Supplementary Information

A reduction and pH dual-sensitive nanodrug for targeted theranostics in hepatocellular carcinoma

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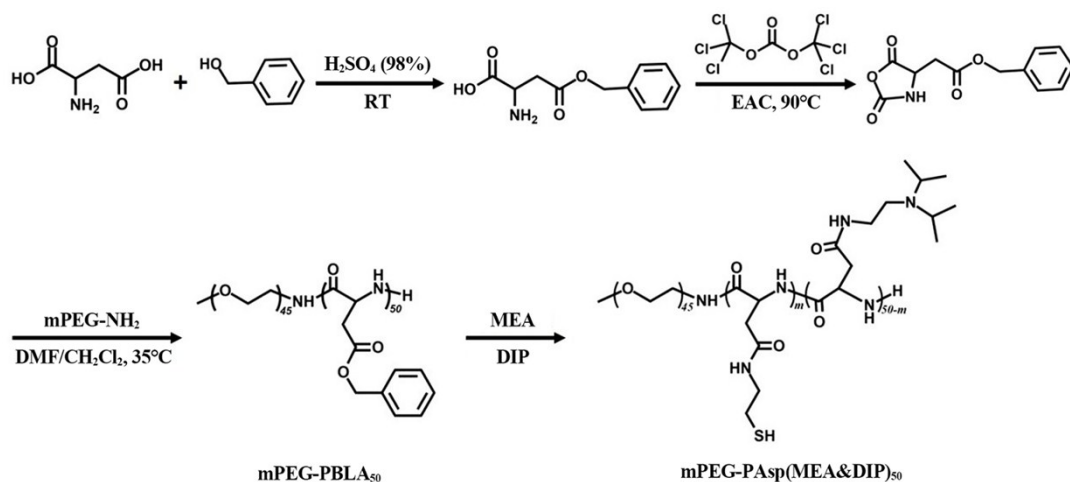
‡These authors contributed equally.

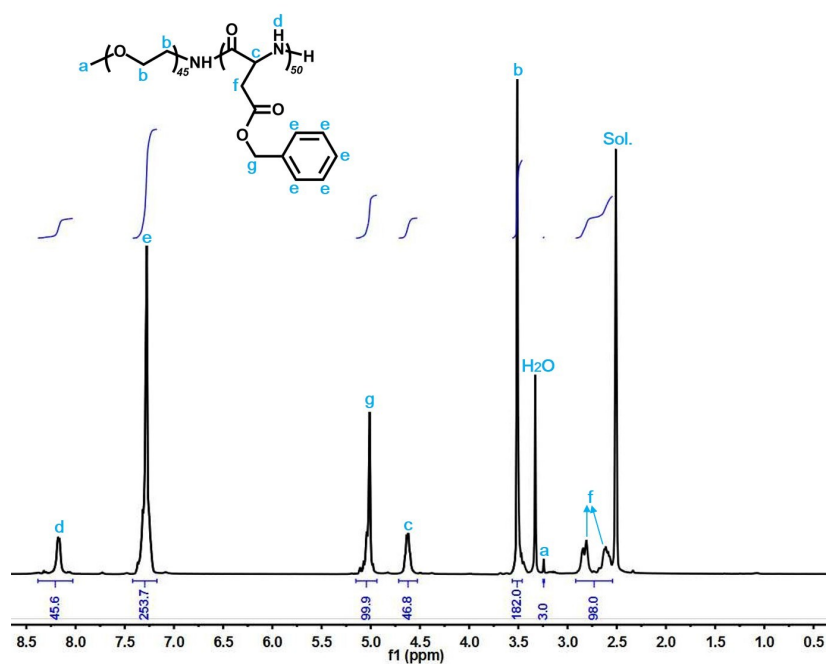**Fig. S1 Synthetic route of the diblock copolymer mPEG-PAsp(MEA&DIP).**

