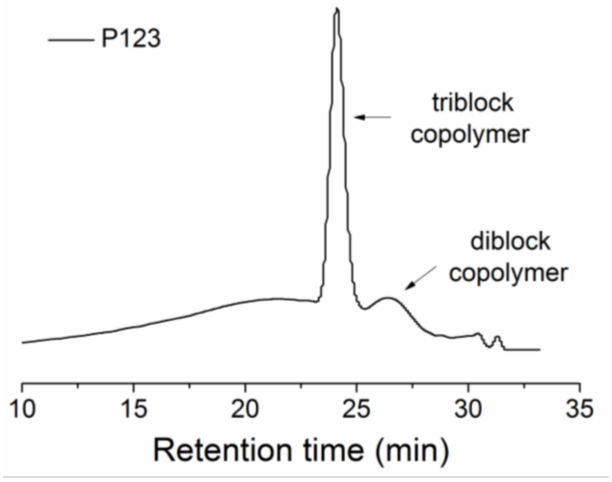

Fig. S4 GPC profile to reflect the molecular weight distribution of P123. The GPC detection was conducted in Agilent 1100 apparatus with a differential refractometer as a detector. Tetrahydrofuran was as an eluting solvent at a flow rate of 1.0 ml/min at 35 ºC. The retention time correlated with the molecular weight. The main peak corresponds to the triblock copolymer, and the second peak at larger retention time and thus lower molecular weight, to the diblock copolymer.

5. Theoretical analysis of the lactone fraction of HCPT in P123 suspensions of different polymer concentrations

Usually the concentration of non-ionized open-ring CPT analogues is too low to be detected. After neglecting [C], we write the lactone fraction in the suspension as

$$f_{\mathrm{lactone}} = \frac{[\mathrm{L}]_{\mathrm{susp}}}{[\mathrm{L}]_{\mathrm{susp}} + [\mathrm{C}^{-}]_{\mathrm{susp}}}$$

This is rewritten as

$$f_{\mathrm{lactone}} = \frac{\varphi[\mathrm{L}]_{\mathrm{in}} + (1-\varphi)[\mathrm{L}]_{\mathrm{out}}}{\varphi[\mathrm{L}]_{\mathrm{in}} + (1-\varphi)[\mathrm{L}]_{\mathrm{out}} + \varphi[\mathrm{C}^{-}]_{\mathrm{in}} + (1-\varphi)[\mathrm{C}^{-}]_{\mathrm{out}}}$$

The equation is further rewritten as

$$f_{\mathrm{lactone}} = \frac{\varphi \mathrm{K_L}[\mathrm{L}]_{\mathrm{out}} + (1-\varphi)[\mathrm{L}]_{\mathrm{out}}}{\varphi \mathrm{K_L}[\mathrm{L}]_{\mathrm{out}} + (1-\varphi)[\mathrm{L}]_{\mathrm{out}} + \varphi \mathrm{K_C}\frac{[\mathrm{L}]_{\mathrm{out}}K_{\mathrm{out}}}{[\mathrm{H}^{+}]} + (1-\varphi)\frac{[\mathrm{L}]_{\mathrm{out}}K_{\mathrm{out}}}{[\mathrm{H}^{+}]}}$$

$$= \frac{\varphi \mathrm{K_L} + (1-\varphi)}{\varphi \mathrm{K_L} + (1-\varphi) + \varphi \mathrm{K_C}\frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]} + (1-\varphi)\frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]}}$$

$$= \frac{\varphi(\mathrm{K_L}-1)+1}{\varphi(\mathrm{K_L}-1)+1+\varphi(\mathrm{K_C}-1)\frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]} + \frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]}}$$

So,

$$f_{\mathrm{lactone}} = \frac{(\mathrm{K_L}-1)sC_{\mathrm{P123}}+1}{(\mathrm{K_L}-1)sC_{\mathrm{P123}}+1+\frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]}(\mathrm{K_C}-1)sC_{\mathrm{P123}} + \frac{K_{\mathrm{out}}}{[\mathrm{H}^{+}]}}$$

Replacing K_{out} by K_{PBS} leads to equation (18) in the main manuscript.