

Electronic Supporting Information (ESI)

Enzymatically-cross-linked peptide hydrogels for enhanced self-assembling capability and controlled drug release

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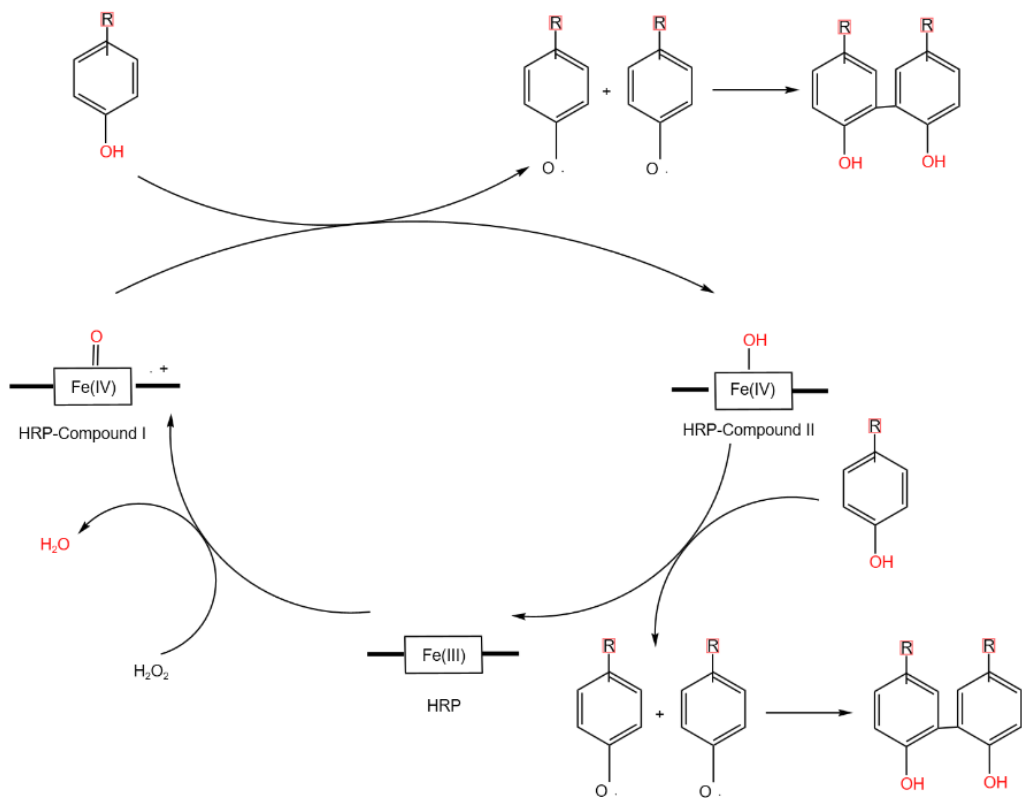
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Scheme S1 The HRP-mediated catalytic cycle of Tyr.

