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Controllable microfluidic fabrication of Janus and microcapsule particles for drug delivery application

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KEYWORDS: microcapsules, Janus, microfluidics, drug delivery, PLGA/PCL

Abstract

Janus and microcapsule particles are very attractive for drug delivery applications due to their capability of targeted and/or programmed drug release. In this paper, a facile yet robust strategy is reported for the first time to fabricate both Janus and microcapsule particles in a simple microfluidic device via the same protocol. According to the classic spreading and partial wetting theory, the key point to fabricate Janus and microcapsule particles in single emulsions is that the two immiscible components should undergo a precisely controlled phase separation, i.e., dewetting for Janus particle and wetting for microcapsule particle. Herein we show that this requirement can be satisfied simply by subtle choice of organic solvents for the dispersed phase. As a model hybrid material, PLGA/PCL Janus and microcapsule particles are obtained via switching the organic solvents between dimethyl carbonate and dichloromethane. ATR-FTIR spectra and acetone treatment demonstrate that PLGA and PCL occupy their own hemisphere in Janus particles. In contrast, the shell on microcapsule particle surface is composed of only PLGA, and the core is composed of PCL in which tiny PLGA beads are embedded. The applications of PLGA/ PCL Janus and microcapsule particles in drug delivery are characterized via in vitro degradation test. The results prove that Janus and microcapsule particles exhibit distinct degradation behaviors, implying their capability of programmable drug delivery in different manners.

1. Introduction

In the past decades, material science community has witnessed an explosion of innovative and effective strategies to fabricate advanced materials for drug delivery applications.¹⁻³ Among the emerging materials so far developed, Janus and microcapsule particles are drawing tremendous attention, mainly due to their capability of targeted and/or programmed drug release.⁴⁻¹⁰ Specifically, Janus and microcapsule particles are two types of particles with distinct architecture: the former possesses two well-defined regions of different surface or bulk composition whilst the latter are of typical core-shell configuration. In other words, Janus particle displays unique asymmetry within a single particle and thus offers diverse chemical or physical properties and/or directionality inconceivable for homogeneous particles or symmetric patchy particles,¹¹ whereas microcapsule particles are usually symmetric (at least from the outside surface) and the encapsulated core components can be released via either degradation of the shell material or stimuli-responsive mechanism (pH, enzyme, temperature, etc).¹² The state-of-the-art fabrication methods for Janus particles include droplet-based microfluidics (often combined with lithographic patterning),¹³ Pickering emulsions,¹⁴ electrohydrodynamic jetting,¹⁵ phase separation in confined volumes etc.¹⁶ Meanwhile, the most employed approaches to prepare microcapsule particles are layer by layer assembly,¹⁷ emulsion polymerization,¹⁸ internal phase separation,¹⁹ flow focusing or co-flowing methods.²⁰ Although the synthetic methods for Janus and microcapsule particles appear partial overlapping at the first glance, one may find after detailed analysis that their operating procedures are quite different. To the best of our knowledge, there is still a big challenge to fabricate simultaneously Janus and microcapsule particles using the same protocol and experimental set-up.

In this paper, we describe a facile yet robust strategy to synthesize both Janus and microcapsule particles in a simple microfluidic device which can solely produce oil-in-water (O/W) single emulsions. According to the famous spreading and partial wetting theory in physical chemistry, the key point to fabricate Janus and microcapsule particles is that the two immiscible components in the as-formed single emulsion should undergo a precisely controlled phase separation, i.e., dewetting for Janus particle and wetting for microcapsule particle.^{21,22} Herein we show that this requirement can be satisfied simply by subtle choice of organic solvents for the dispersed phase.

As a concrete example, hybrid particles composed of biocompatible/biodegradable poly (lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL) are fabricated, and their Janus and microcapsule configurations are achieved via switching the organic solvents between dimethyl carbonate and dichloromethane. In addition to the fabrication and characterization, the possible applications of PLGA/PCL Janus and microcapsule particles in drug delivery are also investigated. We wish this new strategy could open a new way to fabricate particles with complicated architectures in a much easier manner than we had thought before.

2. Experimental section

Materials and reagents: poly (lactic-co-glycolic acid) (PLGA, lactide/glycolide ratio=50/50, $M_w=30$ kDa) and poly (ϵ -caprolactone) (PCL, $M_w=130$ kDa) were purchased from Daigang Biomaterials (Shandong, China). Poly (vinyl alcohol) (PVA, 87-89% hydrolyzed, $M_w=88$ kDa), Rhodamine B and dimethyl carbonate were bought from Aladdin Chemistry (Shanghai, China). Dichloromethane and acetone were obtained from Tianjing Baishi Chemical Co. Ltd (Tianjin, China). Glycerol was purchased from Tianjin Fuyu Chemical Co. Ltd (Tianjin, China). Polydimethylsiloxane (PDMS) (Sylgard 184) and negative resist (NR21-20000P) were purchased from Dow Corning Company and Futurrex Inc (USA), respectively. Deionized water was obtained using a Milli-Q water-purification system. All the reagents were of analytical grade and used as received.

