**Peptide synthesis:** The peptides were synthesized via solid phase peptide synthesis method (SPPS). After cleavage from the resin and deprotection of the side groups and N-terminus using the TFA only, the peptides were collected in cold ether, centrifuged and freeze-dried. The obtained crude products were purified by reverse phase HPLC. MS, $^1$H NMR, HPLC were used to verify the peptide structure and value their purity.

The synthetic routes of these forky peptides were illustrated as Fig.S1.

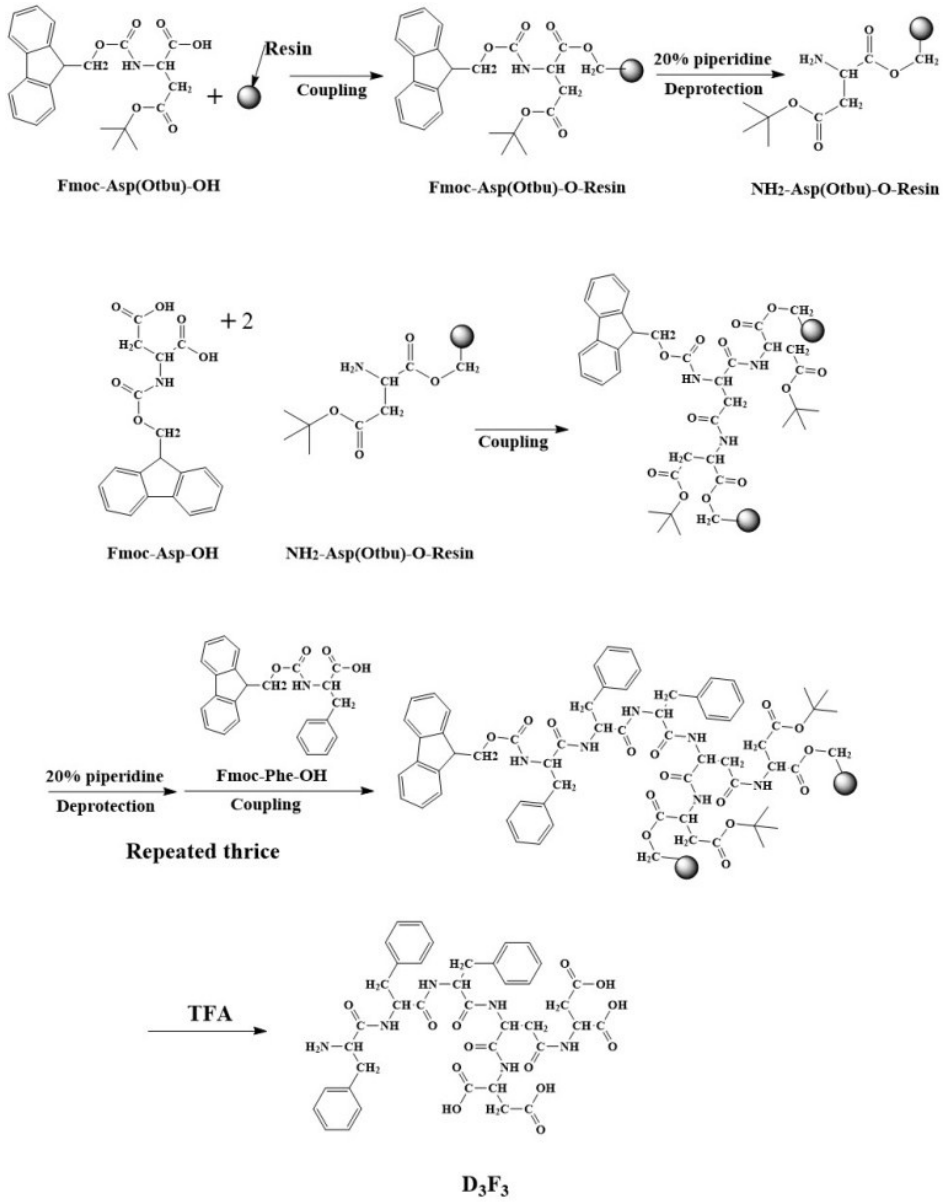


Fig. S1. Schematic diagram of the synthetic routes.

