

# **PLGA Nanoparticle-Reinforced Supramolecular Peptide Hydrogels for Local Delivery of Multiple Drugs with Enhanced Synergism**

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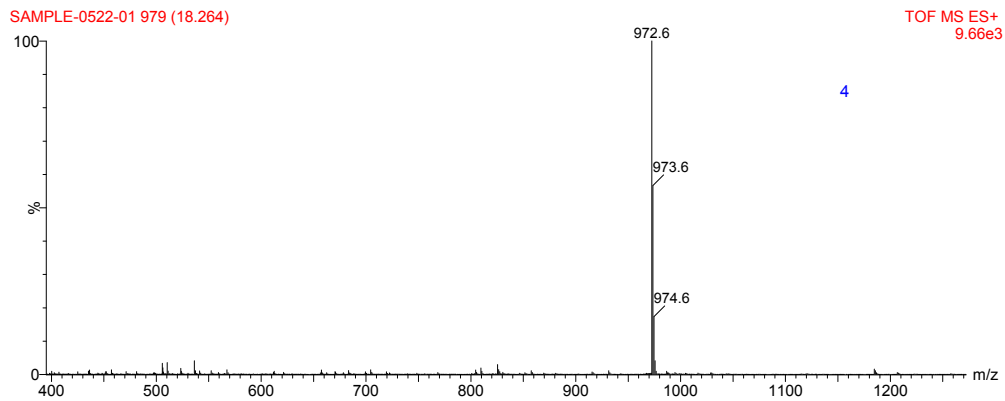
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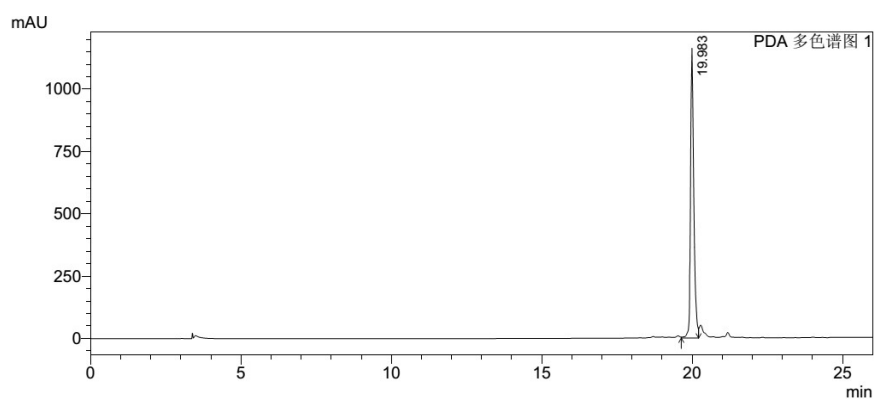
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**Table S1.** The calculated parameters for Ritger-Peppas modeling of 192 h drug release of Cis from various hydrogel formulations.

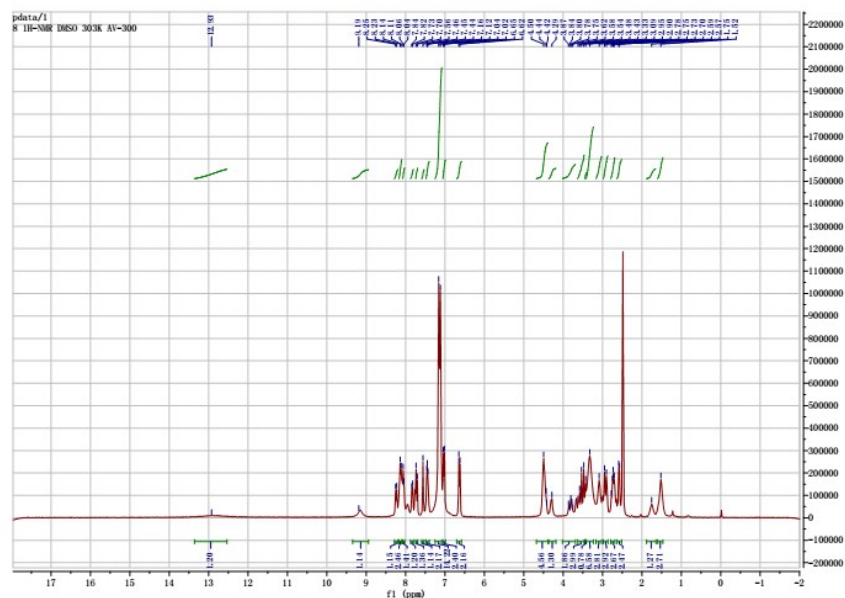
**Table S2.** The calculated parameters for Ritger-Peppas modeling of 192 h drug release of Irino from various hydrogel formulations.



