Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

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.

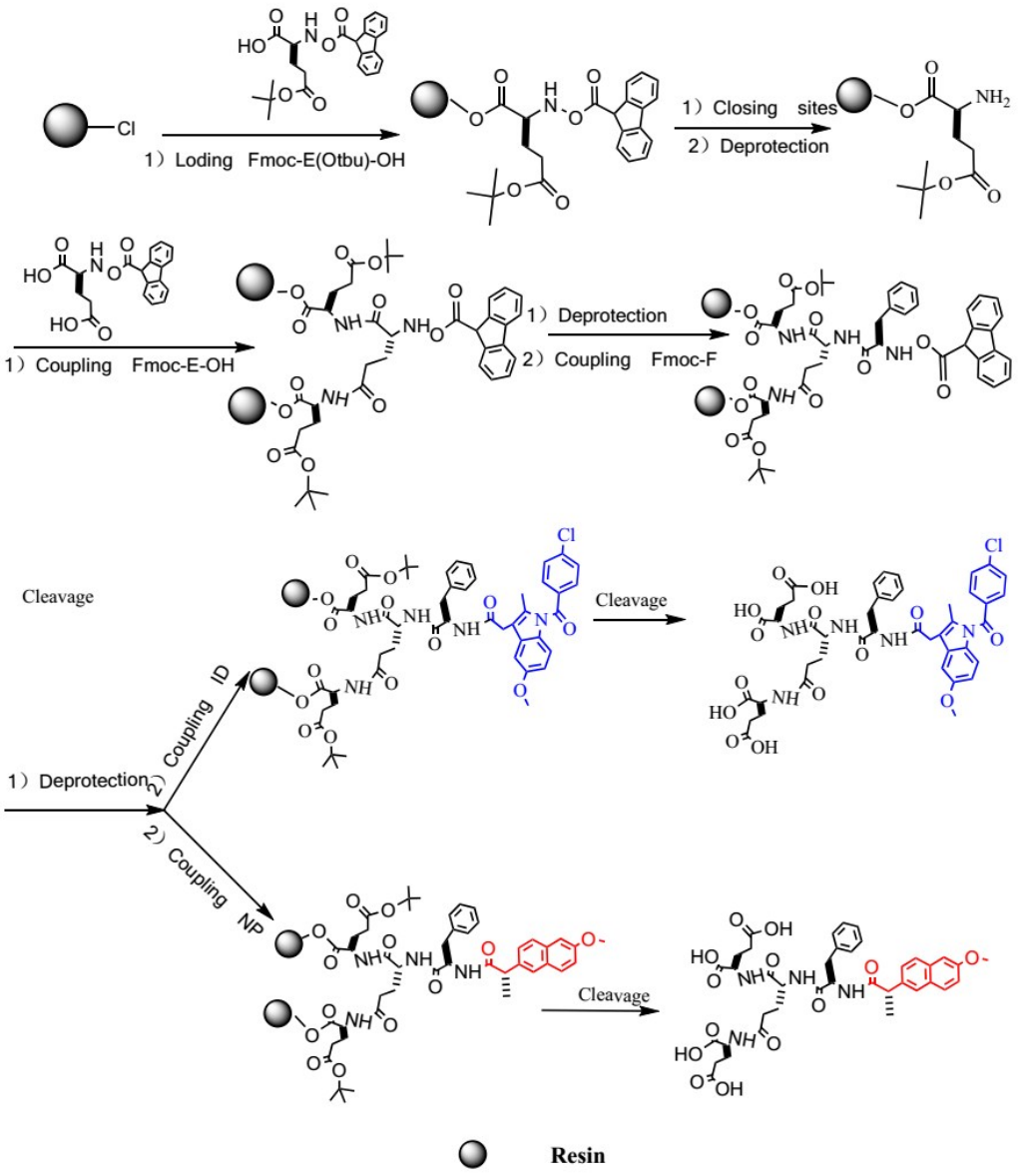

Fig. S1. Schematic diagram of the synthetic routes.

The purification of E_3FID and E_3FNP 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. Fixed mobile phase ratio was 37.5:62.5.Injection volume: 2 mL. Flow rate: 10.0 mL/min. T=35 °C. The DAD monitoring

wavelength was 254 nm and 240nm respectively. The collection time of E_3FID was 12 to 13.5 min according to semi-preparative chromatogram(Fig.S2a). The collection time of E_3FNP was 6.5 to 8.5 min according to semi-preparative chromatogram(Fig.S2b). The elution fluid was concentrated by vacuum rotary evaporation and freeze drying.