**The purification of $D_3F_3$ was handled as follow.**

The purification was performed on liquid chromatograph(Shimadzu LC-20AR). Chromatographic conditions：The semi-preparative Chromatographic column, Shim-pack GIS C18 column(250×20mm i.d.,10um).Mobile phase: The mobile phase consisted of two eluents, phase A was acetonitrile, phase B was 0.1% TFA(trifluoroacetic acid) solution. The mobile phase

ratio using a gradient of acetonitrile. 0～20min，the gradient was 20%～30%. 20～30min，the fixed ratio was 30%. Injection volume: 2 mL. Flow rate: 10.0 mL/min. T=35 °C. The DAD monitoring wavelength was 210 nm. The collection time of $D_3F_3$ was 28.5 to 30 min according to semi-preparative chromatogram(Fig.S2a). The elution fluid was concentrated by vacuum rotary evaporation and freeze drying.

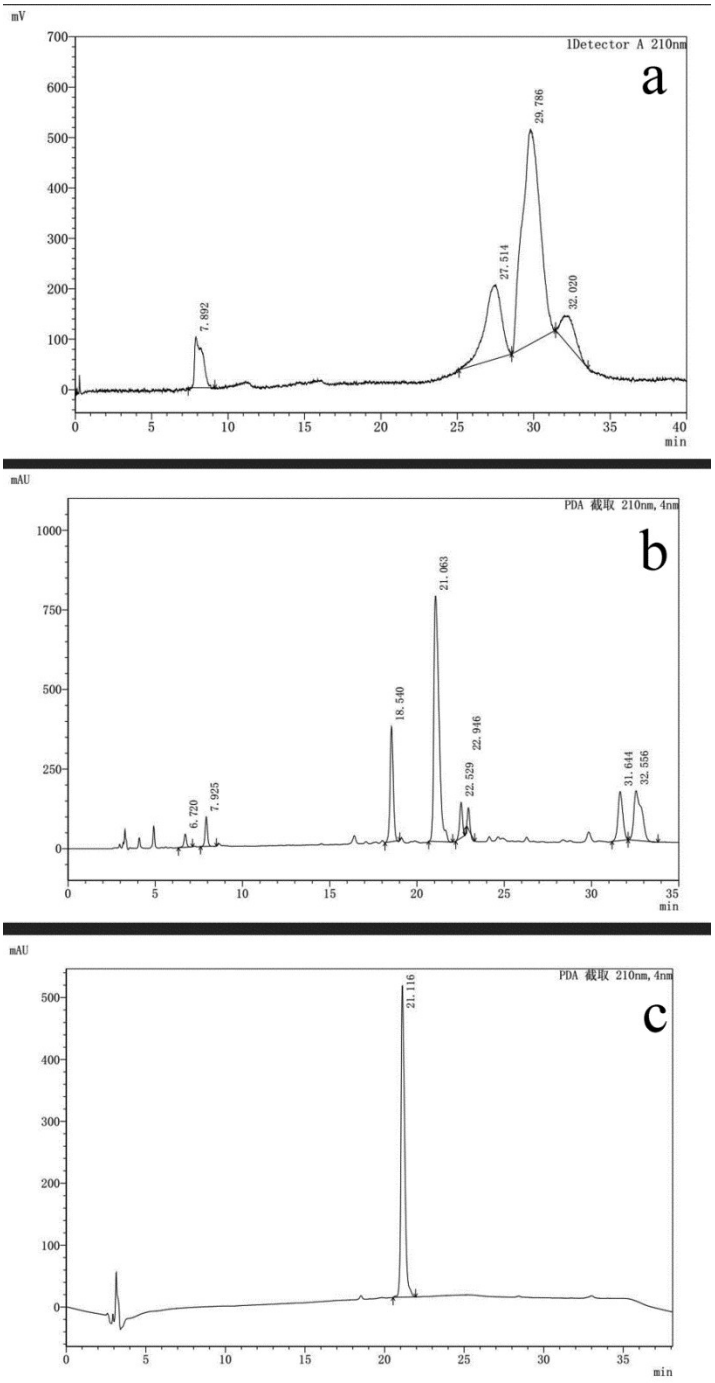


Fig.S2. The chromatogram of conjugates (a: semi-preparative operation; b: before purificating ; c: after purificating.)