**Fig. S1.** TOF-MS of Peptide (NapFFYRGD). (ESI-MS:  $C_{51}H_{57}N_9O_{11}$ , cal.MW = 972, obsvd.  $[M]^+$  = 972.6  $[M+H]^+$  = 973.6,  $[M+2H]^+$  = 974.6.

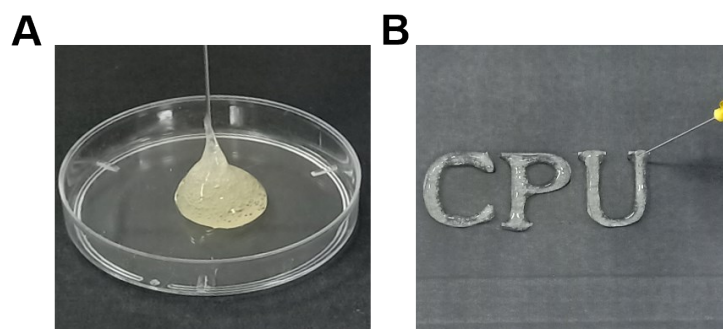


**Fig. S2.** HPLC spectrum of Peptide (NapFFYRGD).

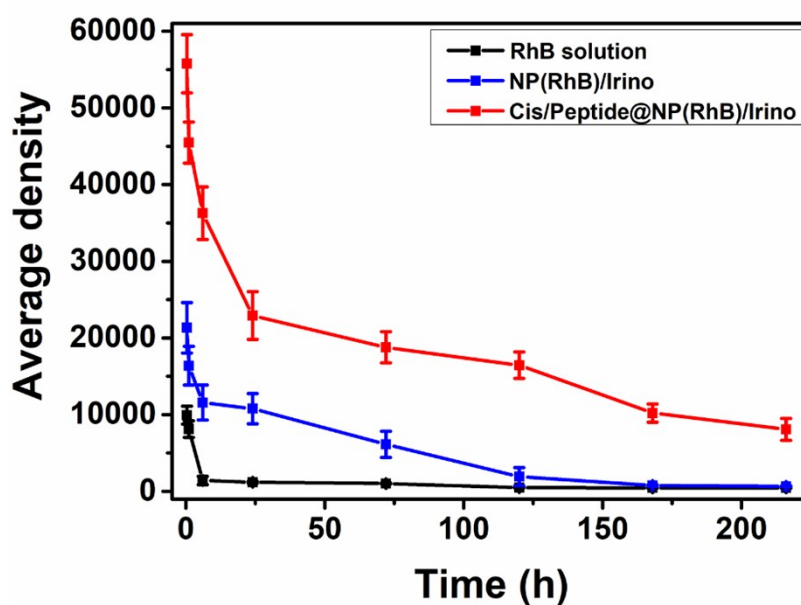


**Fig. S3.**  $^1H$  NMR spectrum of Peptide (NapFFYRGD).  $^1H$ -NMR, 300 MHz, ( $[D_6]$  DMSO)  $\delta$  = 12.93 (s, 1 H), 9.19 (s, 1 H), 8.25-8.23 (d, 1 H,  $J$  = 6 Hz), 8.14-8.11 (d, 2 H,  $J$  = 9 Hz), 8.06-8.04 (d, 1 H,  $J$  = 6 Hz), 7.84-7.82 (d, 1 H,  $J$  = 6 Hz), 7.84-7.82 (d, 1 H,  $J$  = 6 Hz), 7.73-7.70 (d, 1 H,  $J$  = 9 Hz), 7.46-7.44 (m, 2 H), 7.16-7.12 (d, 14 H,  $J$  = 12 Hz), 7.04-7.02 (d, 2 H,  $J$  = 6 Hz), 6.65-