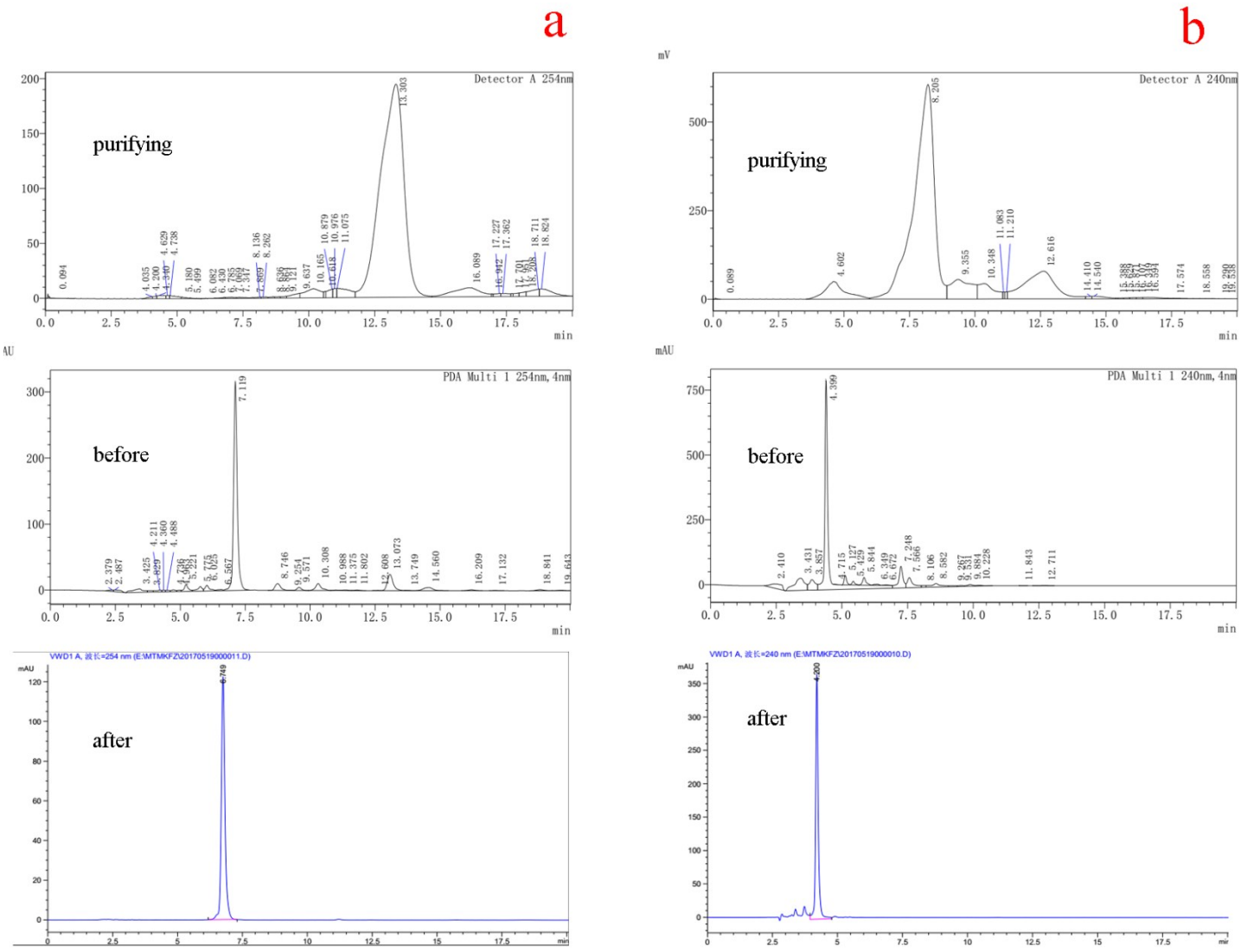

Fig.S2. The chromatogram of conjugates (a: E_3FID ; b: E_3FNP.)

HPLC(Shimadzu LC-20A) was used to confirm operating conditions of the purification and value peptide purity, the chromatogram of E_3FID and E_3FNP before and after purificating was illustrated as Fig.S2a,b.

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. Fixed mobile phase ratio was 37.5:62.5.Injection volume: 10 μL. Flow rate: 1.0 mL/min. T=35 °C. The DAD monitoring wavelength was 254 nm and 240 nm for E_3FID and E_3FNP respectively.

Fig.S3. MS of E3FNp peptide compound

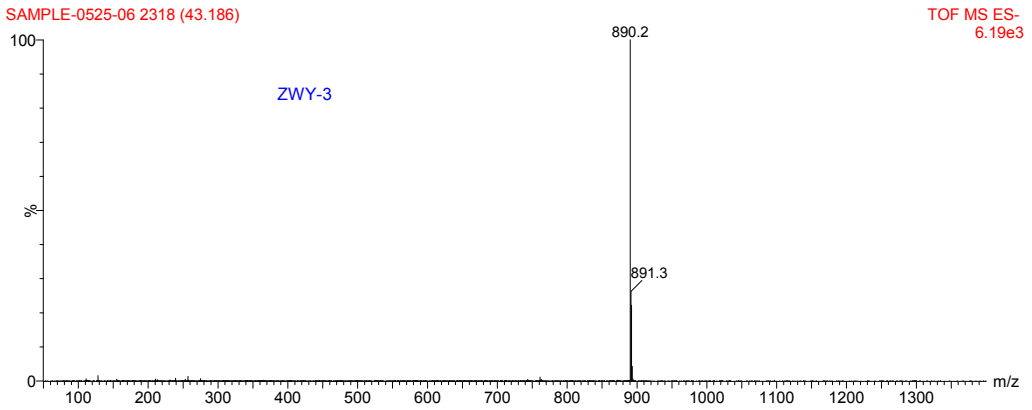

Fig.S3. MS of E3FID peptide compound (M=891.2).

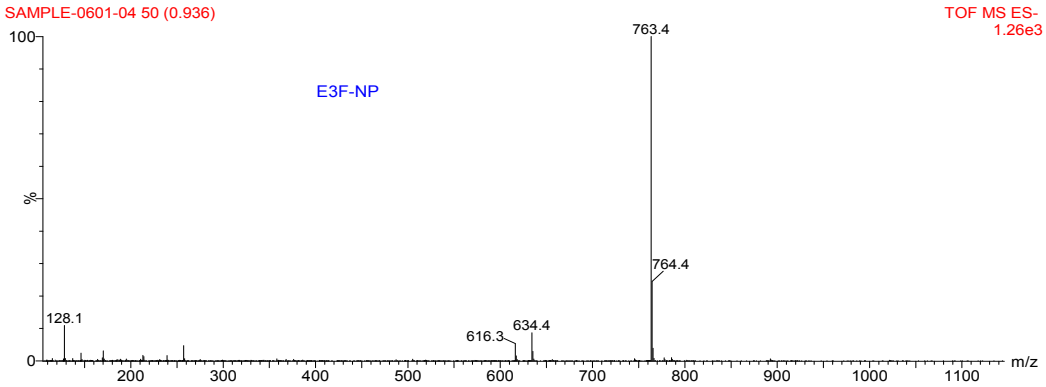

Fig.S4. MS of E3FNp peptide compound (M=764.4).