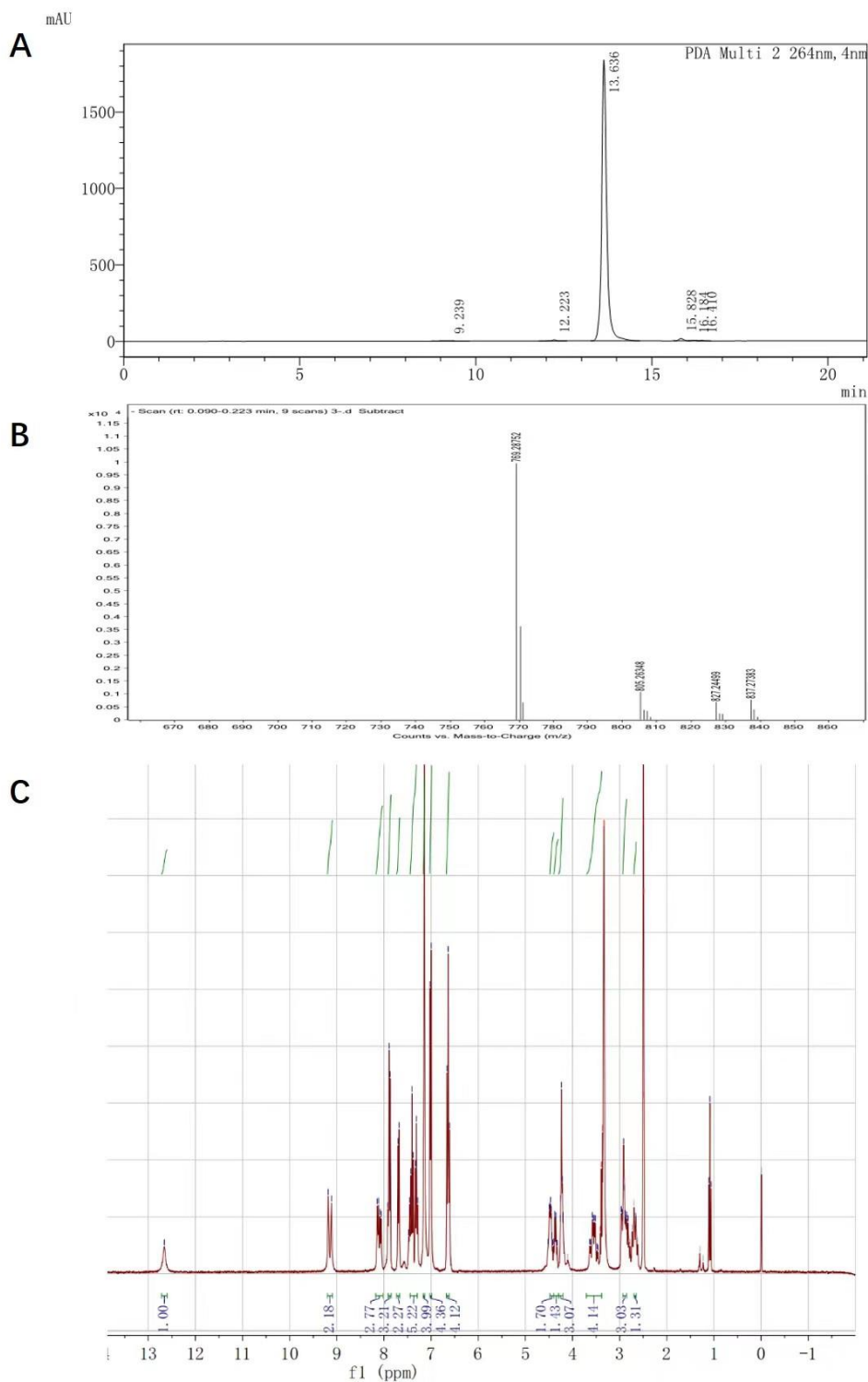


Fig. S1 Structural characterizations of Fmoc-GFYF. (A) HPLC; (B) MS; (C) ¹H NMR. Fmoc-GFYF(C₄₄H₄₂N₄O₉) ¹H NMR (300 MHz, DMSO-d₆) δ 12.66 (s, 1H), 9.15 (d, J = 20.0 Hz, 2H), 8.10 (dd, J = 17.7, 7.9 Hz, 3H), 7.88 (d, J = 7.3 Hz, 3H), 7.69 (d, J = 7.4 Hz, 2H), 7.44 – 7.30 (m, 5H), 7.15 (s, 4H), 7.01 (d, J = 8.2 Hz, 4H), 6.65 (d, J = 8.4 Hz, 4H), 4.44 (dd, J = 14.7, 5.7 Hz, 2H), 4.40 – 4.30 (m, 1H), 4.24 (q, J = 5.6, 4.3 Hz, 3H), 3.55 (qd, J = 16.9, 6.0 Hz, 4H), 2.93 – 2.85 (m, 3H), 2.66 (s, 1H).