Fig. S2 ^{1}H NMR spectrum of mPEG$_{2k}$-PBLA$_{50}$ in DMSO-d$_6$. Characteristic peaks as follows: ^{1}H NMR (400 MHz, DMSO-d$_6$, 298 K): δ (ppm) = 2.52 - 2.88 ppm (-C**H$_2$**COOCH$_2$Ph, f), 3.24 ppm (C**H$_3$**(OCH$_2$CH$_2$) NH-, a), 3.50 ppm (CH$_3$(OC**H$_2$CH$_2$**) NH-, b), 4.62 ppm (-C**H**- of the main chain, c), 5.00 ppm (-CH$_2$COOC**H$_2$**Ph, g), 7.27 ppm (-C**H**- of benzyl group, e), 8.16 ppm (-N**H**- of the main chain, d).
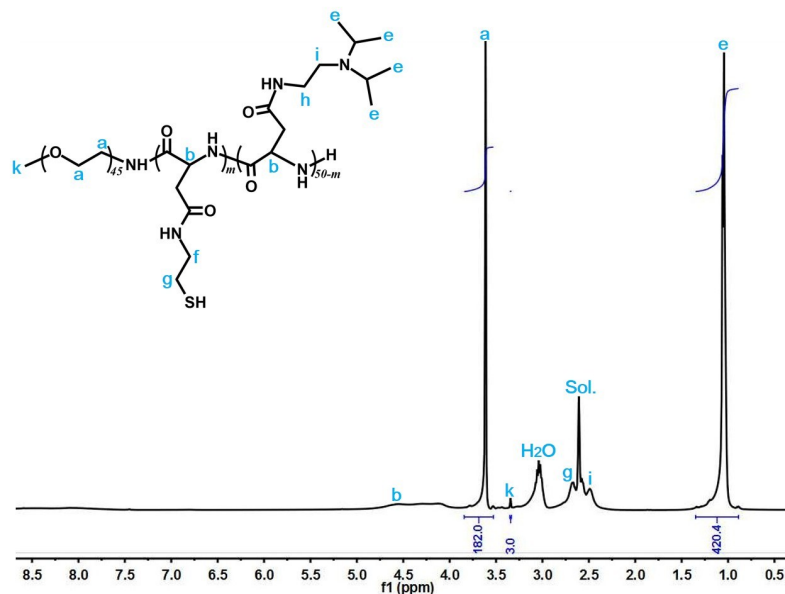
Fig. S3 ^{1}H NMR spectrum of mPEG$_{2k}$-PAsp(MEA&DIP)$_{50}$ in DMSO-d$_6$. Characteristic peaks as follows: ^{1}H NMR (400 MHz, DMSO-d$_6$, 298 K): δ (ppm) = 1.06 ppm ((CH_3)$_2$CH- of DIP, e), 2.49 ppm (-CH$_2$-CH_2-CH-(CH$_3$)$_2$- of DIP, i), 2.68 ppm (-CH$_2$-CH_2-SH of MEA, g), 3.34 ppm (CH_3(OCH$_2$CH$_2$) NH-, k), 3.61 ppm (CH$_3$(OCH_2CH_2) NH-, a), 4.55 ppm (-CH- of the main chain, b). Peak f and peak h are covered by the water peak.
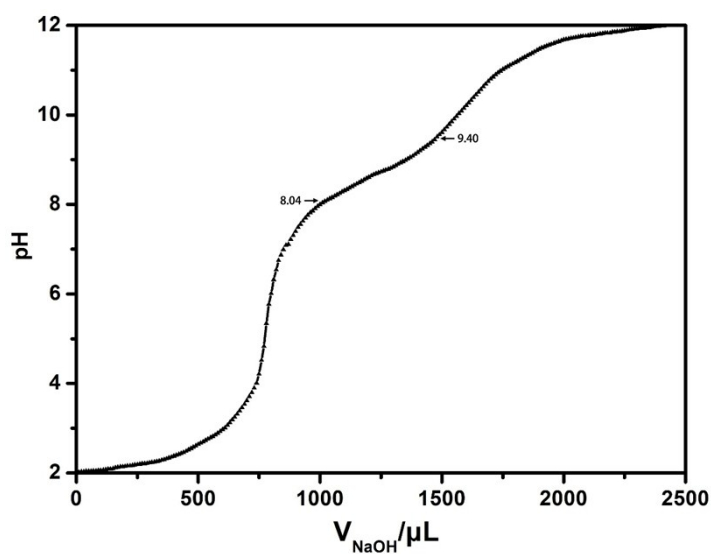

