Supporting information

Janus particle synthesis via aligned non-concentric angular nozzles and electrohydrodynamic co-flow for tunable drug release

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Experimental

1. Materials
Poly(ε-caprolactone) (PCL, 4.5 x10^4 g/mol), Sudan Red G, Indomethacin and Tween 80 were purchased from Sigma-Aldrich, USA. Titanium Dioxide VK-T25N was received from Hangzhou Wanjing New Material Co., Ltd. Carbon Black PRINTEX U was obtained from Evonik Industries AG, Germany. Dichloromethane (DCM) was supplied by Sinopharm Chemical Reagent Co., Ltd, Shanghai, China. Ultrapure water was produced with a Millipore Milli-Q Reference ultrapure water purifier (USA). All materials were of analytical grade and were used as received.

2. Methods

2.1. Preparation of Janus particles
The set-up consists of a high voltage power supply (Glassman high voltage Inc. Series
FC, USA), two syringe pumps (KD Scientific KDS100, USA), novel stainless steel nozzles composed of two symmetric angular nozzles (varying angles) and a ring-shaped grounded electrode. The nozzle was connected to the high power supply to form a static electric field between the device and the ground electrode. The flow rates of co-flowing polymeric solutions (variable) were controlled using high precision syringe pumps. High speed images of the jetting behavior was captured using a CCD camera (Baumer TXG02C, Germany) which was connected to a PC. Janus particles were collected on glass slides and aluminum film.

2.2. Particle characterization

Optical images were captured using an optical microscope (Pheonix BMC503-ICCF, China) with different light sources. TiO$_2$ and Carbon black loaded Janus particles were observed using two different light sources. One of these was used for illuminating Janus particles using a transmission light source directly under the glass substrate to get the overall particle shape as shown in Figure S1(a). Secondly, an LED ring-type light source was placed directly above the glass substrate to illuminate Janus particles. Here, TiO$_2$ loaded compartment of Janus particles displayed distinctively brighter reflection than the carbon black loaded compartment. The bright regions indicate further addition of TiO$_2$ while the dark regions indicate the incorporation of carbon black, as shown in Figure S1(b).

**Figure S1.** (a) Configuration of the optical microscope employed to observe the overall shape of synthesized Janus particles using transmission light through the glass substrate. (b) Configuration of the optical microscope used to observe the distribution
of incorporated optical dyes within Janus particles using an LED ring-type light source around the objective lens for recording the reflected light (from Janus particles).

For SEM analysis, particles were removed from the aluminum film after drying and were mounted on to double-sided conductive tape for sputter coating. A thin layer of gold under vacuum (Ion Sputter MC 1000, Hitachi, Japan) was deposited after 60s. SEM analysis was carried out using a field emission-scanning electron microscope (FE-SEM, FEI Quanta 650 FEG, Hillsboro, Oregon, USA). The diameters of the particles were analyzed using imageJ software (National Institute of Health, USA).

Samples for FTIR analysis were prepared using the KBr pellet pressing method. 2mg of each particle type was dispersed in 200mg KBr medium by grinding. The mixture was then compressed into transparent pellets using a pressure of 12MPa. Pellets were then scanned with FTIR (IR Affinity 1, Shimadzu, Japan) and the spectrum was acquired at a resolution of 4 cm\(^{-1}\) ranging from 4000 to 400 cm\(^{-1}\). Each spectrum was obtained using 45 scans.

### 2.3. In vitro dual-drug release study

#### 2.2.4.1. Procedure of dual-drug release study

*In vitro* studies were performed to investigate the release of incorporated model drug and probe. The release medium was prepared according to a previous report,\(^1\) which involved mixing 2 w/v\% Tween80 in ultrapure water until complete dissolution. Assays to be used in release studies comprised 10 ml release medium with 50 mg Janus particles in 10 ml glass vials for each sample. All assays were fixed on to a swing bed (37°C) at a shaking rate of 200 rpm. Assays were temporarily removed and centrifuged at 4000 rpm for 2 min at predetermined time intervals. For each time interval the supernatant was collected and the same quantity of fresh release medium replaced the withdrawn sample. Supernatants were analyzed for the absorption (UV
measurements). The concentration of Sudan Red G and indomethacin was determined using wavelengths of 249 and 503nm (UV-2600 spectrophotometer, Shimadzu, Japan).

Standard calibration curves for the drug and probe were established. The ultraviolet absorption peak of Sudan Red G is 503 nm at which wavelength the absorption value of indomethacin is approximately equal to zero, thus the concentration of Sudan Red G can be measured by the adsorption value of the supernatant at 503 nm. Both model compounds possess stable UV absorption peaks at 249 nm, and both of the standard curves at this wavelength show good linearity, therefore the absorption value of indomethacin at 249 nm can be calculated by subtracting the absorption value of Sudan Red G at 249 nm which can be calculated from the standard curve of Sudan Red G at 249 nm. The concentration of indomethacin can be calculated from the standard curve. The standard curves of Sudan Red G and indomethacin are shown in Figure S2.

![Standard curves of Sudan Red G and indomethacin](image)
Figure S2. (a) The standard curve of Sudan Red G at 503 nm. The standard curve was expressed as $Y=40.835X+0.95282$; $X$ stands for the Abs, $Y$ stands for concentration of Sudan Red G in release medium (μg/mL). (b) The standard curve of Sudan Red G at 249 nm. The standard curve was expressed as $Y=58.712X+0.27007$; $X$ stands for the Abs, $Y$ stands for concentration of Sudan Red G in release medium (μg/mL). (c) The standard curve of indomethacin at 249 nm. The standard curve was expressed as $Y=29.56X+0.95912$; $X$ stands for the Abs, $Y$ stands for concentration of
indomethacin in release medium (μg/mL).

References