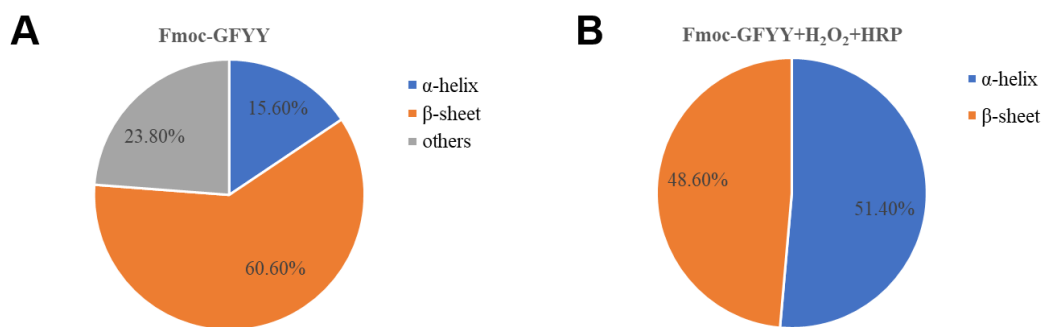


Fig. S2 The secondary conformations of the Fmoc-GFYF (A) and Fmoc-GFYF/enzymatically cross-linked hydrogels (B).

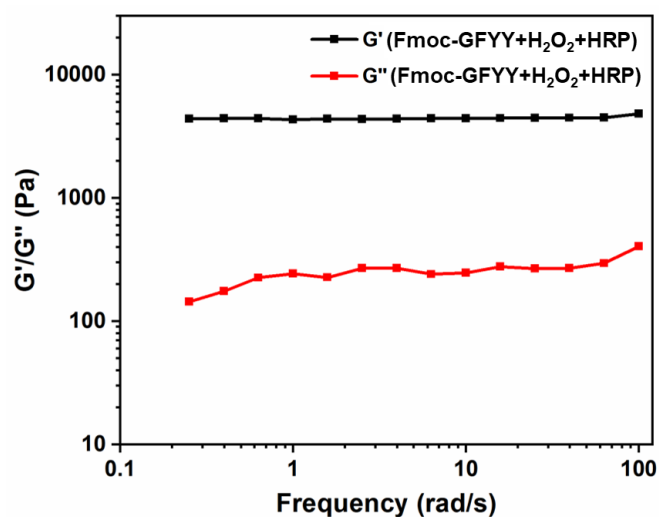


Fig. S3 Frequency sweep of Fmoc-GFYF/enzymatically cross-linked hydrogel.

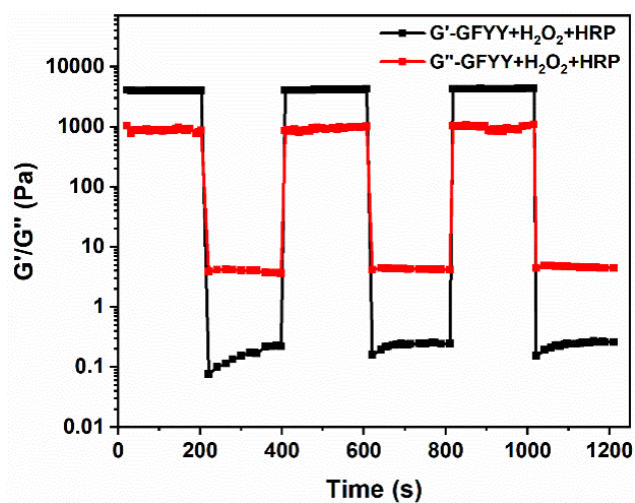


Fig. S4 Cyclic strain sweep of Fmoc-GFYF/enzymatically cross-linked hydrogel.