HPLC(Shimadzu LC-20A) was used to confirm operating conditions of the purification and value peptide purity, the chromatogram of $D_3F_3$ before and after purificating was illustrated as Fig.S2b,c. Chromatographic conditions：Chromatographic column: C8 ODS Hypersil column

(250×4.6 mm, i.d., 5μm).Mobile phase: The mobile phase consisted of two eluents, phase A was acetonitrile, phase B was. 0.1% TFA (trifluoroacetic acid) solution. The mobile phase ratio using a gradient of acetonitrile. 0～20min，the gradient was 20%～30%. 20～30min，the fixed ratio was 30%. Injection volume: 10 μL. Flow rate: 1.0 mL/min. T=35 °C. The DAD monitoring wavelength was 210 nm.

**MS of $D_3F_3$ peptide compound.**

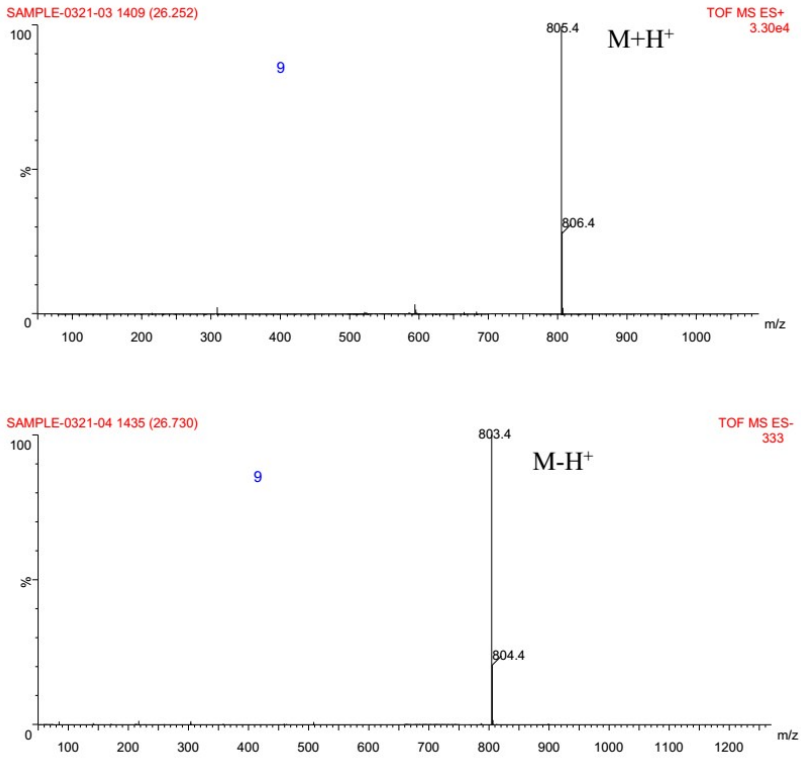


Figure S3 MS spectrum of $D_3F_3$(positive ion mode and negative ion mode; M=804.4).