Fabrication and surface treatment of microfluidic devices: Microfluidic flow-focusing devices were fabricated using standard soft lithography techniques.²³ In brief, clean silicon wafer was first spin-coated with negative photoresist. After baking at 80 °C for 10 min and 150 °C for 5 min, the resist was exposed to UV light through a photo-mask and developed in RD6 developer solution. Mixture of PDMS base and curing agent (10:1, w/w) was then poured onto the silicon wafer and cured at 60 °C to make a PDMS replica which was subsequently sealed with a glass slide via O₂ plasma. The width of branch channel and collection channel were 100 μm and 250 μm , and the depth of all channels was 100 μm . In order to improve the hydrophilicity of microchannels and reduce the swelling of PDMS caused by dichloromethane, surface treatment was conducted by

injecting PVA/glycerol (2/5 wt%) aqueous solution and curing for 1 h.

Synthesis of PLGA/PCL Janus and microcapsule particles: PLGA and PCL (1:1 or 7:3, w/w) dissolved in dichloromethane or dimethyl carbonate with a total concentration of 40 mg/mL were used as the dispersed phase, whilst an aqueous solution containing 2 wt% of PVA was used as the continuous phase. Both the dispersed phase and continuous phase were delivered into the microfluidic devices using syringe pumps (Cole-Parmer, USA). Before introducing the dispersed phase, the microchannels were wetted with the aqueous continuous phase for several minutes. In the case of Janus particles, the flow rates for the continuous and dispersed phases were held at 0.4 and 1.6 mL/h. For microcapsule particles, the flow rates of the continuous and dispersed phase were set as 0.25 and 0.45 mL/h. Droplets were produced continuously at the junction of the microchannels and then collected in 2 wt% aqueous solution of PVA (Figure S1, Movie S1 and S2, Supporting information). After settling at room temperature for 24 h, the solidified microparticles were centrifuged, washed for 3 times with DI water and finally dried in a freeze-drier (Lyophilizer, VIRTIS, USA).

Characterization of PLGA/PCL particles: The fabrication process were monitored using an optical microscope (T240C, SunTime, China) equipped with a high-speed camera (Basler ace, Germany). Rhodamine B-labeled Janus and microcapsule were observed with a confocal laser scanning microscope (CLSM) equipped with a 1 mW helium-neon laser (ZeissLsm-510, Japan). The morphology of the microparticles was observed via a scanning microscope (Nova Nano SEM430, FEI). Attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR, Nexus Por Euro, USA) was carried out to further clarify the configuration of microparticles. The interfacial tension was measured at 25 °C with the wilhelmy plate method (DCAT 30, Dataphysics instruments GmbH), and the polymer surface energy was determined according to the classic Owens-Wendt-Kaelble (OWK) method.

Degradation of PLGA/PCL particles: In vitro degradation test was conducted to investigate the degradation-ability of Janus and microcapsule particles. The microparticles were suspended in 50

mL of PBS (pH 7.4) and incubated in an orbital shaker at 92 rpm and 37 °C for a certain period of time (7, 14, 21, 35 days). The PBS buffer was refreshed every week and the microparticles were collected at predetermined intervals for SEM observation.

3. Results and Discussion

3.1 Fabrication and characterization of Janus and microcapsule particles

A simple flow-focusing microfluidic device was adopted to generate oil-in-water (O/W) single emulsions as the precursors of monodisperse PLGA/PCL Janus and microcapsule particles for the purpose that the solvent extraction rate, particle size and configuration could be precisely controlled (see schematic illustration of the design in Figure S2, supporting information).²⁴⁻²⁶ Figure 1a and b show the SEM images of PLGA/PCL particles prepared using dimethyl carbonate as the solvent of the dispersed phase. An apparent demarcation can be observed on each particle, i.e., one hemisphere exhibits a rough surface and the other displays a smooth surface, indicative of a Janus structure. Interestingly, when dimethyl carbonate is replaced with dichloromethane, microspheres with smooth surface can be formed under the same condition (Figure 1d and e), which implies the material with rough surface might be embedded in the particle so as to generate a core-shell structure. To evaluate the size distribution, one hundred particles were chosen at random and their size was measured by ImageJ software. It is found that the average diameter of Janus particles is 28.42 μm with a coefficient of variation (CV) of 4.25% (Figure 1c). In contrast, the smooth microspheres show more narrow size distribution (CV is 2.74%) and their average diameter was 47.00 μm (Figure 1f). The low CV values (< 5%) of Janus and microcapsule particles prove their excellent monodispersity achieved in microfluidic device. Besides, if a mixture of dimethyl carbonate and dichloromethane (for example, 5:1, v/v) is employed, a transition structure between Janus and microcapsule, or namely an anisotropic configuration with one hemisphere showing smooth morphology and the other hemisphere showing sea-island morphology, can be obtained (Figure S3a, b, Supporting information).