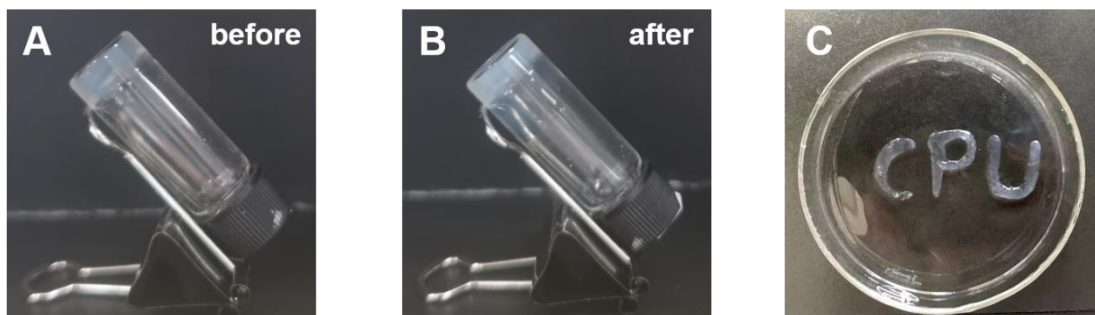


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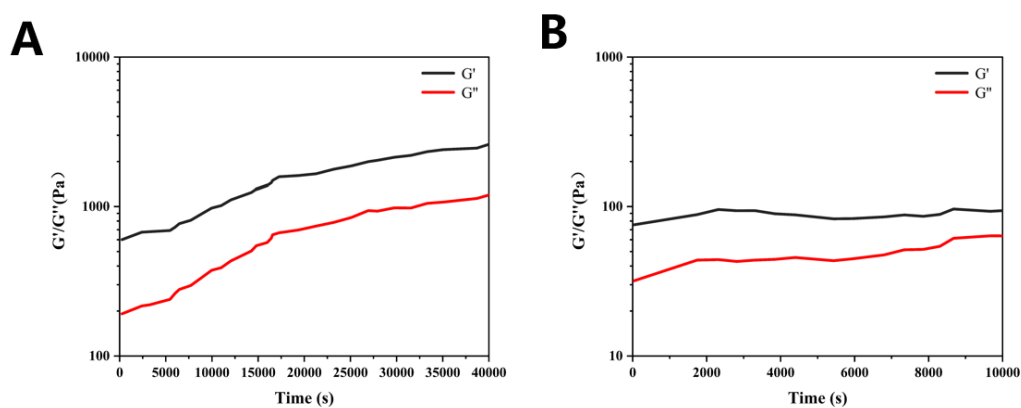


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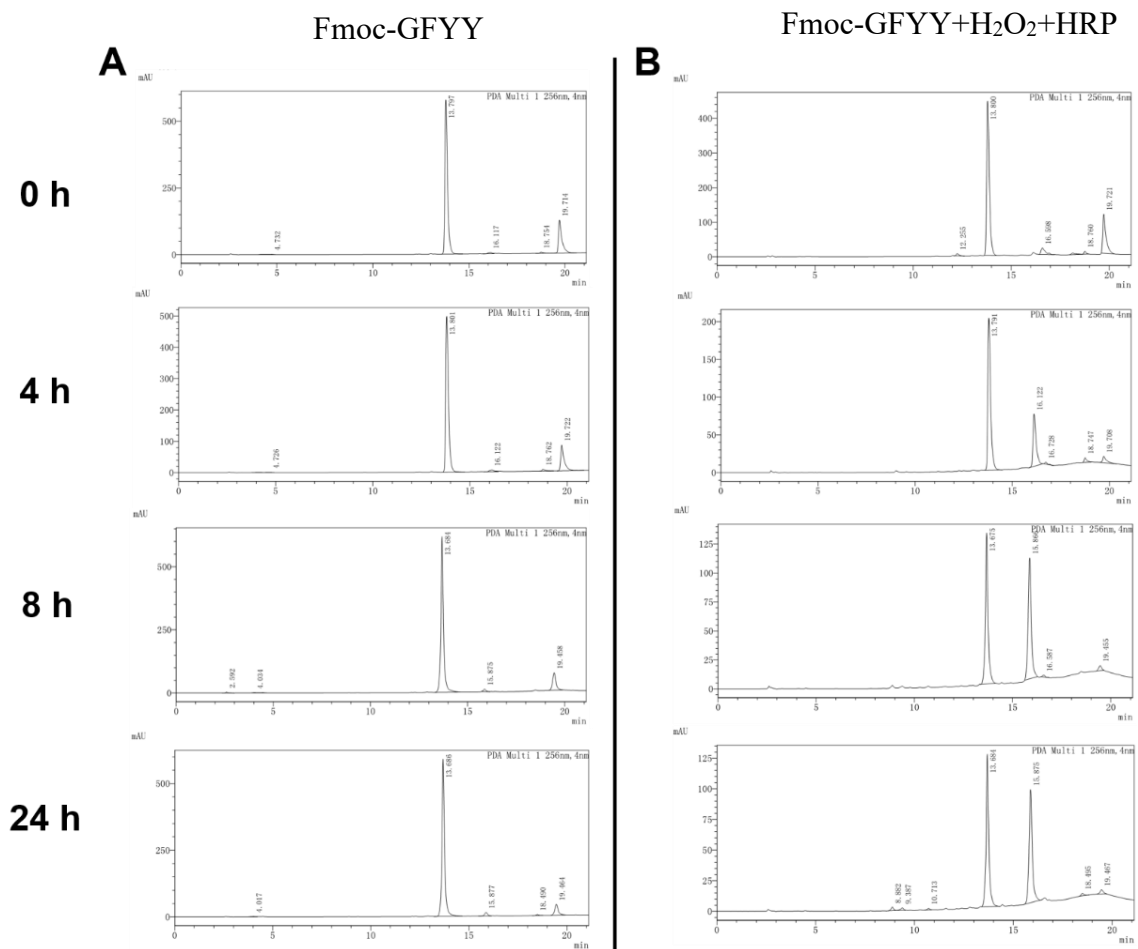