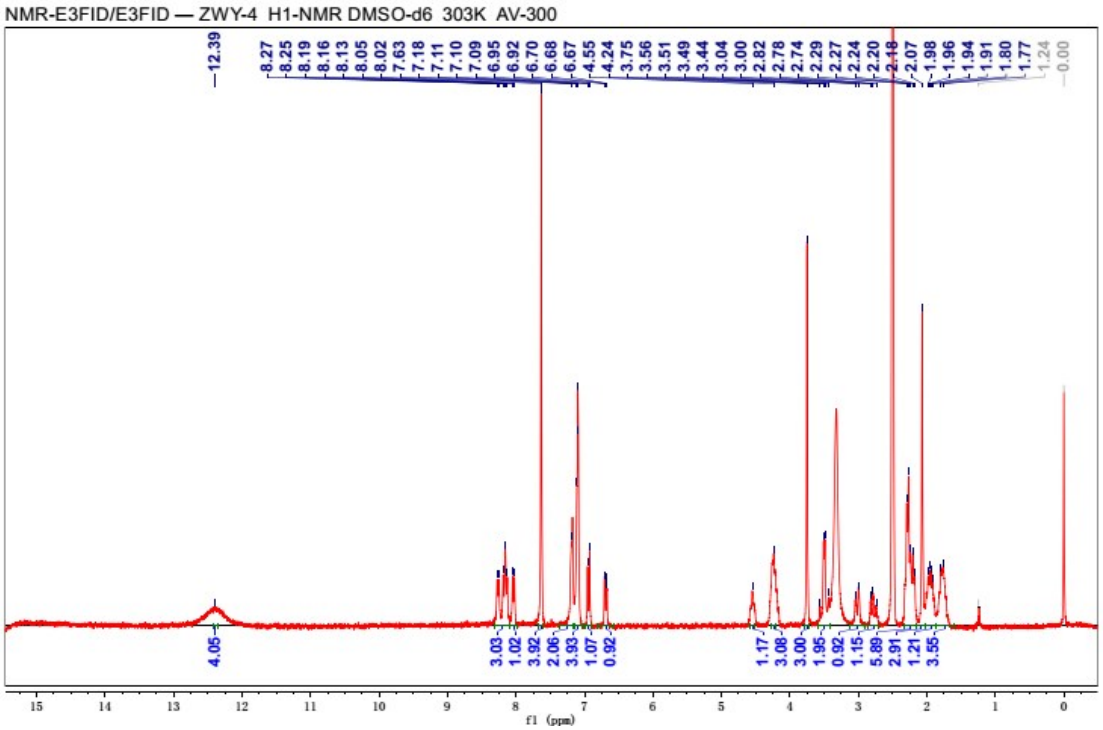

Fig.S5. ^{1}H-NMR of E3FID peptide compound.

NMR (300 MHz, DMSO) of E_3FID δ 12.39 (wide peak, 4H), 8.27~8.25 (d, j=4.0, 1H), 8.19~8.13 (m, 2H), 8.05~8.02 (d, j=6.0, 1H), 7.63 (s, 4H), 7.18~7.09（m，6H）,6.95~6.92(d, j=9.0, 1H), 6.70~6.67 (m, 1H) 4.55 (m,1H), 4.24 (m,3H), 3.75 (s,3H), 3.56~3.44 (m,3H), 3.04~3.00 (d, j=12.0, 1H), 2.82~2.78 (d, j=12.0, 1H), 2.29~2.18 (m, 6H), 2.07 (s, 3H), 1.98~1.91 (m,2H), 1.80~1.77 (m,4H).

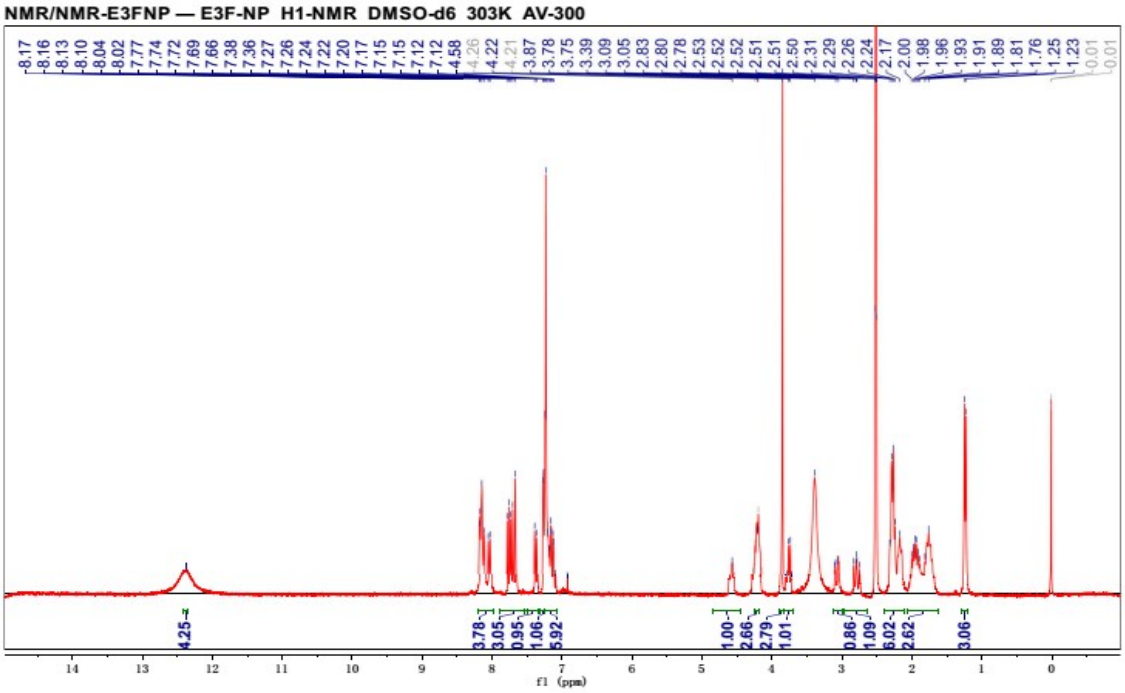

Fig.S6. [1]H-NMR of E3FNp peptide compound.

NMR (300 MHz, DMSO) of E_3FNP δ 12.38 (wide peak, 4H), 8.124~8.062 (m, 4H), 7.77~7.74(d, j=9.0, 1H), 7.72~7.69 (d, j=9.0, 1H), 7.66 (s, 1H), 7.38~7.36 (d, j=9.0, 1H), 7.27~7.26 (d, j=3.0,H), 7.24 (s, 1H), 7.22~7.09(m, 5H), 4.64~4.53（m，1H），4.28~4.16（m，3H），3.87（s，3H), 3.80~3.73（m，1H）， 3.51~3.25(m, 4H), 3.10~3.05 (m，2H), 2.83~2.75 (m，2H), 2.31~2.24 (m，4H), 2.21~2.09 (m，2H), 2.00~1.91 (m，2H), 1.89~1.76 (m，2H), 1.25~1.23 (d, j=6, 3H).

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 E_3FID/ E_3FNP peptides and the trigger concentration of zinc ion and calcium ion.

Peptide category	E_3FID	E_3FNP
MCG	0.8%	1.1%
Trigger concentration of ZIs(μ g/ml)	345.3	385.9

We investigated the rough ion concentration in plasma through summarizing correlational research literature, and recorded as follows. 1.5% E_3FID/ E_3FNP 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 1.5% E_3FID/ E_3FNP peptide solution and one minute shaking. We confirmed the time by observing inversional vial every 30 seconds(Tab.S2).