The surface composition of Janus and microcapsule particles was identified via ATR-FTIR and the spectra are shown in Figure 2. Only the characteristic peaks belonging to PLGA (2998, 2951, 1759, 1129 and 1086 cm^{-1}) can be detected on microcapsule particle surface (curve c), confirming

that PCL is located inside the particle in this case. Comparatively, in addition to the peaks of PLGA at 2997 and 1755 cm^{-1} , the absorption peaks of PCL at 2946, 2865, 1737 and 731 cm^{-1} can be observed on Janus particle surface (curve d). This proves that the surface of Janus particle is composed of both PLGA and PCL.

To figure out the distribution of PLGA and PCL in the Janus and microcapsule particles, we further introduced acetone treatment method since acetone is a good solvent for PLGA but difficult to dissolve PCL in a very short time. After treated with acetone, the smooth half part of Janus particle disappears and the whole particle turns out to be a hemisphere (Figure 3a). This phenomenon validates the existence of a clear interface between PLGA and PCL hemispheres, possibly resulted from the complete phase separation in the formation of Janus particle. To explain the reason why the surface of PCL part is so rough, pure PCL particles were prepared via the same protocol. As can be found, pure PCL particles originally exhibit rough surfaces (Figure 3b), and there is not much difference in particle morphology before and after acetone treatment (Figure 3c). In our opinion, the roughness of PCL surface should be ascribed to its semi-crystalline state. At the same time, after acetone treatment, microcapsule particle still remains the intact spherical structure except that the particle surface is roughened (Figure 3d). Considering the FTIR data as well as the conclusion drawn from Janus particle, it can be deduced that the outmost shell of microcapsule particle is PLGA and the inner core is PCL. More surprisingly, the cross-section of microcapsule particle shows many tiny beads encapsulated in the PCL matrix (Figure 3e). Once subjected to acetone, these beads dissolve quickly, leaving a porous PCL matrix (Figure 3f). These results illustrate that the shell and tiny beads are composed of PLGA and the inner matrix is composed of PCL respectively. For the particle with transition structure shown in Figure S3, one hemisphere and the island on the other hemisphere are dissolved away after acetone treatment, which leads to the formation of a remaining hemisphere with many dents on the surface (Figure S3c). Obviously, in this case, PLGA occupies the smooth hemisphere and the island, while PCL occupies the sea of the other hemisphere.

The fine structure of Janus and microcapsule particles can be tuned by changing the mass ratio of PLGA and PCL. Figure 4 shows the Janus and microcapsule particles synthesized under a mass ratio of 7:3. As can be seen in Figure 4a, Janus particle can be still harvested if dimethyl carbonate

is used. However, the interface between PLGA and PCL doesn't stay at the centerline of the Janus particle but intrudes towards the PCL side. After acetone treatment, PLGA is dissolved away and chesspiece-like PCL particle remains (Figure 4b). With respect to microcapsule particle, no obvious change can be observed on the face of it after increasing the mass percentage of PLGA (Figure 4c), but the sliced particle reveals a remarkable thickening of the PLGA shell (Figure 4d). What's more, PLGA beads are also found in the core matrix (Figure S4, supporting information).

3.2 Formation mechanism of Janus and microcapsule particles

The significant structure difference between Janus and microcapsule particles induced only by organic solvents can be explained according to the classic spreading and partial wetting theory,²¹ in which the equilibrium configuration of two immiscible phase and a third phase can be rationally determined and predicted from the interactive interfacial tensions between different phases (γ_{ij} , γ_{ik} , γ_{jk}) and spreading coefficients (S_i), as defined in Equation (1):