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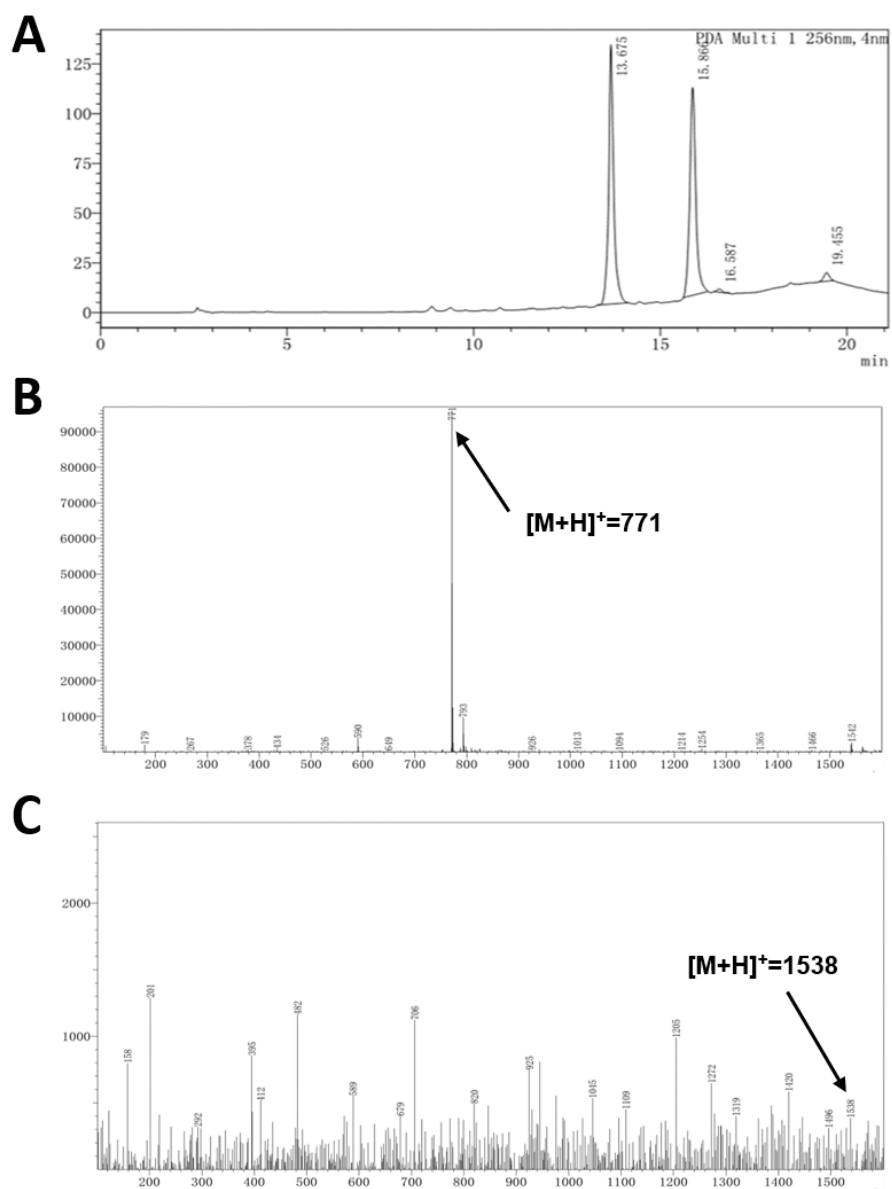


