Supplementary Materials: Scale-Up Synthesis and In Vivo Anti-Tumor Activity of Curcumin Diethyl Disuccinate, an Ester Prodrug of Curcumin, in HepG2-Xenograft Mice

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Figure S1. $^1$H-NMR spectrum of curcumin.

Figure S2. $^1$H-NMR spectrum of curcumin diethyl disuccinate.
Figure S3. Mass spectrum of curcumin.
Determination of chromatographic purity of the prepared curcumin and CurDD

The prepared curcumin and CurDD were injected into an ultra-high performance liquid chromatographic system to determine chromatographic purity. The chromatographic conditions for the assay were described below.
Mobile phase
A = 0.2 % Formic acid in water
B = Acetonitrile

<table>
<thead>
<tr>
<th>Time</th>
<th>A:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (0 min)</td>
<td>A:B = 55:45</td>
</tr>
<tr>
<td>2 min</td>
<td>A:B = 50:50</td>
</tr>
<tr>
<td>2.5 min</td>
<td>A:B = 50:50</td>
</tr>
<tr>
<td>5.0 min</td>
<td>A:B = 25:75</td>
</tr>
<tr>
<td>5.5 min</td>
<td>A:B = 55:45</td>
</tr>
<tr>
<td>7 min</td>
<td>A:B = 55:45</td>
</tr>
</tbody>
</table>

Column
Acquity UPLC BEC C18 (50 mm x 2.1 mm, 1.7 µm)

Flow rate 0.5 mL/min
Column oven temperature 35 °C
Injection volume 2 µL
Detection wavelength λ = 400 nm for CurDD, 425 nm for curcumin

Figure S5. UHPLC chromatogram of curcumin.

Figure S6. UHPLC chromatogram of curcumin diethyl disuccinate.

Figure S7. Powder X-ray diffraction spectrum of curcumin.
Figure S8. Powder X-ray diffraction spectrum of CurDD.

Figure S9. Particle size distribution analysis by laser diffraction of CurDD.

Figure S10. Particle size distribution analysis by laser diffraction of curcumin.