Tab.S2 The MTG for E_3F_3 peptide.

Serial number	1	2	3	4	5	average	SD
MTG of E_3**FID** (min)	4	5	4	6	5	4.9	0.74
MTG of E_3**FNP** (min)	9.5	10	11	8.5	9	9.6	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. E_3FID/ E_3FNP solution was mixed with the whole blood，the concentration of peptide was 3wt%.After one minute shaking and ten minute standing, the vial was inclined, the mixture was mobile.

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 30 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 2% and the high level was 60%.

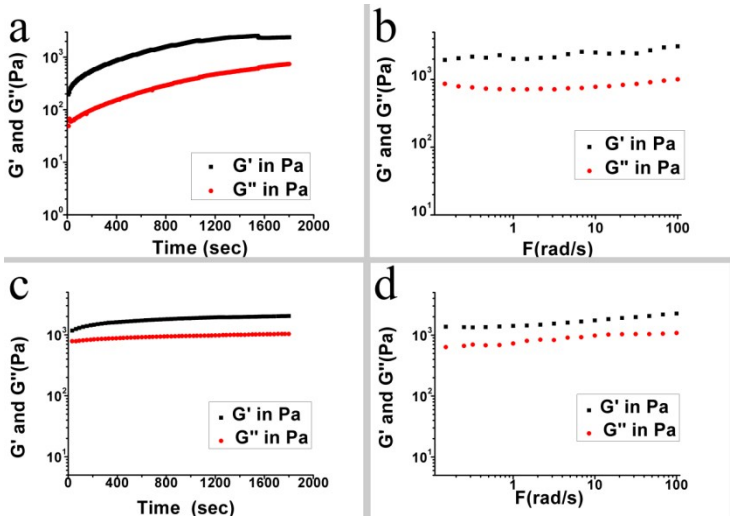

Fig.S7 Viscoelastic properties (The concentration of gel was 1.5wt%, pH was 7.4): Dynamic time sweep(a:E_3FID;c: E_3FNP); Dynamic frequency sweep (b:E_3FID; d:E_3FNP).

Determination the content of DTX:

The chromatogram of pure DTX, E_3FID/ E_3FNP peptide and hydrogel loaded DTX was illustrated as Fig.S8-12. The experiment was carried out three times at least. The calibration curve of DTX was illustrated as Fig.S13. The equation is A=5.815*C_{DTX}-37.159, R was 0.9993.

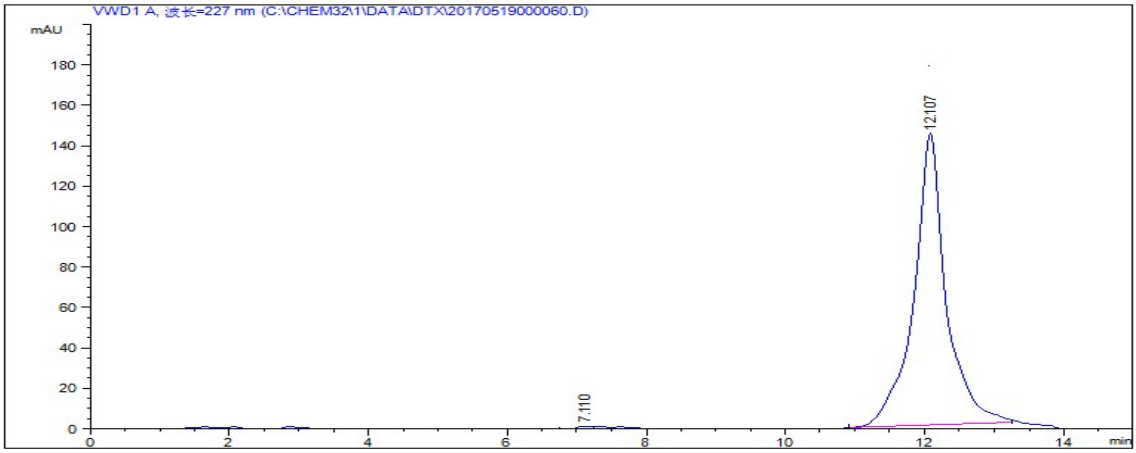

Fig.S8. The chromatogram of pure DTX.

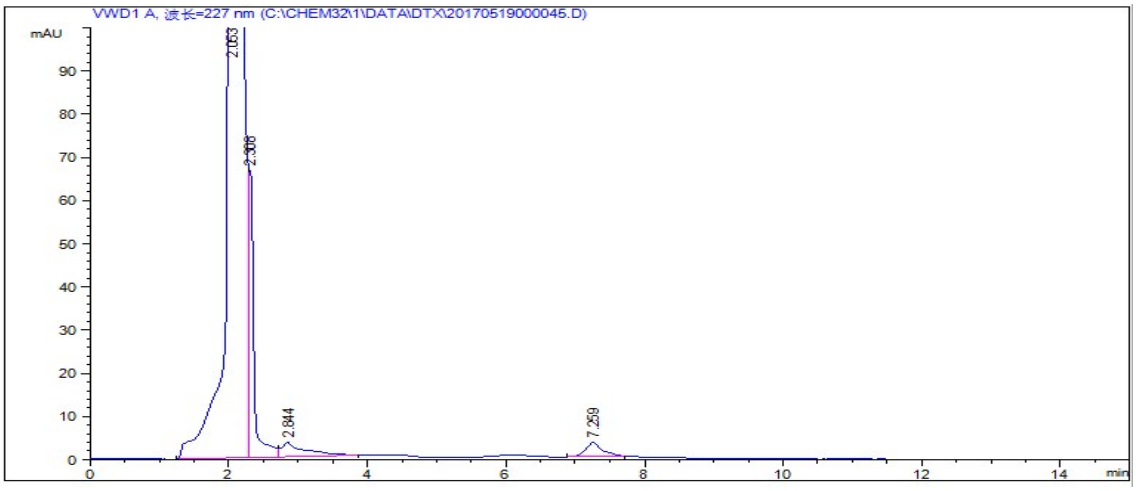

Fig.S9. The chromatogram of E_3FID compound.

