Electronic Supplementary Information

Carbamoylmannose Enhances Tumor Targeting of Supramolecular Nanoparticles Formed through Host-Guest Complexation of a Pair of Homopolymers

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3-O-carbamoyl-2-propynyl-2,4,6-tris-O-acetyl-α-D-mannopyranoside

![Chemical structure of 3-O-carbamoyl-2-propynyl-2,4,6-tris-O-acetyl-α-D-mannopyranoside](image)

Into a solution of 1,2,4,6-tetra-O-acetyl-3-O-carbamoyl-α-D-mannopyranoside (1.5 g, 3.8 mmol) and propargyl alcohol (1.15 mL, 19.2 mmol) in 20 mL of anhydrous DCM was added BF₃·Et₂O (4.74 mL, 38.4 mmol) dropwise at 0 °C under nitrogen. The mixture was stirring at 0-20 °C for 24 h. The reaction was quenched with saturated aqueous NaHCO₃ at 0 °C, and the mixture was extracted with DCM. The organic layer was washed subsequently with water, saturated aqueous Na₂CO₃, and brine, dried by Na₂SO₄ and concentrated. The crude product was purified by silica gel column chromatography (EtOAc/petroleum ether 2:1) to yield 3-O-carbamoyl-2-propynyl-2,4,6-tris-O-acetyl-α-D-mannopyranoside as a white solid (0.74 g, 50.2%). [α]D +56 (0.1, CHCl₃), m.p. 110.5-112.5 °C. Optical rotations were measured at 25°C using a Rudolph Autopol VI. 1H and 13C spectra were recorded on a Bruker Ascend400 (400 MHz and 100 MHz). High-resolution mass spectral analyses were run on a microTOF 10293.

1H NMR (400 MHz, CDCl₃) δ 5.35 – 5.20 (m, 3H), 5.05 (s, 1H), 4.85 (s, 2H), 4.29 (dd, J = 14.1, 3.7 Hz, 3H), 4.11 (dd, J = 12.3, 2.2 Hz, 1H), 4.06 – 4.00 (m, 1H), 2.49 (t, J = 2.2 Hz, 1H), 2.16 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H);

13C NMR (101 MHz, CDCl₃) δ 170.66, 169.94, 169.92, 155.27, 96.28, 77.98, 77.38, 77.06, 76.75, 75.59, 69.85, 69.01, 66.16, 62.35, 55.01, 20.91, 20.75;

HR-MS m/z: 410.1058, (calculated for C_{16}H_{21}NNaO_{10}, 410.1058).

2-propynyl-3-O-carbamoyl-D-mannose (PCM)

![Chemical structure of 2-propynyl-3-O-carbamoyl-D-mannose](image)

To a cooled (0 °C) solution of 3-O-carbamoyl-2-propynyl-2,4,6-tris-O-acetyl-α-D-mannopyranoside (584 mg, 1.5 mmol) in 12 mL of anhydrous MeOH was added K₂CO₃ (30 mg, 0.2 mmol) in portion. The mixture was reacted at 0 °C for 3 h. The solution was then neutralized by addition of iron-exchange resin until pH 7, filtered, and concentrated. The crude product was purified by silica gel column chromatography (0% - 5% MeOH: CH₂Cl₂) to yield PCM as a white solid (340 mg, 86.5%). [α]D +79 (0.12, MeOH), m.p. 146-148 °C.

1H NMR (400 MHz, MeOD) δ 4.99 (s, 1H), 4.83 (dd, J = 9.9, 3.2 Hz, 1H), 4.31 (d, J = 2.2 Hz, 2H), 4.00 (s, 1H), 3.91 – 3.80 (m, 2H), 3.74 (dd, J = 11.7, 5.7 Hz, 1H), 3.66 – 3.58 (m, 1H), 2.88 (d, J = 2.2 Hz, 1H);

13C NMR (101 MHz, MeOD) δ 159.37, 99.74, 79.89, 76.14, 75.90, 75.28, 70.15, 65.97, 62.64, 54.90, 49.67, 49.45, 49.24, 49.03, 48.82, 48.60, 48.39.

HR-MS m/z: 284.0728, (calculated for C_{10}H_{15}NNaO_{2}, 284.0741).
Scheme S1. The synthesis route of β-CD-PVP-PCM.
Scheme S2. The synthesis route of β-CD-PVP-PM.
Scheme S3. The synthesis route of FITC-labeled β-CD-PVP.
Scheme S4. The synthesis route of NIR797-labeled β-CD-PVP.
Scheme 55. The structure of used various monosaccharides and polysaccharides.
**Table S1.** The characteristics of these platinum-incorporating nanoparticles.

<table>
<thead>
<tr>
<th>No.</th>
<th>Formation</th>
<th>Diameter (nm)</th>
<th>PDI</th>
<th>Zeta-potential (mV)</th>
<th>Drug Loading Content (DLC)</th>
<th>Drug Encapsulation Efficiency (DEE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PVPA-Pt NPs</td>
<td>65</td>
<td>0.16</td>
<td>-13.11 ± 2.31</td>
<td>39%</td>
<td>52%</td>
</tr>
<tr>
<td>2</td>
<td>PM-PVPA-Pt NPs</td>
<td>63</td>
<td>0.19</td>
<td>-15.46 ± 1.75</td>
<td>42%</td>
<td>56%</td>
</tr>
<tr>
<td>3</td>
<td>PCM-PVPA-Pt NPs</td>
<td>66</td>
<td>0.18</td>
<td>-14.15 ± 3.21</td>
<td>41%</td>
<td>55%</td>
</tr>
</tbody>
</table>
Table S2. The IC50 values of different formations after incubated with three various cancer cells for 48 h.

