Molecular design of peptide amphiphiles for controlled self-assembly and drug release

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Scheme S1. Chemical structures of peptide amphiphiles (PAs) with different capping groups and hydrophilic domains.

Table S1. Values of MGC and CAC of PA molecules with varying capping groups

<table>
<thead>
<tr>
<th>Sequence</th>
<th>MGC (%)</th>
<th>CAC (μM)</th>
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<tr>
<td>C_{12}-VVAADD</td>
<td>2.8</td>
<td>378.4</td>
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<tr>
<td>Fmoc-C_{12}-VVAADD</td>
<td>2.2</td>
<td>131.7</td>
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<tr>
<td>Nap-C_{12}-VVAADD</td>
<td>2.0</td>
<td>107.3</td>
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</table>

Note: MGC: minimal gelation concentration; CAC: critical aggregation concentration.
Fig. S1. HPLC elution curves of C₁₂-VVAADD (A), Fmoc-C₁₂-VVAADD (B), and Nap-C₁₂-VVAADD (C). Purity > 90%.
Fig. S2. TOF-MS spectra of C$_{12}$-VVAADD (A), Fmoc-C$_{12}$-VVAADD (B), and Nap-C$_{12}$-VVAADD (C).

Fig. S3. (A) $^1$H NMR spectrum of C$_{12}$-VVAADD (300 MHz, DMSO).

$^1$H NMR (300 MHz, DMSO) δ 12.84 (s, 3 H), 8.26 – 7.94 (m, 6 H), 4.55 (dd, $J = 13.5$, 7.8 Hz, 2 H), 4.42 (s, 2 H), 4.25 (dd, $J = 7.1$, 4.9 Hz, 2 H), 2.82 – 2.52 (m, 8 H), 2.01 – 1.92 (m, 2 H), 1.23 (s, 16 H), 1.18 (dd, $J = 7.0$, 2.1 Hz, 10 H), 0.81 (d, $J = 6.8$ Hz, 12 H).

(B) $^1$H NMR spectrum of Fmoc-C$_{12}$-VVAADD (300 MHz, DMSO).

$^1$H NMR (300 MHz, DMSO) δ 12.50 (s, 3 H), 8.01 – 7.88 (m, 6 H), 7.73 – 7.65 (m, 3 H), 7.41 (d, $J = 7.2$ Hz, 2 H), 7.35 – 7.16 (m, 4 H), 4.67 – 4.36 (m, 4 H), 4.28 (s, 2 H), 4.26 (s, 2 H), 3.38 (s, 1 H), 2.98 – 2.92 (m, 2 H), 2.61 (qd, $J = 16.8$, 5.8 Hz, 6 H), 2.12 (dd, $J = 15.0$, 7.2 Hz, 2 H), 1.21 (s, 16 H), 1.17 (d, $J = 7.0$ Hz, 8 H), 0.80 (d, $J = 6.8$ Hz, 12 H).

(C) $^1$H NMR spectrum of Nap-C$_{12}$-VVAADD (300 MHz, DMSO).

$^1$H NMR (300 MHz, DMSO) δ 8.15 – 7.91 (m, 6 H), 7.80 (d, $J = 8.1$ Hz, 3 H), 7.69 (d, $J = 8.6$ Hz, 1 H), 7.52 – 7.39 (m, 4 H), 4.57 – 4.48 (m, 2 H), 4.27 – 4.15 (m, 4 H), 3.55 (s, 2 H), 3.08 – 3.01 (m, 2 H), 2.78 – 2.51 (m, 6 H), 2.13 (dd, $J = 14.5$, 7.3 Hz, 2 H), 1.99 – 1.91 (m, 2 H), 1.43 (d, $J = 24.6$ Hz, 6 H), 1.20 (s, 16 H), 0.82 (t, $J = 5.4$ Hz, 12 H).
Fig. S4. HPLC elution curves of Nap-C_{12}-VVAAG (A) and Nap-C_{12}-VVAAD (B). Purity > 90%.

Fig. S5. TOF-MS spectra of Nap-C_{12}-VVAAG (A), and Nap-C_{12}-VVAAD (B),
Fig. S6. (A) $^1$H NMR spectrum of Nap-C$_{12}$-VVAAG (300 MHz, DMSO).

$^1$H NMR (300 MHz, DMSO) $\delta$ 12.53 (s, 1 H), 8.11 (t, $J = 5.8$ Hz, 1 H), 7.99 – 7.86 (m, 4 H), 7.81 (d, $J = 8.3$ Hz, 3 H), 7.69 (d, $J = 8.7$ Hz, 1 H), 7.47 (ddd, $J = 15.2$, 10.3, 6.3 Hz, 4 H), 4.32 – 4.25 (m, 2 H), 4.21-4.13(m, 2 H), 3.79 – 3.71 (m, 2 H), 3.56 (s, 2 H), 3.44 (s, 2 H), 3.05 (dd, $J = 12.7$, 6.6 Hz, 2 H), 2.14 (dq, $J = 13.7$, 6.8 Hz, 2 H), 1.97 (dd, $J = 13.1$, 6.6 Hz, 2 H), 1.39 (t, $J = 27.3$ Hz, 6 H), 1.21 (d, $J = 3.4$ Hz, 16 H), 0.83 (t, $J = 5.5$ Hz, 12 H).

(B) $^1$H NMR spectrum of Nap-C$_{12}$-VVAAD (300 MHz, DMSO).

$^1$H NMR (300 MHz, DMSO) $\delta$ 12.60 (s, 2 H), 8.04 (dd, $J = 27.4$, 14.4 Hz, 5 H), 7.91 (dd, $J = 11.7$, 3.9 Hz, 3 H), 7.69 (d, $J = 8.7$ Hz, 1 H), 7.46 (ddd, $J = 14.3$, 8.0, 2.2 Hz, 4 H), 4.52 (d, $J = 7.7$ Hz, 1 H), 4.29 (d, $J = 7.0$ Hz, 2 H), 4.17 (d, $J = 7.1$ Hz, 2 H), 3.56 (s, 2 H), 3.05 (d, $J = 6.0$ Hz, 2 H), 2.63 (qd, $J = 16.7$, 6.2 Hz, 4 H), 2.17 – 2.10 (m, 2 H), 2.00 – 1.93 (m, 2 H), 1.43 (d, $J = 24.9$ Hz, 6 H), 1.20 (s, 16 H), 0.84 (d, $J = 4.7$ Hz, 12 H).
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