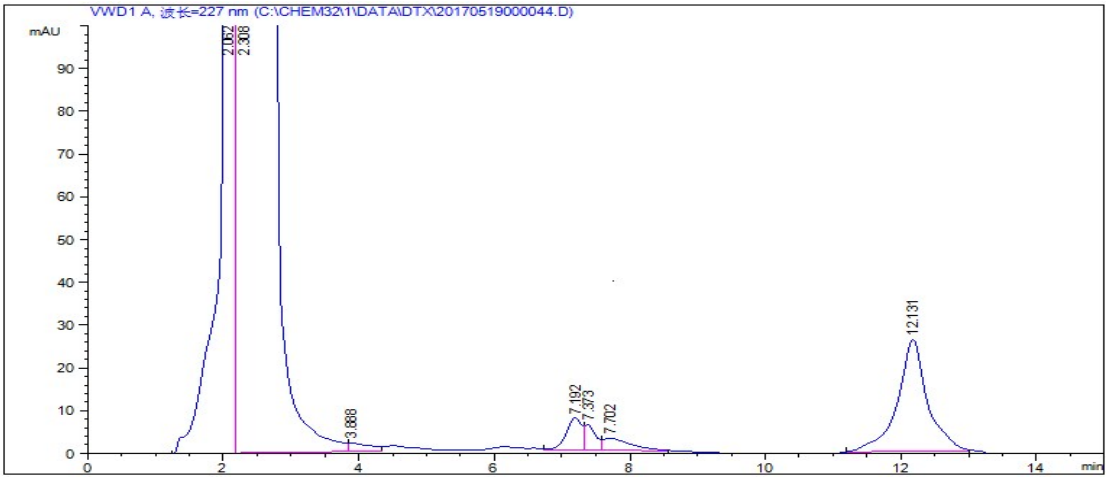

Fig.S10 The chromatogram of E_3FID hydrogel loaded DTX.

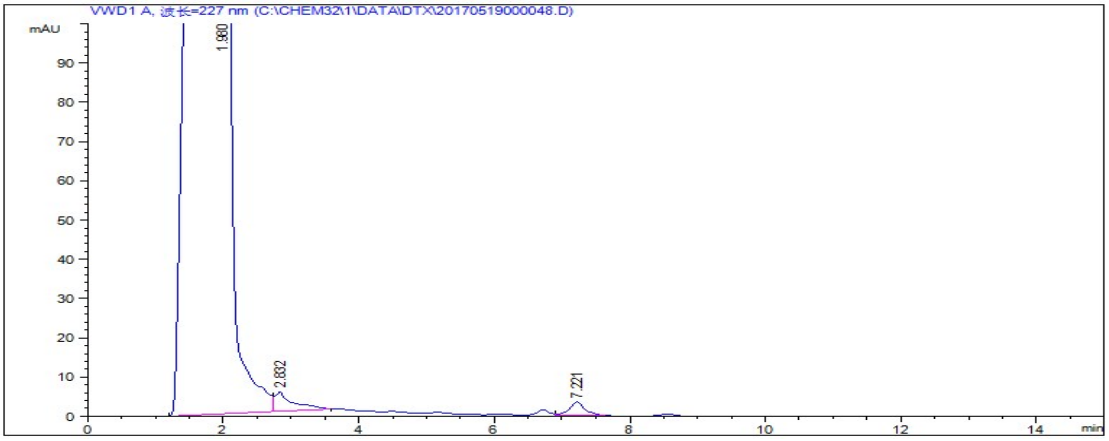

Fig.S11. The chromatogram of E_3FNP compound.

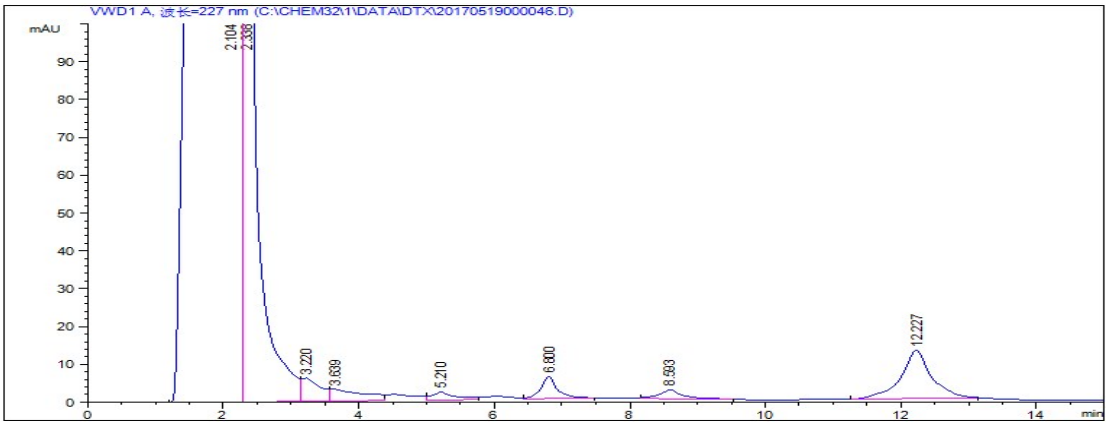

Fig.S12. The chromatogram of E_3FNP hydrogel loaded DTX.

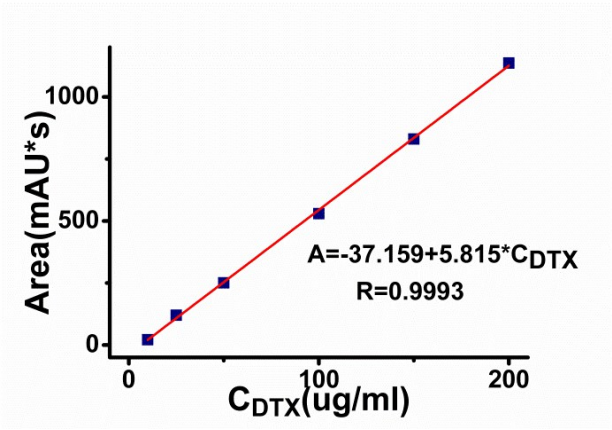

Fig.S13. The calibration curve of DTX.

