In order to obtain micelle powders, the solution of VP loaded micelles was lyophilized with PEG-3350 (5%, w/v) as lyoprotectant. To determine the DL and EE, 50 mg of the freeze-dried powders of VP loaded micelles (corresponding to 10 mg VP) was rehydrated in 100 mL distilled water and stirred for 5 min. 5 mL of the solution was filtrated with a 0.45 μm cellulose nitrate membrane to separate the unloaded VP from micelles solution, for its very low solubility in water. Then 1 mL of the filtrated solution was diluted with methanol (micelle solution: methanol = 1:9, v/v) to dissociate micelle nanoparticles. The amount of VP in the resulting solution was measured by a reversed phase-HPLC method described in the following paragraphs.

**Supplemental table 1. Composition of different preparation methods of VP loaded micelles.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Preparation method | VP/polymer mass ratio (%) | organic solvent | solvent/water volume ratio | hydration / evaporation temperature (°C) | hydration / evaporation / dialysis time |
| Thin-film hydration | 20 | DCM |  | 60 | 3 |
| 20 | DCM |  | 70 | 3 |
| 20 | DCM |  | 80 | 3 |
| Solvent evaporation | 20 | acetonitrile | 1:6 | 40 | 4 |
| 20 | acetone | 1:6 | 40 | 4 |
| 20 | acetone | 1:10 | 40 | 4 |
| Dialysis | 20 | DMF |  |  | 12 |
| 20 | THF |  |  | 12 |
| 20 | DMSO |  |  | 12 |

**Supplemental table 2. Factor-level table of orthogonal design.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Preparation method | VP/polymer mass ratio (%) | organic solvent | solvent/water volume ratio | hydration / evaporation temperature (°C) | hydration / evaporation / dialysis time |
| Thin-film hydration | 20 | DCM |  | 60 | 3 |
| 20 | DCM |  | 70 | 3 |
| 20 | DCM |  | 80 | 3 |
| Solvent evaporation | 20 | acetonitrile | 1:6 | 40 | 4 |
| 20 | acetone | 1:6 | 40 | 4 |
| 20 | acetone | 1:10 | 40 | 4 |
| Dialysis | 20 | DMF |  |  | 12 |
| 20 | THF |  |  | 12 |
| 20 | DMSO |  |  | 12 |

**Supplemental table 3. Ymax and Ymin values of the two indices used for normalization.**

|  |  |  |
| --- | --- | --- |
| Factor | Ymax | Ymin |
| DL (%) | 25 | 1 |
| EE (%) | 70 | 5 |

**Supplemental table 4. Analysis of variance (ANOVA).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor | Sum of squares | Degrees of freedom | Mean square | F |  |
| A | 0.1222 | 2 | 0.0611 | 54.95 | \*\* |
| B | 0.2193 | 2 | 0.1097 | 98.66 | \*\*\* |
| C | 0.0617 | 2 | 0.0308 | 27.76 | \* |
| Error | 0.0011 | 2 | 0.0006 |  |  |