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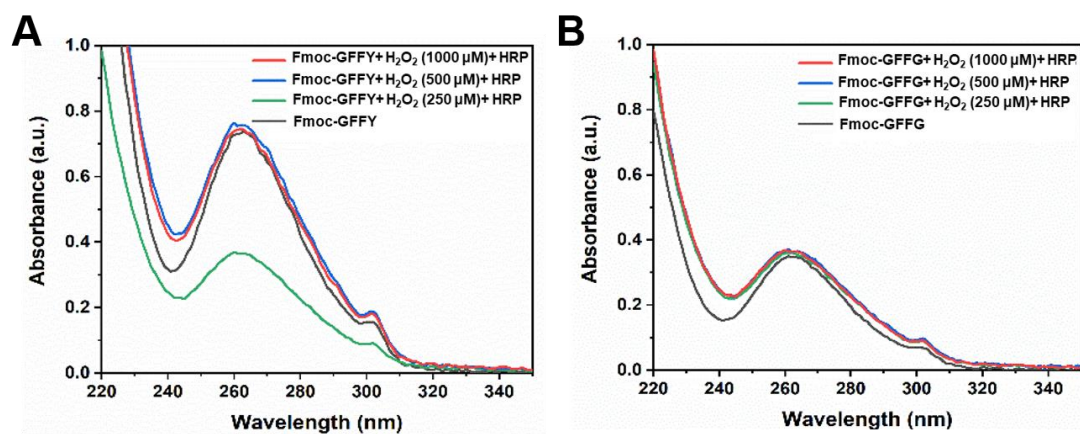


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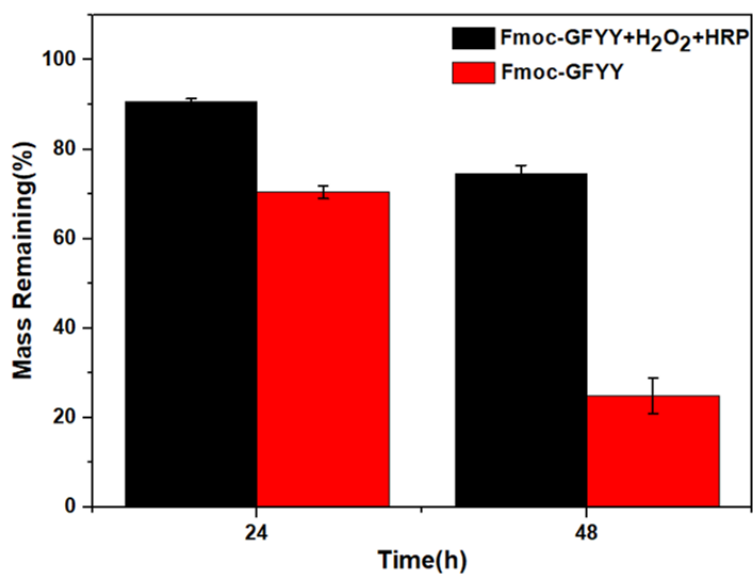


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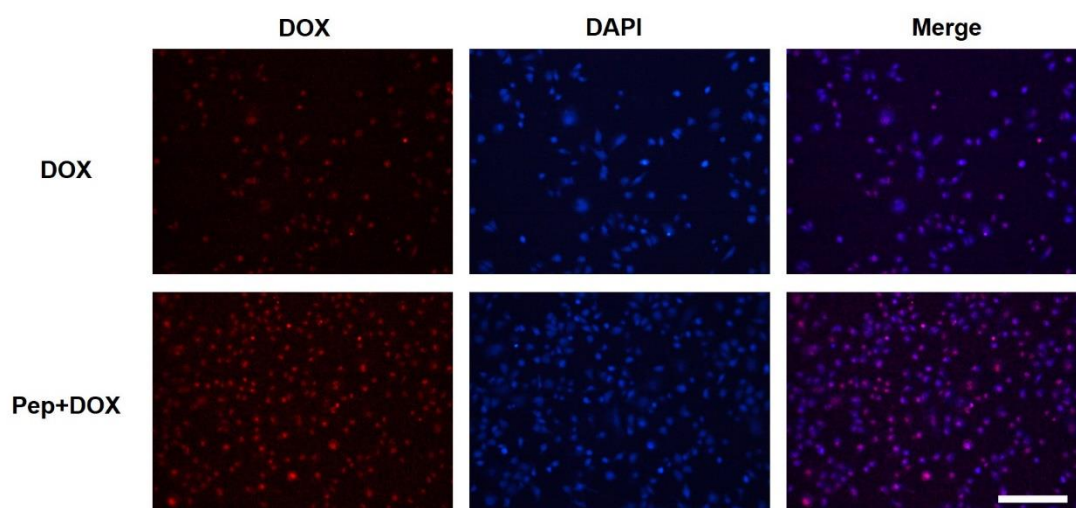