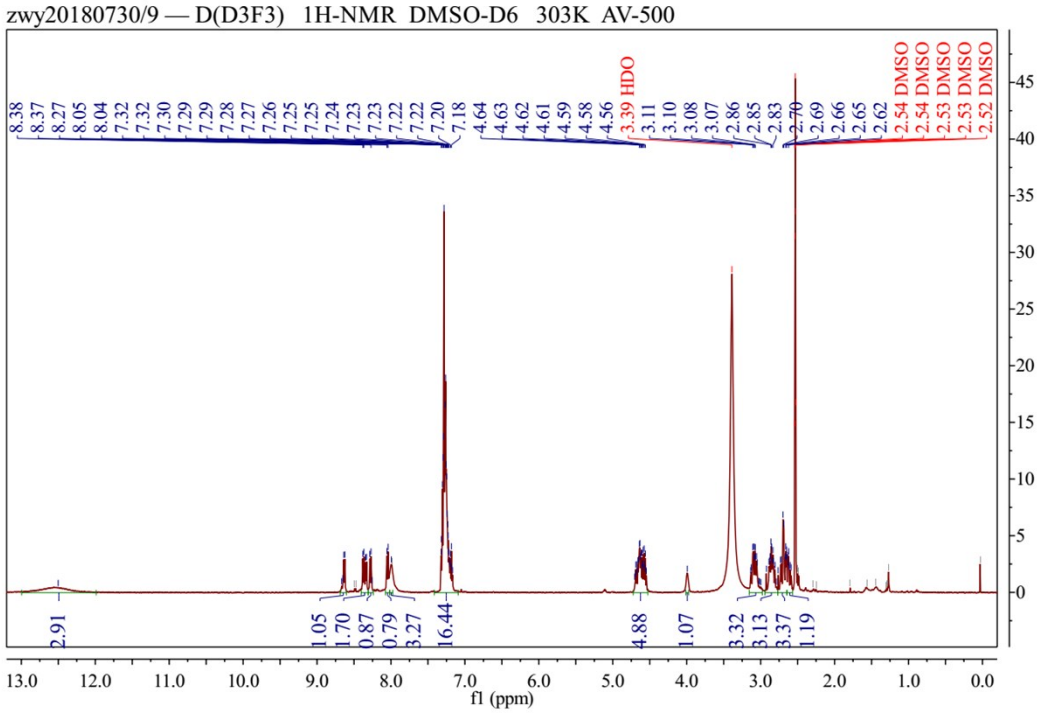


Fig.S4. $^{1}$H-NMR of $D_3F_3$ peptide compound.

TOF-MS of $D_3F_3$: m/z 805.4 [M+H], 803.4 [M-H]。$^{1}$H NMR (500 MHz, DMSO) of $D_3F_3$: δ 12.50 (wide peak, 4H), 8.64～8.62 (d, j=10.0, 2H), 8.64～8.62 (d, j=10.0, 1H), 8.38～8.37 (d, j=5.0, 1H), 8.35～8.33 (d, j=10.0, 1H), 8.29～8.27 (d, j=10.0, 1H), 8.05～8.04 (d, j=5.0, 1H), 7.32～7.17（m,15H）, 4.70～4.55（m,5H）, 4.0～3.98 (m, 1H), 3.13～2.82（m,6H）, 2.73～2.58（m,6H）。

**Gelling properties：**

A series peptide solution，at different concentration level, was prepared and placed overnight, then zinc ions(ZIs) were added into stepwise. The apparent minimum gelation concentration(MGC) of each dendron peptide was confirmed by vial inversion and recorded (Tab.S1).

Tab.S1 The MCG of different $D_3F_3$ peptides and the trigger concentration of zinc ion and calcium ion.

| Peptide category | $D_3F_3$ |
|---|---|
| MCG | 0.4% |
| Trigger concentration of ZIs( μ g/ml) | 162.5 |

We investigated the rough ion concentration in plasma through summarizing correlational research literature, and recorded as follows. 1.% $D_3F_3$ solution was prepared and various divalent cation was added into, for determining of the ions trigger concentration.

The minimum time needed for gelation (MTG) were confirmed through a series parallel experiments, in which we recorded the gelling time after adding 5Mm zinc ion into 1.0% $D_3F_3$ peptide solution and one minute shaking. We confirmed the time by observing inversional vial every 30 seconds(Tab.S2).