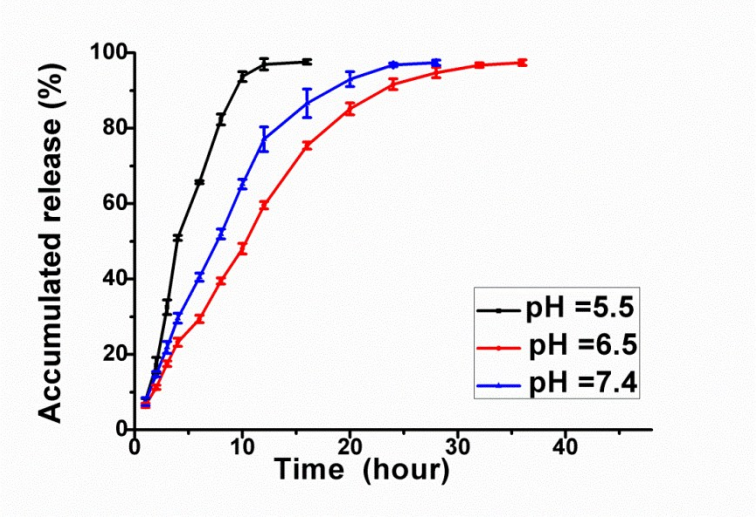

Fig.S14. The cumulative release of DTX from E_3FNP hydrogels. Mean±SD (n=3).

Release mechanism: To provide an explanation about the conceivable mechanism of the DTX 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_∞ is fractional drug release, M_t is the amount of drug released at time t, M_∞ 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.S3. The calculated data of DTX hydrogel in drug release experiment of different peptide.

		Ritger-Peppas		
Peptide category	pH	k	R^2	n
	5.5	0.1563	0.9269	0.5662
E_3FID	6.5	0.0573	0.9863	0.7244
	7.4	0.0612	0.9876	0.7402
	5.5	0.1107	0.9434	0.9406
E_3FNP	6.5	0.0774	0.9763	0.765
	7.4	0.1032	0.9644	0.7383

Cytotoxicity assay in vitro

Tab.S4. The IC_{50} value of DTX to DU145 cells or PC3 cells (μg/ml).

Compound	E_3FID		E_3FNP	
Group	DU145	PC3	DU145	PC3
Free DTX	6.12	21.41	6.12	21.41
DTX-PEP	5.17	**11.36**	5.579	**18.17**
DTX-PEP-Zn	**4.27**	9.67	5.285	14.25

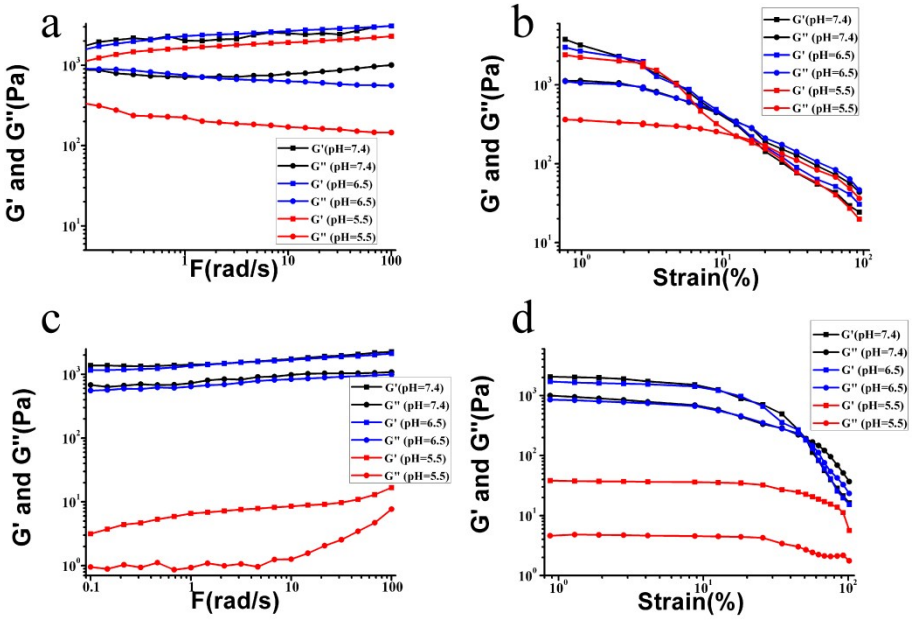

Fig.S15 Viscoelastic properties (The concentration of gel was 1.5wt%.): Dynamic frequency sweep(a:E_3FID;c: E_3FNP); Dynamic strain sweep (b:E_3FID; d:E_3FNP).

We have employed photoluminescence (PL) to study the structural identifications of these materials (free and DTX-loaded hydrogels). 1.5% E_3FID (or E_3FNP) hydrogel and hydrogel loaded DTX was prepared for PL, these sample was diluted with deionized water and the final peptide concentration was 150 μ g/ml. In both experiments, the excitation and emission slits were 5nm , the assay volume was 1.0 mL, PMT Voltage was 400V.

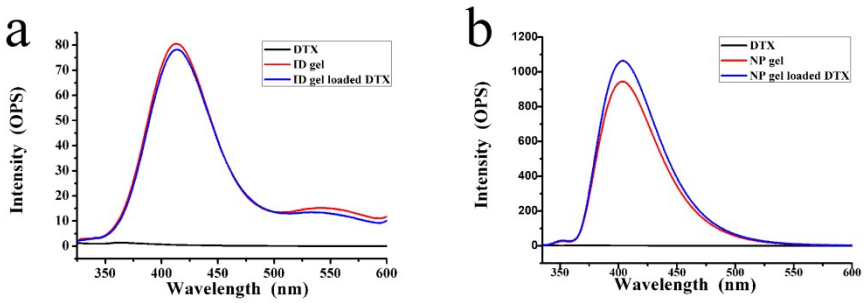

Fig.S16 Fluorescence spectroscopy (a:E_3FID;b: E_3FNP)

We have employed Zeta potential to study the structural identifications of these materials (free and DTX-loaded hydrogels). 1.5% E_3FID (or E_3FNP) hydrogel and hydrogel loaded DTX was prepared for Zeta potential, the solution of E_3FID (or E_3FNP) with or without DTX was prepared as the control, all of these sample was diluted with deionized water and the final peptide concentration was 300 μ g/ml.

