Supporting Information

Materials and general methods:

Chemicals materials: Carbamazepine (CBZ) was purchased from Aladdin (Shanghai, China). 2-Cl-trityl chloride resin, 2-(1H-benzotriazol-1-yl)-1,1,3,3 –tetramethyluronium hexafluorophosphate (HBTU), 1-hydroxy-benzotriazole monohydrate (HOBT), diisopropylethylamine (DIPEA), trifluoroacetic acid (TFA) and Fmoc-amino acids were obtained from GL Biochem (Shanghai, China). N,N-Dimethylformamide (DMF) and tetrahydrofuran (THF) were purchased from Sinopharm Chemical Co., Ltd (Shanghai, China). All other reagents and solvents were commercially available and were used without further purification, unless noted otherwise.

General methods: The synthesized compounds were characterized by \(^1\text{H}-\text{NMR}\) (AV-500. Bruker) and ESI-TOF (Q-TOF. micro. Waters). Infrared spectra were scanned on a FTIR-8400S spectrophotometer (Shimadzu). Fluorescence emission spectra were operated on RF-5301PC spectrofluorophotometer (Shimadzu).

Drug release of CBZ was carried out by a LC-20AD (Shimadzu) system.

The morphologies were performed on transmission electron microscope (TEM, JEM-2100, Japan) and scanning electron microscope (SEM, Ultra Plus. Zeiss).

Circular dichroism (CD) data were collected on a Jasco J-810 CD spectropolarimeter.

Rheology test was performed on a RheoStress 600 (Thermo) system by using 60 mm parallel plates at a gap of 500 \(\mu\)m.

Synthesis and characterization:

Synthesis of CBZ-acyl isocyanate: 1 mmol CBZ (236 mg) and 15 mL anhydrous 1, 2-dichloroethane were added into a three-neck flask and cooled to 0-5 \(^\circ\)C with ice water. 1.5 mmol (0.13 mL) oxalyl chloride was added dropwise. The reaction mixture was stirred at room temperature for 1 h, then kept at 50-55 \(^\circ\)C for about 3 h, further heated to approx. 65 \(^\circ\)C and refluxed for 4 h. HCl and unreacted oxalyl chloride were evaporated under reduced pressure. The residual carbamazepine isocyanate was dissolved in dry THF (5mL) and directly employed in the subsequent reaction.
Scheme S-1. The synthesis route of carbamazepine isocyanate.

**Synthesis of CBZ-FFG:**

The peptide derivative was prepared by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin (1.0~1.2 mmol/g) and the corresponding N-Fmoc protected amino acids. The resin was swelled in dry DCM for 20 minutes, followed by washing with DCM for three times (2 min×3). Then the first amino acid Fmoc-Gly-OH (2 equiv.) and DIPEA (2 equiv.) in DCM were added to the SPPS reactor. After shaking 1-2 hour, the first amino acid was loaded onto the resin. After washing the resin with DCM for three times (2 min×3), the unreacted sites in resin were quenched with mixture solution (DCM/MeOH/DIPEA=80/15/5) for two times (10 min×2). Here, wash the resin with anhydrous DMF for five times (2 min×5). Then the 20% piperidine (in DMF) was added for 30 min to remove the protecting group, followed by washing with DMF for five times (2 min×5). Then the next Fmoc-Phe-OH (2 equiv.) was coupled to the free amino group using HBTU (2 equiv.) and HOBT (2 equiv.) as the coupling reagents and DIPEA (4 equiv.) as catalysis reagent. The growth of the peptide chain was according to the established Fmoc SPPS protocol. The next deprotection and coupling steps were consistent with the above. At the final step, carbamazepine isocyanate (2 equiv.) was used to attach on the peptide using THF as solvent in presence of DIPEA (2 equiv.). After carbamazepine isocyanate was coupled, excessive reagents were removed through five times of DMF wash (2 min×5), followed by five steps of DCM wash (2 min×5). The cleavage of the peptide from the resin was achieved by using TFA for 30 minutes. Filtered the resin and washed it 2 ~ 3 times with fresh TFA. TFA was removed by rotary-evaporate process. Then, the residue was poured into a moderate amount of ice-cold diethylether. The
resulting mixture was centrifuged for 15 min at 10,000 rpm. Afterward, decanting the supernatant, the precipitate was dispersed in double-distilled water and lyophilized. The resulting solid product was purified by reverse phase HPLC. 