Fig. S4 Acid–base titration curve of mPEG$_{2k}$-PAsp(MEA&DIP)$_{50}$. (NaOH concentration: 0.2 N).
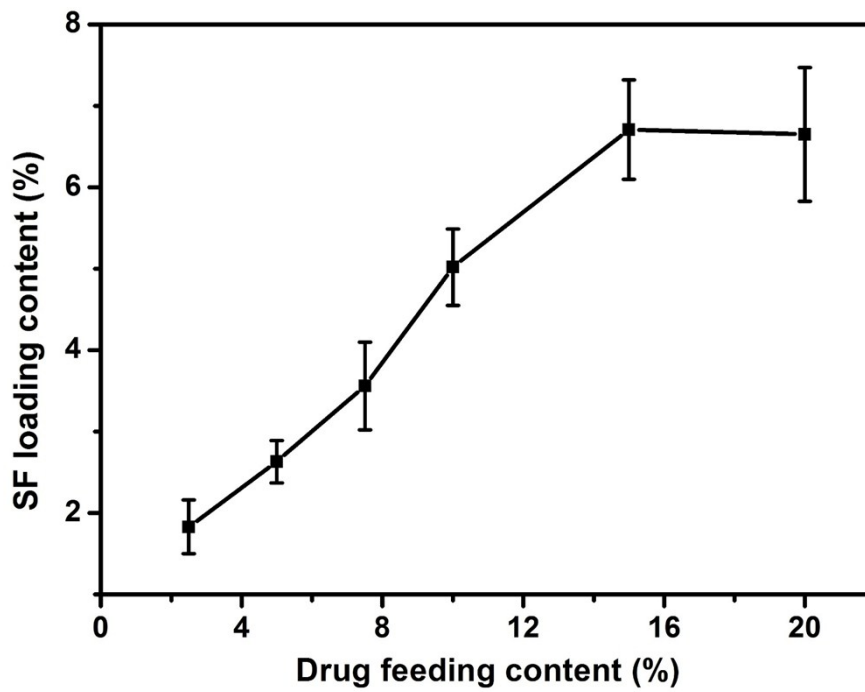
Fig. S5 SF loading contents of GPPSS prepared at different drug feeding contents.
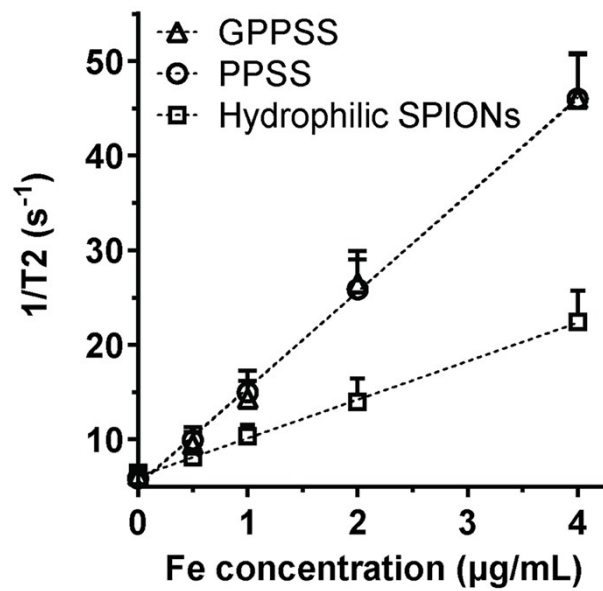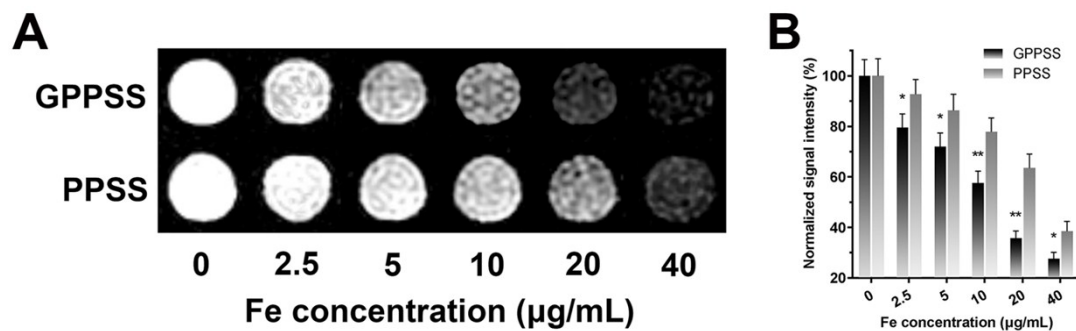