$$S_i = \gamma_{jk} - (\gamma_{ij} + \gamma_{ik}) \quad (1)$$

Herein, the oil phase containing PLGA, the aqueous solution containing PVA and the oil phase containing PCL are designated as phase 1, phase 2 and phase 3, respectively. Table 1 lists the interfacial tensions measured by the Wilhelmy plate method and the calculated spreading coefficients. Since dimethyl carbonate owns high solubility in water (13.9 wt% at 20 °C²⁷) and can be extracted from the emulsion very fast (less than 30 s), the interfacial tension between dissolved PLGA and PCL in dimethyl carbonate is calculated based on the surface energy of PLGA and PCL (see Table S1, Supporting information). Compared with dimethyl carbonate, dichloromethane shows much lower solubility in water (2 wt% at 20 °C). As a result, the dissolved PLGA and PCL in dichloromethane are completely miscible for a considerable long time (~3-4 h) and their interfacial tension is assumed as zero. In terms of the emulsion using dimethyl carbonate as organic solvent, the spreading coefficient S_2 is positive and the other two (S_1 and S_3) are negative, satisfying the condition of dewetting. The dewetting process is schematically illustrated in Scheme 1a. As dimethyl carbonate in oil phase diffuses into water, phase separation between PLGA and PCL occurs. These two materials segregate towards the opposite poles and a clear

interface gradually builds at the centerline of the particles, ultimately causing the formation of Janus structure. In the case of dichloromethane, there are two situations in regards of the spreading coefficients. At the low concentration of PLGA and PCL (for example, 40 mg/mL) where the droplets are initially generated, the positive S_1 and negative S_2 and S_3 meet the criteria of complete wetting. That is, a core-shell structure with PLGA as the shell and PCL as the core can be achieved (Scheme 1b). However, with the extraction of more dichloromethane into the water, the concentrations of PLGA and PCL increase (In our study, oil phases containing 80 mg/mL of PLGA and PCL were used for the measurement of interfacial tension in high concentration), accompanying by the increase of γ_{12} and decrease of γ_{23} . This triggers the inversion of S_1 and S_3 , leading to the encapsulation of PLGA in the PCL matrix. It should be pointed out that the movement of PLGA molecules would be greatly slowed down in high concentration and thus the coalescence of tiny PLGA beads into bigger PLGA core are restricted. Although Janus and microcapsule particles were obtained in dimethyl carbonate and dichloromethane systems respectively, it doesn't mean that the particle configurations were constant in these two solvents. Any factor that changes the interfacial tensions between different phases and spreading coefficients (such as temperature, concentration of PLGA and PCL, extraction rate of solvent, etc), may result in different particle structure.

3.3 Possible applications of PLGA/PCL Janus and microcapsule particles in drug delivery

In our work, PLGA/PCL Janus and microcapsule particles are fabricated not only because of their excellent biocompatibility and biodegradability as approved by the US Food and Drug Administration (FDA), but also because of their complementary properties in mechanical strength, degradation rate and hydrophobicity/ hydrophilicity etc.^{28, 29} Since PLGA is hydrophilic and PCL is hydrophobic, it is of much possibility that drugs with different hydrophilicity/ hydrophobicity may distribute unevenly in PLGA and PCL. To prove this hypothesis, Rhodamine B, a hydrophilic fluorescence dye, was used to stain Janus and microcapsule particles. The fluorescence images (Figure 5) show that Rhodamine B mainly dyes PLGA rather than PCL, indicating that Rhodamine B can selectively distributes in different compartments of Janus and microcapsule

particles. As a result, with the respective degradation of PLGA and PCL, these drugs can be released in a controllable mode. To compare the degradation behaviors of PLGA/PCL Janus and microcapsule particles, *in vitro* biodegradation test was performed in phosphate buffered saline (PBS, pH 7.4). Figure 6a and b show the particle morphologies after incubation for various times. On the 7th day, both Janus and microcapsule particles hardly show any change (Figure 6 a₁ and b₁). However, after 14 days of incubation, PLGA hemisphere in Janus particle displays obvious roughening effects, so does the PLGA shell on microcapsule particle (Figure 6 a₂ and b₂). What's more, ATR-FTIR profile proves that both PLGA and PCL can be detected on microcapsule particle surface after 14 days, implying that part of PLGA shell has been degraded (data not shown here). When the degradation test proceeds to the 21st day, the PLGA part in Janus particle become much smaller and the whole particle loses its spherical architecture, as shown in Figure 6a₃. In addition, the microcapsule particle returns to sound microspheres again but its morphology resembles pure PCL particle (Figure 6b₃), indicative of the complete degradation of PLGA shell. By the time of the 35th days, the residual PLGA in Janus particles is swollen due to the penetration of water³⁰ and the particle looks like a mushroom with a fluffy and porous canopy (Figure 6a₄). Meanwhile, pores are also observed on PCL-coated microcapsule particle, which can be attributed to the degradation of tiny PLGA beads embedded in PCL matrix (Figure 6b₄). These data reveal that PLGA degrades much faster than PCL, indicating that Janus and microcapsule particles can also exhibit distinct degradation behaviors. Although one may argue that drugs can also be released from the particles without the degradation of PLGA and PCL, our primary results demonstrate that only 7 wt% Tanshinone II A (a drug for coronary heart disease and angina pectoris) can be released before PLGA starts to degrade (data will be shown in another paper). Therefore, it is still reasonable to conclude that the distinct degradation behaviors of PLGA/PCL Janus and microcapsule particles prove their capability of programmable drug delivery, as vividly illustrated in Figure 6c and d.