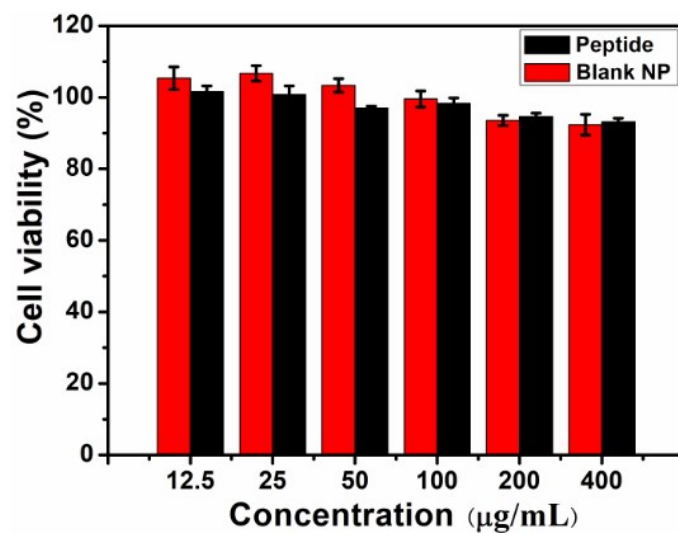
6.62 (d, 2 H, J = 9 HZ), 4.50-4.42 (m, 5 H), 4.29 (s, 1 H), 3.87-3.75 (m, 2 H), 3.62-3.48 (m, 2 H), 3.43 (s, 1 H), 3.33 (s, 6 H), 3.09 (s, 2 H), 2.95-2.90 (d, 2 H, J = 15 HZ), 2.78-2.70 (m, 2 H), 2.59-2.57 (d, 2 H, J = 6 HZ), 1.75 (s, 1 H), 1.52 (s, 2 H).



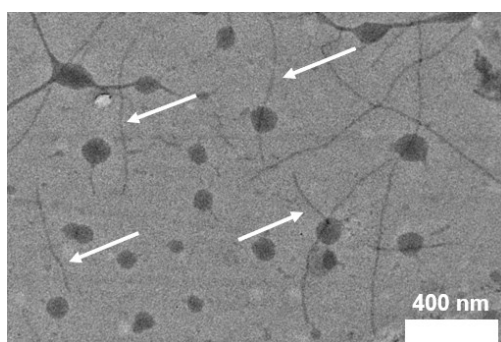
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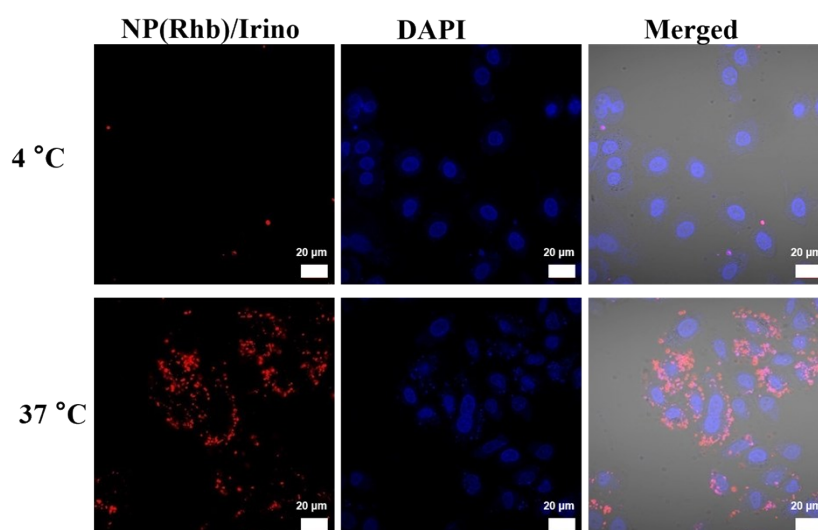
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**Table S1.** The calculated parameters for Ritger-Peppas modeling of 192 h drug release of Cis from various hydrogel formulations.

	n	k	R <sup>2</sup>
Cis/Peptide (0.2 eq./0.8 wt%)	0.7303	0.0252	0.9513
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@0.25 wt%)	0.7125	0.0243	0.9686
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@0.5 wt%)	0.7274	0.0212	0.9672
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@1.0 wt%)	0.7358	0.0191	0.9612

**Table S2.** The calculated parameters for Ritger-Peppas modeling of 192 h drug release of Irino from various hydrogel formulations.

	n	k	R <sup>2</sup>
NP/Irino	0.5093	0.0535	0.9830
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@0.25 wt%)	0.8095	0.0042	0.9833
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@0.5 wt%)	0.7732	0.0029	0.9597
<b>Cis/Peptide@NP/Irino</b> (0.2 eq./0.8 wt%@1.0 wt%)	0.7347	0.0018	0.9509