Fig. S6 T2 relaxivities of the micelles.

Fig. S7 T2WI image of the HepG2 cell samples. (A) T2WI images of HepG2 cells incubated with micelles at various Fe concentrations for 2 h. (B) Normalized signal intensities of cell samples on T2WI images ($^{*}P < 0.05$ and $^{**}P < 0.01$, compared with PPSS).
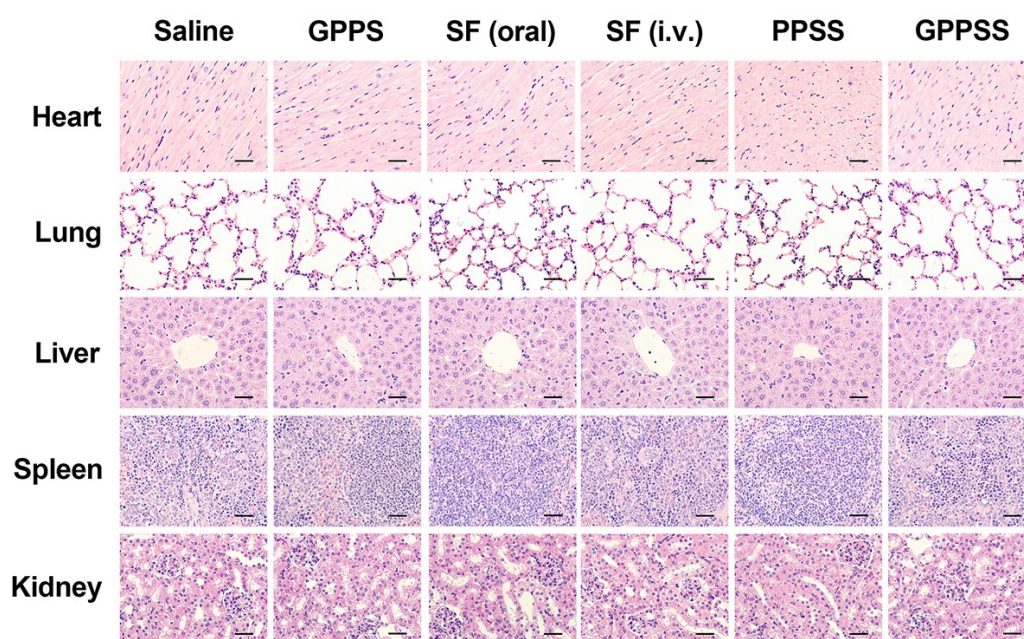

Fig. S8 H&E staining images of major organs from the mice in different treatment groups (scale bar: 20 μm).

Table S1. The IC$_{50}$ values of micellar nanodrug for HepG2 cells

Incubation time	IC$_{50}$ (μg mL^{-1})		
	Free SF	GPPSS	PPSS
24 h	4.55	4.99	9.05
48 h	2.96	2.85	5.24
72 h	1.93	1.79	3.54

IC$_{50}$, half maximal inhibitory concentration.