4. Conclusion

In summary, we present a novel and versatile microfluidic approach to fabricate PLGA/PCL Janus and microcapsule particles simply by changing the organic solvents of the dispersed phase

between dimethyl carbonate and dichloromethane. As confirmed through FTIR and acetone treatment, the smooth hemisphere in Janus particle is PLGA and the rough hemisphere is PCL. In comparison, the smooth shell in microcapsule particle is PLGA and the core is composed of PCL in which tiny PLGA beads are embedded. The formation mechanisms of these two types of particles are discussed via the well-known spreading and partial wetting theory. It is revealed that the distinct particle configurations are rooted in the variation of interfacial tensions and spreading coefficients in the two solvents. We believe this strategy opens a new way when synthesizing particles with various architectures. Additionally, in view of the vast difference of PLGA and PCL in mechanical strength, hydrophobicity/hydrophilicity and especially biodegradation rate, Janus and microcapsule particles show promising applications for controllable and programmable drug release.

ASSOCIATED CONTENT

Supporting Information Available:

Schematic illustration of the flow focusing microfluidic device, the optical images and movies of the droplet generation process in microfluidic devices, the transition structure between Janus and microcapsule particles fabricated using a mixture of dimethyl carbonate and dichloromethane, schematic illustration on controllable and programmable drug release accompanying with the biodegradation of PLGA/PCL Janus and microcapsule particles. This material is available free of charge via the Internet at <http://www.rsc.org>.

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ACKNOWLEDGMENTS

This research work was financially sponsored by the National Natural Science Foundation of China (Grant NO. 51373056, 51372085) and the Program for New Century Excellent Talents in University (NCET-11-0150, NCET-11-0148) and Fundamental Research Funds for the Central Universities (2012ZZ0089, 2013ZZ0005).

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Figures

Figure 1

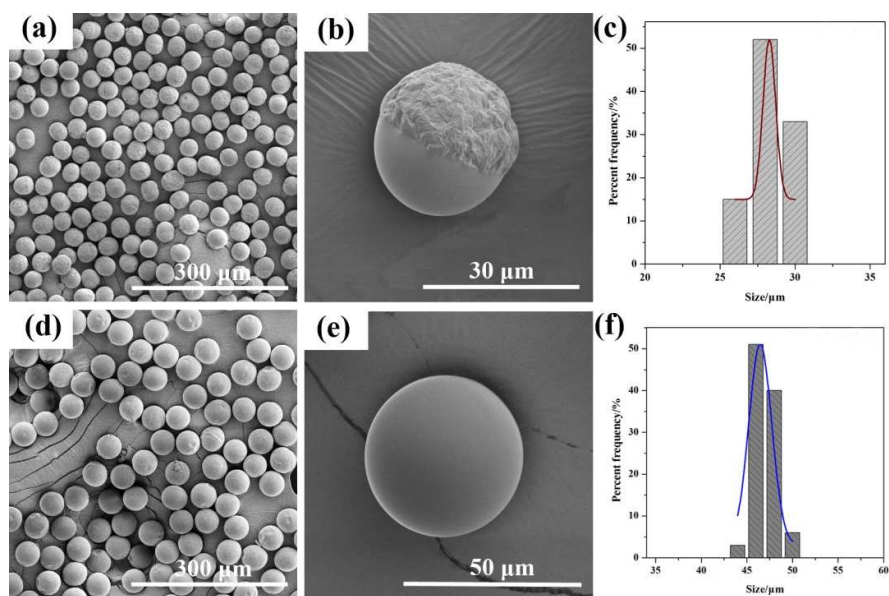


Figure 1. SEM images and size distribution of Janus and microcapsule PLGA/PCL particles. (a-c) Janus particles prepared using dimethyl carbonate as the solvent of the dispersed phase, (d-f) microcapsule particles prepared using dichloromethane as the solvent of the dispersed phase. The flow rates of the dispersed and continuous phase to generate Janus particle were 0.4 and 1.6 mL/h, respectively, whilst the flow rates of the dispersed and continuous phase to generate microsphere particle were 0.25 and 0.45 mL/h, respectively. The weight ratio between PLGA and PCL was 1:1.