Tab.S2 The MTG for $D_3F_3$ peptide.

| Serial number | 1 | 2 | 3 | 4 | 5 | average | SD |
|---|---|---|---|---|---|---|---|
| MTG of $D_3F_3$ (min) | 7.5 | 8 | 8.5 | 6 | 7 | 7.4 | 0.96 |

We investigated the rough ion concentration in plasma through summarizing correlational research literature, and recorded as follows. 1ml whole blood was collected from the heart of healthy SD rat(SPF), 4wt% disodium citrate was chose as anticoagulation and added into at the ratio 1:16. $D_3F_3$ solution was mixed with the whole blood，the concentration of peptide was 2wt%.After one minute shaking and ten minute standing, the vial was inclined, the mixture was mobile.

Tab.S3 The trigger concentration of different divalent cation for $D_3F_3$

| Category | Zn | Ca | Mg | Cu | Ni | Fe |
|---|---|---|---|---|---|---|
| Plasma concentration(μg/mL) | 0.83 | 47.20 | 12.72 | 1.36 | 0.0005 9 | 0.92 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Trigger concentration(μg/mL) | 162.5 | 256.0 | 106.9 | 419.4 | 117.4 | 513.8 |

**Oscillatory rheology:** Rheological tests including dynamic time sweep, dynamic frequency sweep, and dynamic strain sweep were performed on a RheoStress 600 (Thermo) instrument using 60 mm parallel plates at a gap of 0.5 mm. The tests were conducted to record the change between storage (G′) and loss (G″) modulus at 37 °C. Firstly, the gel was carried out dynamic time sweep with a constant frequency of 6.28 rad/s and constant strain value of 1% within 60 min. During the dynamic time sweep, hydrogels were firstly transformed to solution state by vortex vibration(5min), then recovery of hydrogels was examined by recording viscoelastic properties of hydrogels with the increase of time. Then, the gel was characterized by the mode of dynamic frequency sweep within the region of 0.1-100 rad/s at the strain of 1%. Next, the gel was conducted dynamic strain sweep test, in the strain region of 0.1-100% at the frequency of 6.28 rad/s. Finally, the circle sweep was conducted, the low level of shear strain was 1% and the high level was 50%.

**Determination the content of DOX:**

HPLC(Shimadzu LC-20A) was used to determinate the content of DOX. Chromatographic conditions：Chromatographic column: C8 ODS Hypersil column (250×4.6 mm, i.d., 5μm).Mobile phase: The mobile phase consisted of two eluents, phase A was acetonitrile, phase B was. 0.1% TFA (trifluoroacetic acid) solution. The mobile phase ratio using a gradient of acetonitrile. 0～20min，the gradient was 20%～30%. 20～30min，the fixed ratio was 30%. Injection volume: 10 μL. Flow rate: 1.0 mL/min. T=35 °C. The DAD monitoring wavelength was 233 nm.

The chromatogram of pure DOX, $D_3F_3$ peptide hydrogel loaded DTX was illustrated as Fig.S6a,b. The experiment was carried out three times at least. The calibration curve of DTX was illustrated as Fig.S5. The equation is $A=70.263*C_{DTX}+63.978$, R was 0.9998.