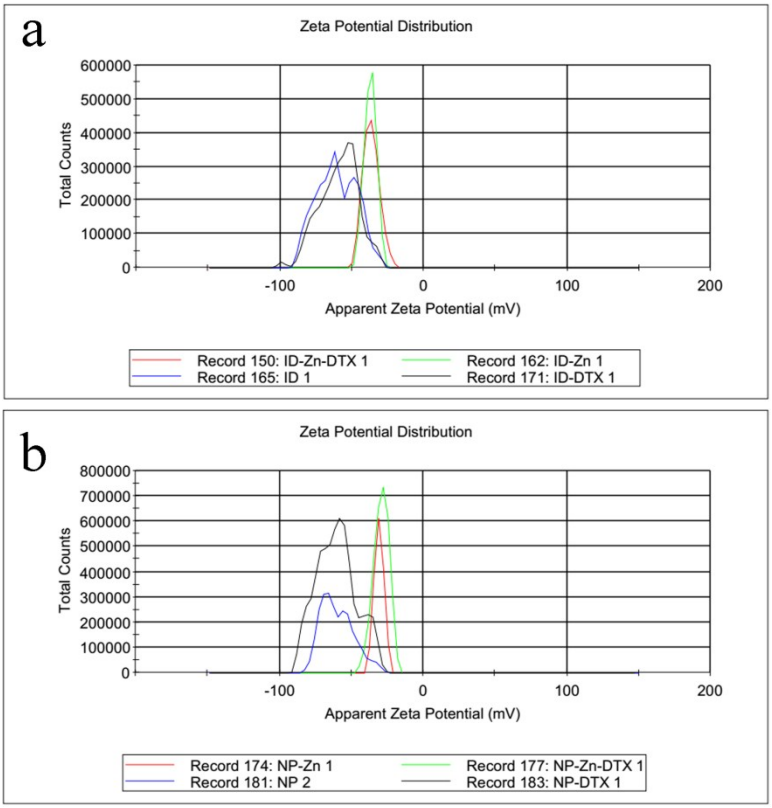

Fig.S17 The Zeta Potential of E_3FID(a) and E_3FNP(b)

Tab.S5. The Zeta Potential (mV) of sample.

System	E_3FID（mv）	E_3FNP（mv）
Peptide	-60.3	-59.5
Peptide with Zn(hydrogel)	-37	-28.8
Peptide mixed with DTX	-64.5	-60.9
Peptide with Zn and DTX(hydrogel loaded DTX)	-38.2	-29.8

Determination the content of ID and NP:

ID: The mobile phase consisted of two eluents, phase A was acetonitrile and phase B was deionized water, the fixed ratio was 45:55. Injection volume:10μL. Flow rate: 1.0 mL/min. T was 35 °C. The UVD monitoring wavelength was 320 nm. The chromatogram of pure ID and E_3FID hydrogel degraded by PK was illustrated as Fig.S18. The experiment was carried out three times at least. The equation of ID is $A=23.63*C_{ID}-9.62$, R was 0.9989(The scope was 10.0~100 μ g/ml).

NP: The mobile phase consisted of two eluents, phase A was acetonitrile and phase B was deionized water, the fixed ratio was 60:40. Injection volume:10μL. Flow rate: 1.0 mL/min. T was

35 °C. The UVD monitoring wavelength was 271 nm. The chromatogram of pure NP and E_3FNP hydrogel degraded by PK was illustrated as Fig.S19. The experiment was carried out three times at least. The equation of NP is $A=29.31*C_{NP}+21.88$, R was 0.9982(The scope was 5.625~45 μ g/ml).

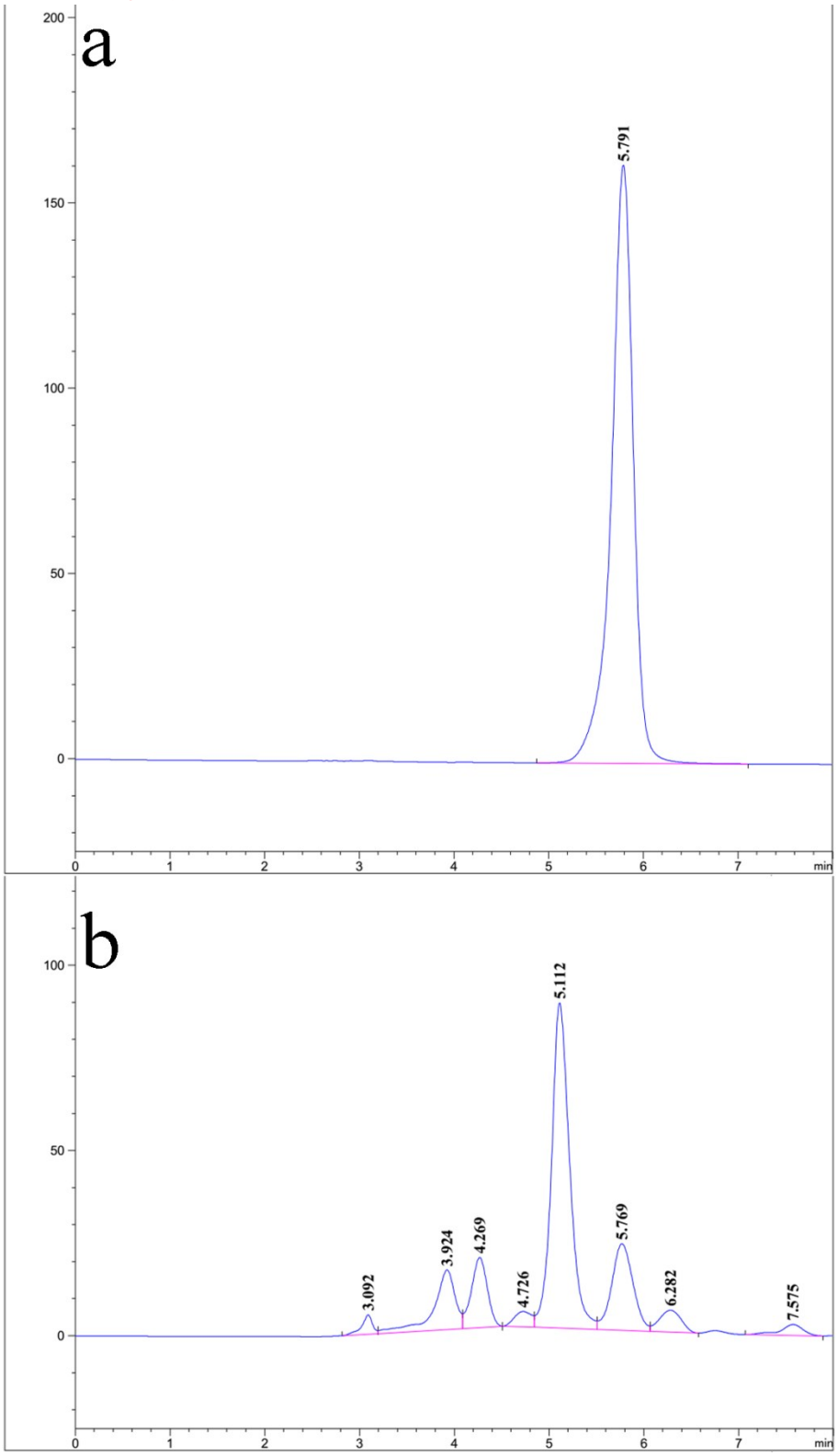

Fig.S18. The chromatogram of pure ID(a) and hydrogel(b) degraded by PK.