Figure 2

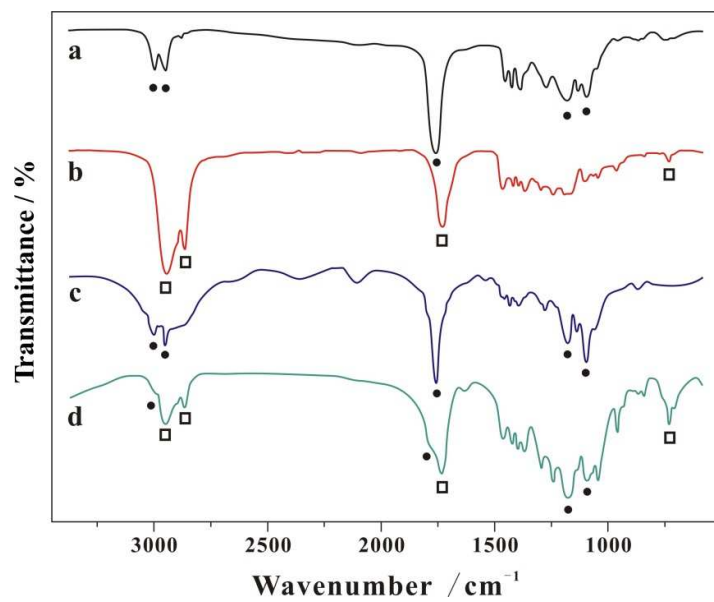


Figure 2. ATR-FTIR spectra of (a) pure PLGA film, (b) pure PCL film, (c) PLGA/PCL microcapsule particle, and (d) PLGA/PCL Janus particle. The weight ratio between PLGA and PCL was 1:1.

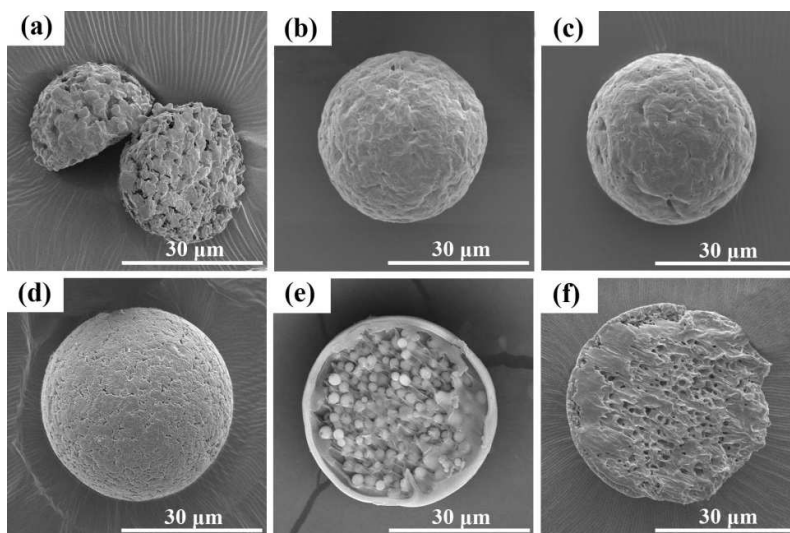
Figure 3

Figure 3. Effects of acetone treatment on Janus and microcapsule particles: (a, c, d, f) SEM images of (a) Janus, (c) pure PCL, (d) microcapsule and (f) cross-sectioned microcapsule particles after treatment with acetone for 30 s. For comparison, (b) pure PCL and (e) cross-sectioned microcapsule particles without acetone treatment are also included. The weight ratio between PLGA and PCL was 1:1.