Fig. S11 Cellular uptake of DOX in A549 cells after 2 h treatment of DOX solution or Fmoc-GFYF+H₂O₂+HRP/DOX. Fmoc-GFYF, 300 μM; DOX, 10 μg/mL. Scale bar, 100 μm.

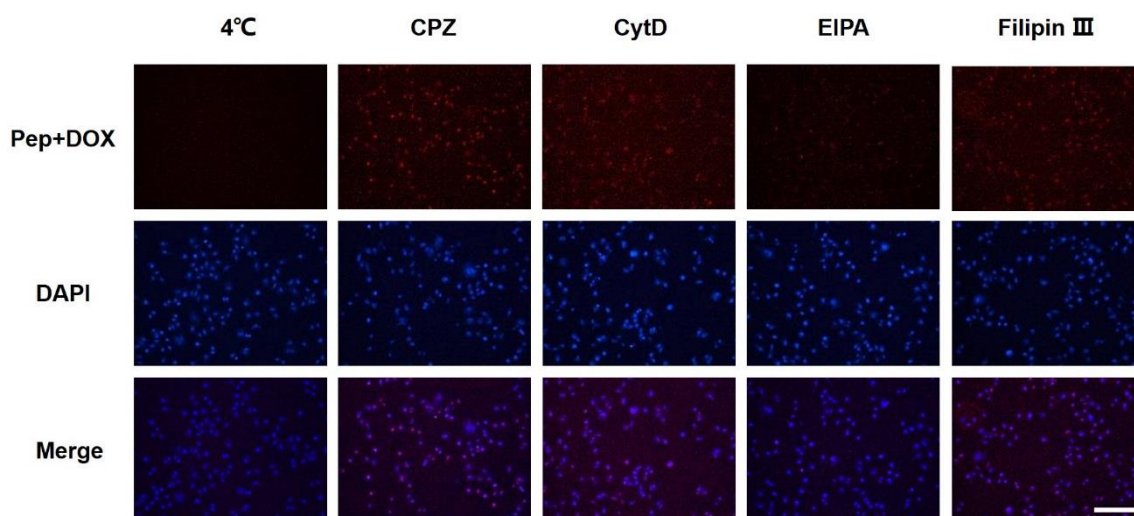


Fig. S12 Cellular uptake of DOX in Fmoc-GFYF+H₂O₂+HRP/DOX-treated cells at 4 °C or 37°C receiving pretreatment of various endocytosis inhibitors. Fmoc-GFYF, 300 μM; DOX, 10 μg/mL. Scale bar, 100 μm.

Table S1 The parameters calculated in Ritger-Peppas modelling of 24 h drug release of DOX from Fmoc-GFYY or Fmoc-GFYY+H₂O₂+HRP hydrogels.

Formulation	n	K	R ²
Fmoc-GFYY	0.76	2.93	0.8656
Fmoc-GFYY+H ₂ O ₂ +HRP	0.70	0.70	0.8562

Table S2 Values of IC₅₀ in A549 for DOX, Fmoc-GFYY/DOX and Fmoc-GFYY+H₂O₂+HRP/DOX.

Formulation	IC ₅₀ (ng/mL)
DOX	542 ± 43
Fmoc-GFYY/DOX	258 ± 24***
Fmoc-GFYY+H ₂ O ₂ +HRP/DOX	386 ± 23**

Note. Results are shown as the mean values ± standard deviation (n = 3).

IC₅₀ of Fmoc-GFYY/DOX and Fmoc-GFYY+H₂O₂+HRP/DOX were significantly different from DOX. (**, $P < 0.01$; ***, $P < 0.001$.)