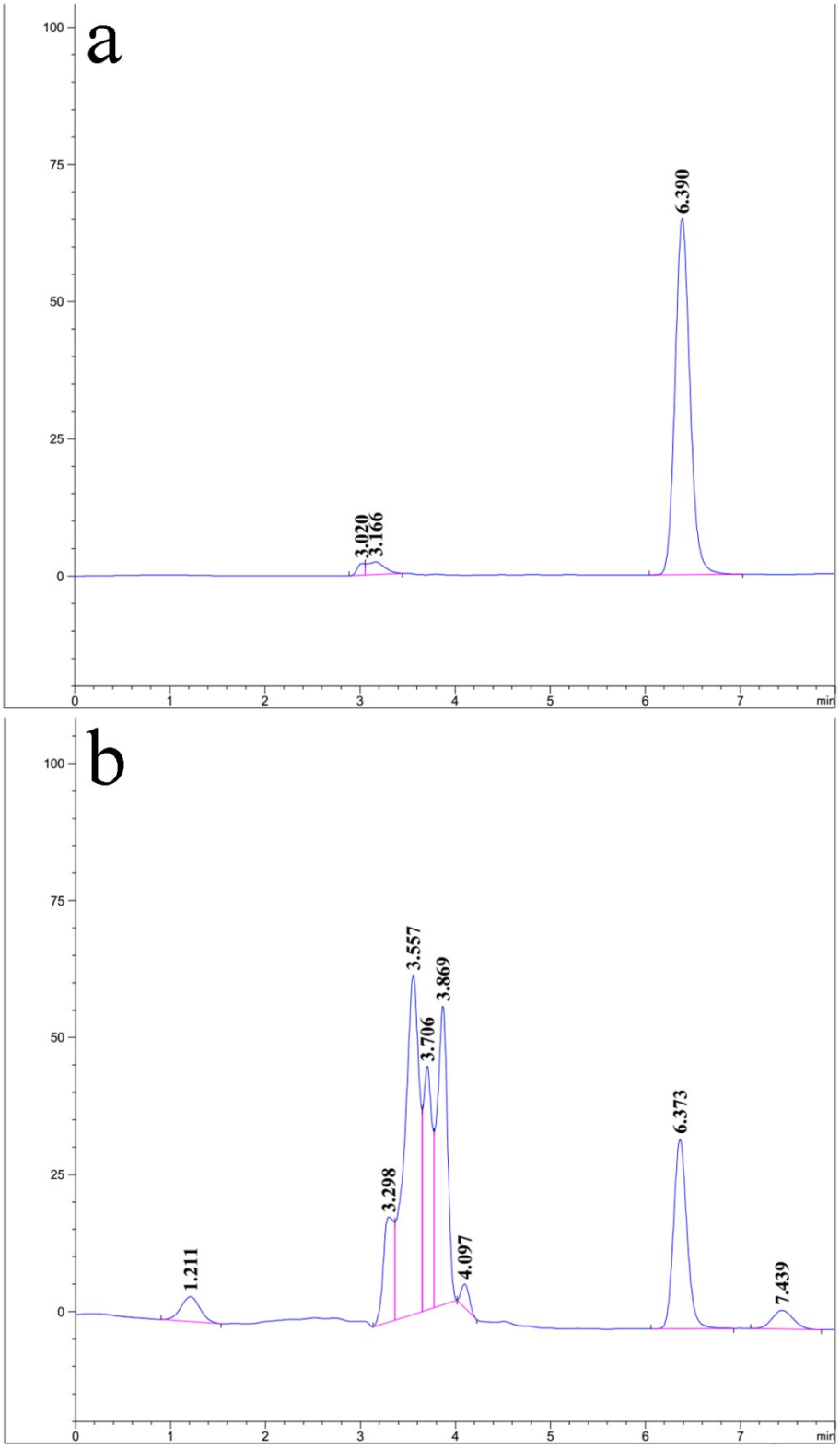

Fig.S19. The chromatogram of pure NP(a) and hydrogel(b) degraded by PK.

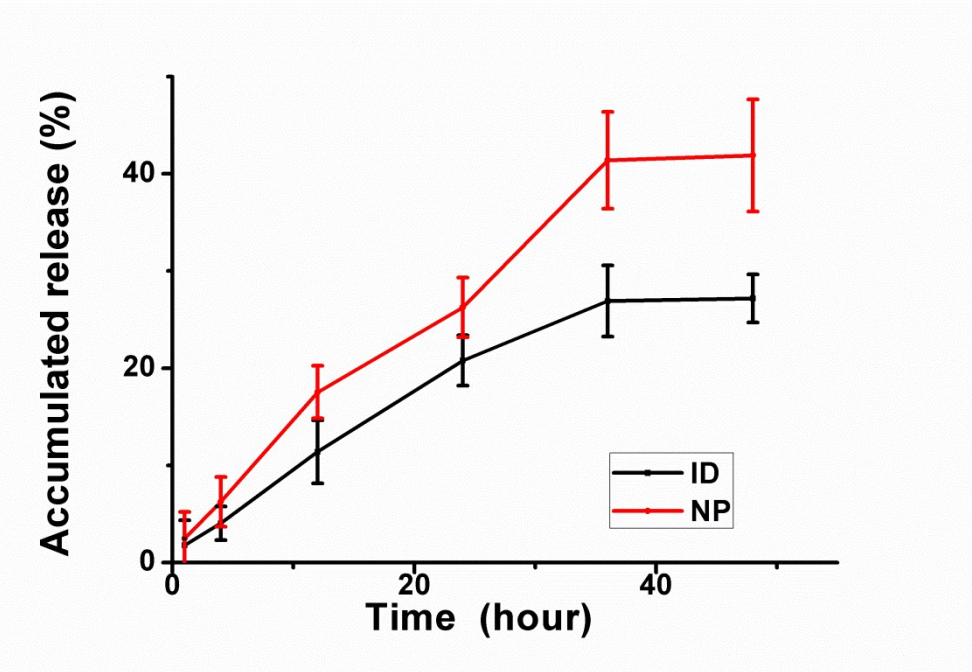

Fig.S20 The cumulative release of ID or NP from hydrogels (Mean±SD; n=3)