<table>
<thead>
<tr>
<th>No.</th>
<th>Cells</th>
<th>Free CDDP</th>
<th>PVPA-Pt NPs</th>
<th>PM-PVPA-Pt NPs</th>
<th>PCM-PVPA-Pt NPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A549</td>
<td>25.1</td>
<td>50.1</td>
<td>46.8</td>
<td>40.7</td>
</tr>
<tr>
<td>2</td>
<td>SH-SY5Y</td>
<td>26.9</td>
<td>37.2</td>
<td>36.3</td>
<td>32.4</td>
</tr>
<tr>
<td>3</td>
<td>H22</td>
<td>1.9</td>
<td>30.9</td>
<td>17.0</td>
<td>12.0</td>
</tr>
</tbody>
</table>
Figure S1. The FT-IR spectra of various β-CD-PVP polymers.
Figure S2. The $^1$H NMR spectrum of β-CD-PVP-PCM (solvent: DMSO-d$_6$).
Figure S3. The fluorescent spectrum of β-CD-PVP-FITC. Excitation: 450 nm.
Figure S4. The fluorescent spectrum of β-CD-PVP-NIR797. Excitation: 704 nm.
Figure S5. The relative DLS intensity curves of these platinum-incorporating nanoparticles during the preparation.
Figure S6. The relative DLS intensity of these platinum-incorporating nanoparticles in deionized water at 37 °C.
Figure S7. The dissociation behaviours of these platinum-incorporating nanoparticles in 10 mM PBS containing 150 mM NaCl.
Figure S8. The 2D NOESY spectra of PVPA (A), PM-PVAP (B), PVPA-Pt NPs (C), and PM-PVPA-Pt NPs (D), respectively (solvent: D$_2$O).
Figure S9. The relative FITC fluorescent intensity of these platinum-incorporating nanoparticles. Excitation: 450 nm.
Figure S10. The CLSM images of NIH3T3 cells after incubated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h. (A) is the FITC channel, (B) is the bright field, (C) is the Hoechst 33258 channel, and (D) is the merged image.
Figure S11. The CLSM images of A549 cells (A), SH-SY5Y cells (B) and H22 cells (C) after treated with PCM-PVPA-Pt NPs at 4 °C or 37 °C for 4 h. (D) Quantitative data for the relative fluorescent intensity. (n = 10 in at least three different CLSM images, ** represents P < 0.01)
Figure S12. The CLSM images of A549 cells (A), SH-SY5Y cells (B) and H22 cells (C) after treated with PCM-PVPA-Pt NPs in the absence (-) or presence (+) of 3 μM phosphocreatine (PC) at 37 °C for 4 h. (D) Quantitative data for the relative fluorescent intensity. (n = 10 in at least three different CLSM images, ** represents P < 0.01)
Figure S13. The CLSM images of A549 cells, SH-SY5Y cells and H22 cells after treated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for different time.
Figure S14. The CLSM images of A549 cells, SH-SY5Y cells and H22 cells after treated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h in the absence (-) or presence (+) of 600 μM Mannose.
Figure S15. The CLSM images of A549 cells, SH-SY5Y cells and H22 cells after treated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h in the presence of D-mannosamine (MA), D-glucosamine (GA), chitosan, and hyaluronic acid (HA).
Figure S16. The quantification of fluorescent intensity in A549 cells, SH-SY5Y cells and H22 cells after incubated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h in the presence of various saccharides.
**Figure S17.** The CLSM images of A549 cells, SH-SY5Y cells and H22 cells after incubated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h in the presence of various endocytosis inhibitors.
Figure S18. The quantification of fluorescent intensity in A549 cells, SH-SY5Y cells and H22 cells after incubated with FITC-labeled PCM-PVPA-Pt NPs at 37 °C for 4 h in the presence of various endocytosis inhibitors.
Figure S19. The *in vitro* A549 cell viability after treated with PCM-PVAP pseudo block polymer at 37 °C for 48 h on different polymer concentration.
Figure S20. The *in vitro* SH-SY5Y cell viability after treated with PCM-PVAP pseudo block polymer at 37 °C for 48 h on different polymer concentration.
Figure S21. The *in vitro* H22 cell viability after treated with PCM-PVAP pseudo block polymer at 37 °C for 48 h on different polymer concentration.
Figure S22. The NIRF images of same amount of NIR797-labeled nanoparticles.
Figure S23. The NIRF images of the tumor and major organs from the mice treated with NIR797-labeled PVPA-Pt NPs (A) and PM-PVPA-Pt NPs (B) after the experiment.
**Figure S24.** The CLSM images of H22-tumor tissues from the mice treated with FITC-labeled PCM-PVPA-Pt NPs for 12 h (A), 24 h (B), PM-PVPA-Pt NPs for 24 h (C), and PVPA-Pt NPs for 24 h (D).
Figure S25. Quantitative relative intensity of these platinum-incorporating nanoparticles with distance from blood vessels. (about ten CLSM images were chosen for the quantitation of each formation, * represents $P < 0.05$, ** represents $P < 0.01$)