Figure 4

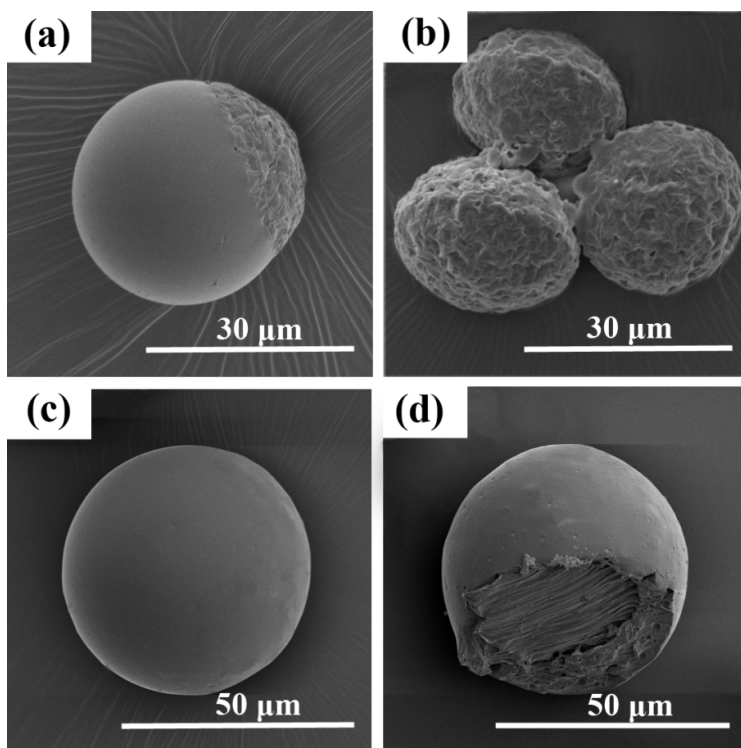
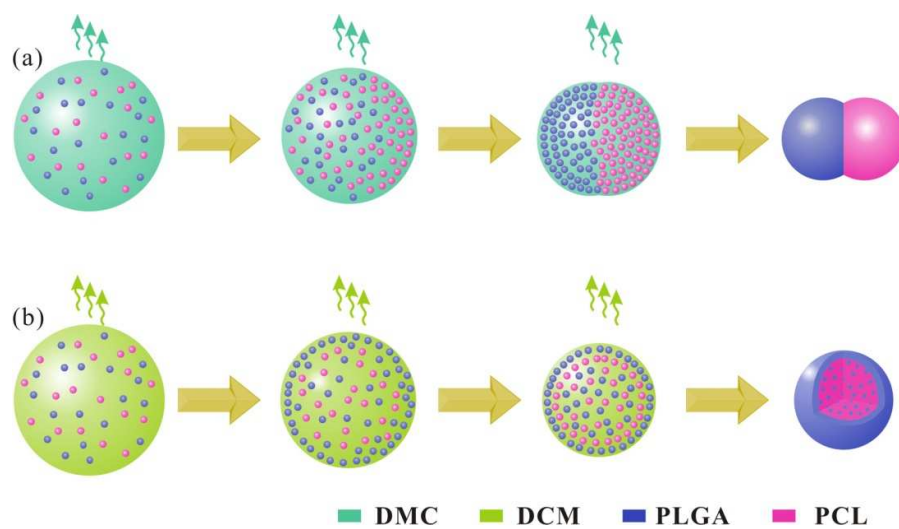


Figure 4. SEM images of Janus and microcapsule particles prepared under the mass ratio of PLGA and PCL (7:3, w/w). (a) Janus particle without acetone treatment; (b) chesspiece-like PCL particle after treating Janus particle with acetone; (c) microcapsule particle; (d) sliced microcapsule particle.

Scheme 1



Scheme 1. Schematic illustration on the formation mechanism of (a) Janus particles and (b) microcapsule particles. DMC: dimethyl carbonate; DCM: dichloromethane.

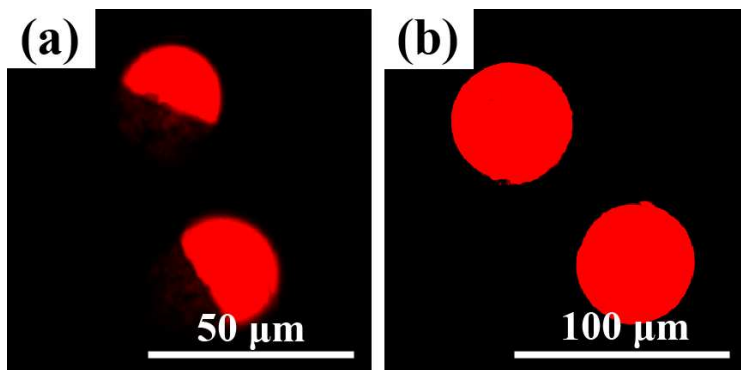
Figure 5

Figure 5. Fluorescence images of (a) Janus and (b) microcapsule particles after stained by Rhodamine B.