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\text{Scheme S-2. The synthesis route of CBZ-FFG}
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a). Fmoc-Gly-OH, DIPEA, DCM  
b). 20% piperidine in DMF  
c). Fmoc-Phe-OH, HOBT, TBTU, DIPEA, DMF  
d). carbamazepine isocyanate, DIPEA, THF  
e). TFA 

**Fig. S-1.** MS of compound CBZ-FFG
Formation of the gel: 4 mg of CBZ-FFG was dispersed in a vial with 0.2 mL PBS buffer (pH=7.4) containing 1 equiv. 0.1M Na$_2$CO$_3$. The suspension was ultrasoniced for 10 min followed by a water bath (40 °C) to make the peptide totally dissolve. An opaque gel produced after kept at room temperature within 10 minutes or incubated at 37 °C for 1 h. This was confirmed by vial inversion.

**Fig. S-2.** 1H-NMR of CBZ-FFG

**Fig. S-3.** TEM image of 3 months stored gel (A) and TEM image of gel after releasing drug for 5 days (B). The inset photo is the local amplified image
Fig. S-4. IR spectra of CBZ-FFG and xerogel

Fig. S-5. Fluorescence emission spectra of the gelator and gel. The excitation wavelength was 324 nm
**Fig. S-6.** A schematic illustration of the internal self-assembly of the gelator in gel state (All simulations and calculations were performed using Accelrys Discovery Studio 2.5)

**Rheology measurements:**
Rheology test was performed on a RheoStress 600 (Thermo) system using 60 mm parallel plates at a gap of 500 μm. The test was conducted to monitor the change in storage (\(G'\)) and loss (\(G''\)) modulus at 37 °C. The gel was firstly characterized by the mode of dynamic strain sweep, within the strain region of 0.1-100 % and the frequency of 6.28 rad/s. Then, the gel was carried out a dynamic frequency sweep in the region of 0.1-100 rad/s at the strain of 1%. Finally, the dynamic time sweep was conducted at a constant frequency of 6.28 rad/s and constant strain value of 1%.

**Drug release determination:** 0.3 mL of fresh PBS buffer solutions (pH = 7.4) was added upon the surface of 0.2 mL gel (2.0 wt%). 0.2 mL of the upper buffer solution was taken out at the desired time point for CBZ content determination using a LCMS-20AD (Shimadzu) system, and 0.2 mL of fresh PBS buffer solution was added back. The experiment was conducted three times at 37 °C.

**Chromatographic conditions:**
Chromatographic column: C18 ODS Hypersil column (250×4.6 mm, i.d., 5 μm).
Mobile phase: The mobile phase consisted of two eluents, A phase was ammonium acetate buffer (20 mM) using acetic acid adjusted to pH =6
B phase consisted of methanol and acetonitrile (1/1, v/v)
Injection volume: 20 μL
Flow rate: 1.0 mL/min
T=37 °C
The DAD monitoring wavelength was 285 nm.

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Fig. S-7. The chromatogram of pure CBZ

Fig. S-8. The chromatogram of a typical release buffer
Cytotoxicity Study: The biocompatibility of the hydrogel was evaluated by MTT assay. The HUV cells were seeded in a 96-well plate at a density of 10000 cells per well with 0.2 mL medium (DMEM) contained 10% FBS and 1% penicillin-streptomycin solution. After incubating 24 h, the solutions of the hydrogel at a series of different concentrations were added (100 μL per well). 24 h later, added 20 μL of MTT reagent per well. After another 4 h, removed the medium and MTT reagent. And then 0.15 mL DMSO was added to each well to dissolve the formazan crystals. The final result was performed on an absorbance microplate reader at 490 nm. Cells without the treatment of the hydrogel were used as the control. The cell viability was calculated by the following formula: The cell viability rate (%) = \frac{OD_{sample}}{OD_{control}} \times 100\%.
Fig. S-10. MTT assay of the gel on HUV cells

Fig. S-11. The chemical bond breaking mechanism of CBZ-FFG