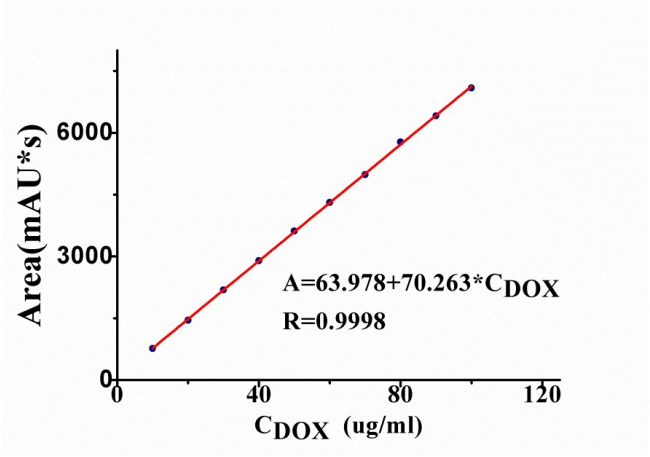


Fig.S5 The calibration curve of DOX

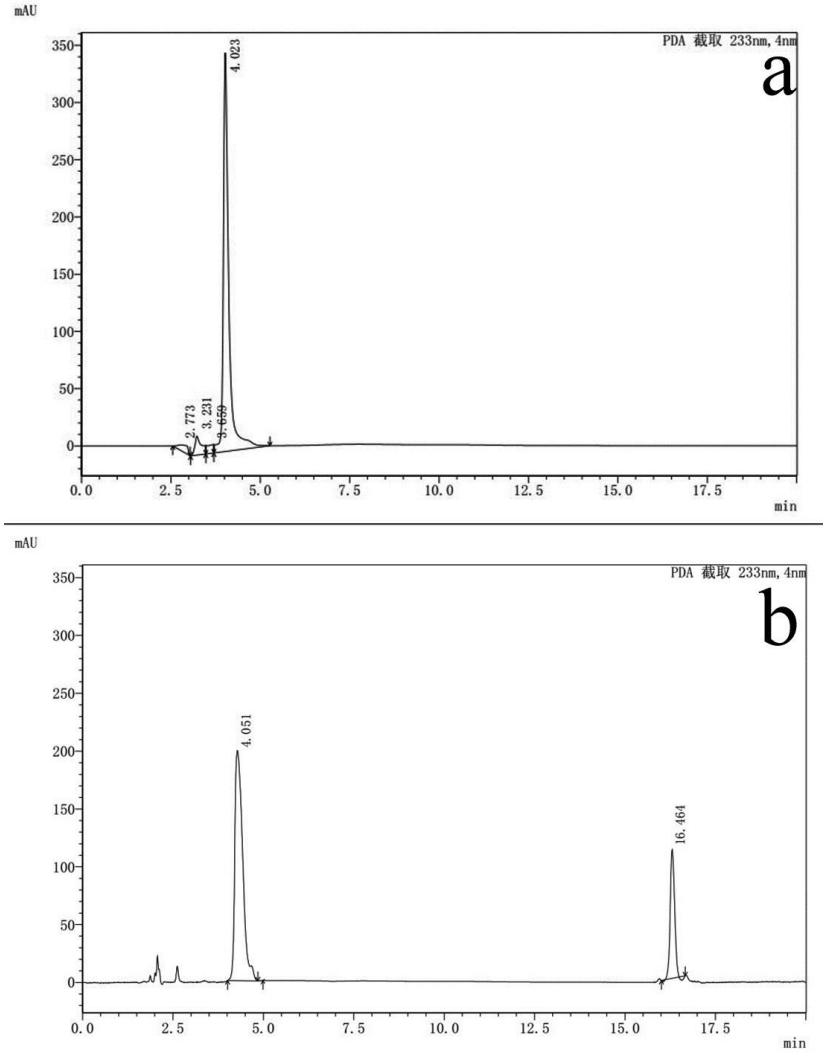


Fig.S6 The HPLC chromatogram (a:DOX;b:$D_3F_3$-DOX)

**Release mechanism**: To provide an explanation about the conceivable mechanism of the DOX release from the hydrogels, the data were analyzed fitting to the following empirical equations:
Model: Ritger-Peppas equation

$M_t / M_\infty = k \cdot t^n$

Where $M_t/M_\infty$ is fractional drug release, $M_t$ is the amount of drug released at time t, $M_\infty$ is the maximum amount of drug released at time ∞, t is the release time, k is a rate constant of kinetic release, and n is the diffusion exponent, characteristic of the drug release mechanism. For $n< 0.5$, it indicates that the drug release follows the Fickian diffusion, whereas the non Fickian drug release process has a value of n between 0.5 and 1.

