Supporting information of

Human serum albumin-based doxorubicin prodrug nanoparticles with tumor pH-responsive aggregation-enhanced retention and reduced cardiotoxicity

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Figure S1. (a) Synthetic scheme of DMDOX. (b) $^1$H NMR spectrum of DMDOX in DMSO-$d_6$.

Figure S2. ESI-MS spectrum of DMDOX.
**Figure S3.** Fluorescence intensity of DMDOX and DOX in different pH conditions. (a-b) Fluorescence emission spectra of DMDOX at pH 7.4 (a) and 6.5 (b) within 12 h. (c-d) Fluorescence emission spectra of DOX at pH 7.4 (a) and 6.5 (b) within 12 h.
Table S1. DLCs and DLEs of HSA-DOX and HSA-DMDOX with different feeding molar ratios of HSA to DOX.

<table>
<thead>
<tr>
<th>Samples</th>
<th>Feeding molar ratio of HSA to DOX</th>
<th>DLCs</th>
<th>DLEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSA-DOX 1:5</td>
<td>1:5</td>
<td>3.3%</td>
<td>78.9%</td>
</tr>
<tr>
<td>HSA-DMDOX 1:5</td>
<td>1:5</td>
<td>1.8%</td>
<td>37.6%</td>
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<tr>
<td>HSA-DOX 1:10</td>
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<td>6.9%</td>
<td>85.8%</td>
</tr>
<tr>
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<td>36.1%</td>
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<tr>
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<td>7.2%</td>
<td>48.9%</td>
</tr>
<tr>
<td>HSA-DMDOX 1:20</td>
<td>1:20</td>
<td>3.6%</td>
<td>21.6%</td>
</tr>
</tbody>
</table>
Figure S4. Fluorescence emission spectra (excited at 480 nm) of HSA, DOX, HSA-DOX and HSA-DMDOX.
**Figure S5.** The H&E histological analysis (100×) of heart, liver, spleen, lung, kidney, and tumor in different groups (saline, DOX, HSA-DOX and HSA-DMDOX).