Supporting information

iRGD-decorated reduction-responsive nanoclusters for targeted drug delivery

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Figure S1. $^1$H NMR spectra of HES-SS-C18 with varied MS of C18.

Table S1. Characterization of HES-SS-C18 with varied MS of C18.

<table>
<thead>
<tr>
<th>Sample</th>
<th>$\text{MS}_{\text{C18}}$ (%)</th>
<th>$\text{MS}_{\text{PDA}}$ (%)</th>
<th>Diameter (nm)</th>
<th>PDI</th>
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</thead>
<tbody>
<tr>
<td>HES-SS-C18</td>
<td>8.8</td>
<td>1.8</td>
<td>187.7 ± 3.5</td>
<td>0.28 ± 0.05</td>
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<tr>
<td>HES-SS-C18</td>
<td>7.1</td>
<td>3.6</td>
<td>162.3 ± 1.9</td>
<td>0.26 ± 0.02</td>
</tr>
<tr>
<td>HES-SS-C18</td>
<td>5.1</td>
<td>5.3</td>
<td>31.3 ± 9.8</td>
<td>0.26 ± 0.08</td>
</tr>
</tbody>
</table>
Figure S2. Characterization of HES-SS-C18 with low MS of C18 (5.1 %). (A) Size distribution of HES 130/0.4 and HES-SS-C18 (MS_{C18} = 5.1 %) measured by DLS. (B) TEM image of individual HES-SS-C18 (MS_{C18} = 5.1 %) nanoparticles. (C) Size distribution of the particles in Figure B. (D) TEM image of large HES-SS-C18 (MS_{C18} = 5.1 %) NCs.

Figure S3. TEM image of HES-SS-C18 NCs with high MS of C18 (8.8 %).
Figure S4. Size and morphology characterization of HES-SS-C18 and iRGD-HES-SS-C18 NCs. (A) Size distribution of HES-SS-C18 NCs measured by DLS. (B) Size distribution of iRGD-HES-SS-C18 NCs measured by DLS. (C) TEM image of HES-SS-C18 NCs. (D) TEM image of iRGD-HES-SS-C18 NCs.

Figure S5. CAC determination of HES-SS-C18 and iRGD-HES-SS-C18. Intensity ratio ($I_{337}/I_{334}$)
of pyrene excitation spectra as a function of log C for HES-SS-C18 (A) and iRGD-HES-SS-C18 (B) in deionized water. The concentration of pyrene was fixed at $6 \times 10^{-7}$ mol/L.

![Figure S6](image)

Figure S6. (A) Stability of DOX@HES-SS-C18 and DOX@HES-SS-C18 NCs in PBS buffer (pH 7.4, 6.7 mmol/L). (B) Fluorescence spectra of free DOX, DOX@HES-SS-C18 NCs, and DOX@HES-SS-C18 NCs (10 µg/mL as DOX) in PBS buffer (pH 7.4, 6.7 mmol/L). Data represent the mean ± SD ($n = 3$).

![Figure S7](image)

Figure S7. Size changes of DOX@iRGD-HES-SS-C18 NCs after incubation with 20 mmol/L of DTT.
Figure S8. In vitro drug release profiles of DOX@HES-SS-C18 NCs in PBS buffer (pH 7.4, 10.0 mmol/L) with and without 20 mmol/L of DTT.
Figure S9. IC_{50} values of free DOX, DOX@HES-SS-C18 NCs, and DOX@iRGD-HES-SS-C18 NCs against HepG-2 (A, C, E) and 4T1 cells (B, D, F) after incubation for 6 h (A, B), 24 h (C, D), and 48 h (E, F). * p < 0.05, ** p < 0.01, *** p < 0.001. n.s. as not significant. Data represent the mean ± SD (n = 4).
The in vitro cytotoxicity of DOX-free HES-SS-C18 and iRGD-HES-SS-C18 NCs against HepG-2 and 4T1 cells was evaluated, as shown in Figure S10. The cell viability of HepG-2 and 4T1 cells treated with HES-SS-C18 and iRGD-HES-SS-C18 NCs (from 1 µg/mL to 1 mg/mL) are all over 90 %, indicating the excellent biocompatibility of our NCs.

Figure S10. In vitro cytotoxicity of HES-SS-C18 and iRGD-HES-SS-C18 NCs against HepG-2 (A) and 4T1 cells (B). Data represent the mean ± SD (n = 4).