Tab.S4. The calculated data of DOX hydrogel in drug release experiment of different peptide.

| pH | k | $R^2$ | n |
|---|---|---|---|
| 5.5 | 0.0812 | 0.9412 | 0.6471 |
| 6.5 | 0.0641 | 0.9764 | 0.6383 |
| 7.4 | 0.0572 | 0.9756 | 0.6457 |

**Cytotoxicity assay in vitro**

**Preparation of hydrogels loaded DOX with trigger ions（Zn）:**

20mg $D_3F_3$ peptide was dissolve in 750 μL phosphate buffered saline (PBS) solution (pH = 7.4), 250 μL 0.1M sodium carbonate solution was dropped in, 500 μL DOX solution at 1 mg/mL was added into correspondingly. Then 380 μL PBS was added into. The above solution was incubated at room temperature overnight, then 120 μL zinc ions solution(0.1M) was added in to trigger the formation of the translucent hydrogel.

**Preparation of peptide precursor solution loaded DOX without trigger ions（Zn）:**

20mg $D_3F_3$ peptide was dissolve in 750 μL phosphate buffered saline (PBS) solution (pH = 7.4), 250 μL 0.1M sodium carbonate solution was dropped in, 500 μL DOX solution at 1 mg/mL was added into correspondingly. Then 500 μL PBS was added into.

Tab.S5. The $IC_{50}$ value of DOX to DU145 cells ( μg/ml ).

| Group | Free DOX | DOX-PEP | DOX-PEP-Zn |
|---|---|---|---|
| $IC_{50}$ | 12.46 | 11.14 | 9.30 |

**Zeta Potential** :We have employed Zeta potential to study the structural identifications of

these materials (pure peptide and peptide mixed with zinc-ions). 1% $D_3F_3$ hydrogel and precursor solution without zinc ions were prepared for Zeta potential, all of these sample was diluted with deionized water and the final peptide concentration was 300 μg/ml.

Tab.S6. The Zeta Potential (mV) of sample.

| | |
|---|---|
| Peptide | -43.0 |
| Peptide with Zn(hydrogel) | -27.5 |

**Gelling test in vivo:**

To verify the hydrogel formation could happen at the prostate, gelling test in vivo was conducted, using rat as experiment animal. Doxorubicin was mixed into 1wt% $D_3F_3$ solution was prepared. The concentration of doxorubicin was 0.25mg/ml consistently. All rats were adult male, SD (SPF), weight was about 300~350g. 10wt% chloral hydrate was used as anesthetic. After the anesthesia through intraperitoneal injecting, both the solution of doxorubicin and the $D_3F_3$ peptide solution was injected into ventral page of prostate. Each ventral page were injected at two sites, the amount was 50μl respectively. 4 ,8,24hours after the injection respectively, the rat was executed and excised its prostate immediately, then the prostate was observed by stereomicroscope（Olympus SZX7, Japan）.

**Critical Micelle Concentration (CMC):**The CMC values of $D_3F_3$ in water solution was determined by dynamic light scattering (DLS). Solutions containing different concentration of peptide were tested and the light scattering intensity was recorded for determining the CMC.

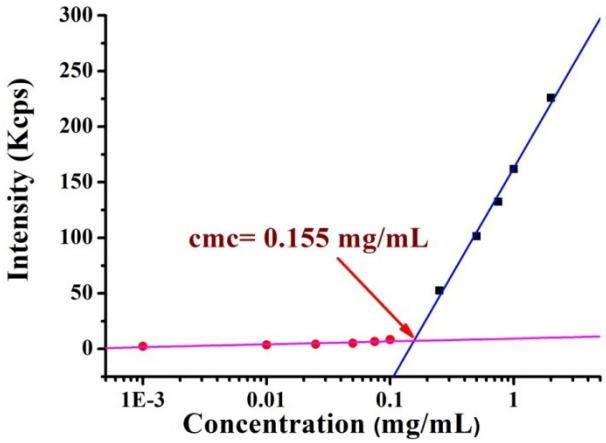


Figure S7. CMC values of $D_3F_3$