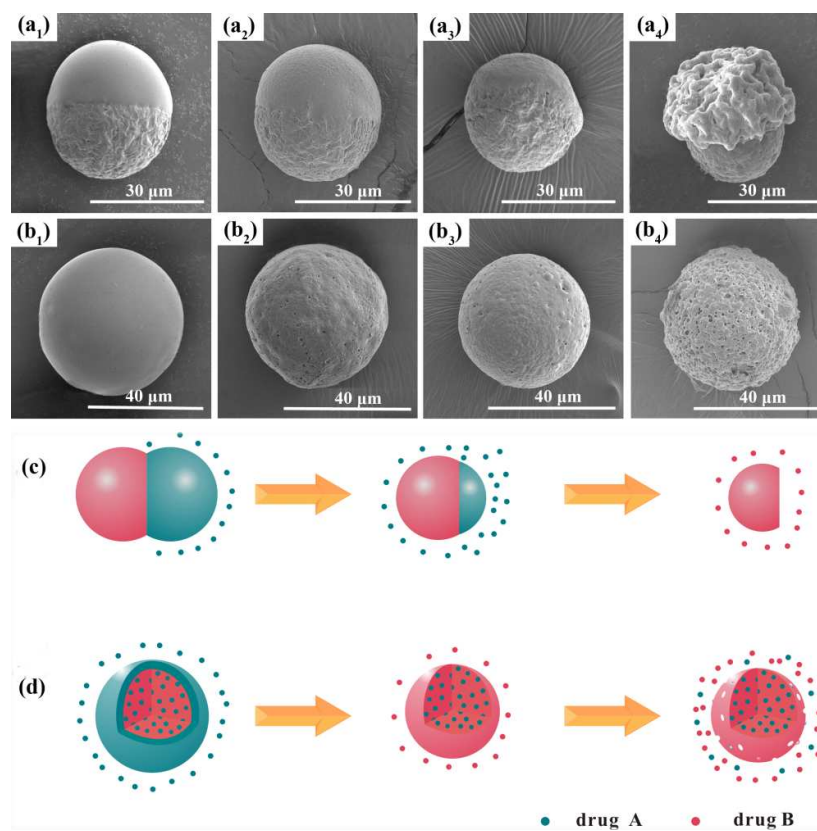
Figure 6

Figure 6. Possible applications of PLGA/PCL Janus and microcapsule particles in drug delivery. (a and b) in vitro degradation of PLGA/PCL Janus and microcapsule particles in PBS solution after (a₁, b₁) 7 days, (a₂, b₂) 14 days, (a₃, b₃) 21 days and (a₄, b₄) 35 days; (c and d) schematic illustration on programmable drug delivery with the degradation of PLGA/PCL Janus and microcapsule particles.

Table 1**Table 1.** Interfacial tensions measured by the Wilhelmy plate method and spreading coefficients.

Emulsion system	γ_{12}	γ_{13}	γ_{23}	S_1	S_2	S_3	Type
PLGA/DMC-PVA-PCL/DMC	3.08	7.48	2.92	-7.64	+1.48	-7.32	Dewetting
PLGA/DCM-PVA-PCL/DCM ^(a)	2.17	0	2.33	+0.16	-4.50	-0.16	Wetting
PLGA/DCM-PVA-PCL/DCM ^(b)	2.87	0	1.72	-1.15	-4.59	+1.15	Wetting

^{a)} The concentrations of PLGA and PCL in the oil phase are 40 mg/mL; ^{b)} the concentrations of PLGA and PCL in the oil phase are 80 mg/mL. The units of interfacial tensions and spreading coefficients were all mN/m. DCM: dichloromethane, DMC: dimethyl carbonate.

(Supporting Information)

**Controllable microfluidic fabrication of Janus and
microcapsule particles for drug delivery application**

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(1) Stable generation of droplets in microchannels

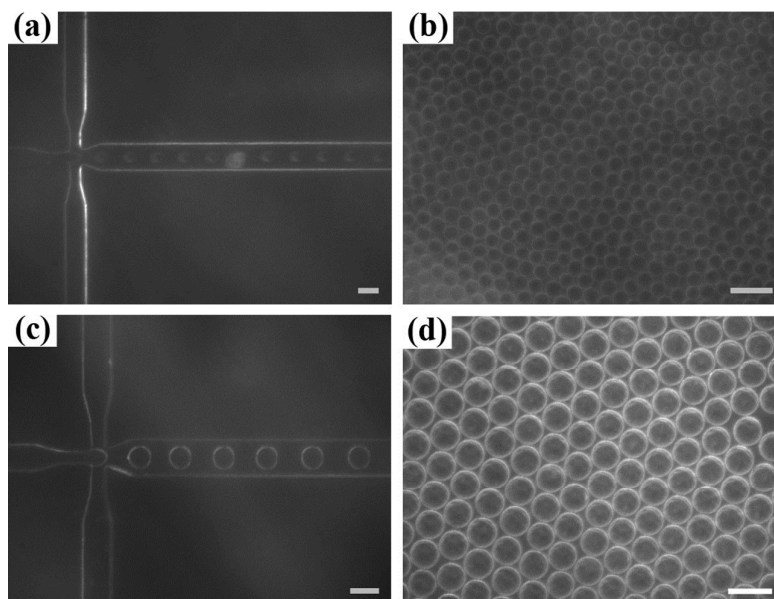


Figure S1. Optical images showing (a, c) generation of droplets in the flowing focusing region and (b, d) monodisperse droplets collected at the outlet of microfluidic devices. The solvent used in a and b is dimethyl carbonate, whilst the solvent used in c and d is dichloromethane. All the scale bars are 200 μm .

(2) Schematic illustration of droplet-based microfluidic device

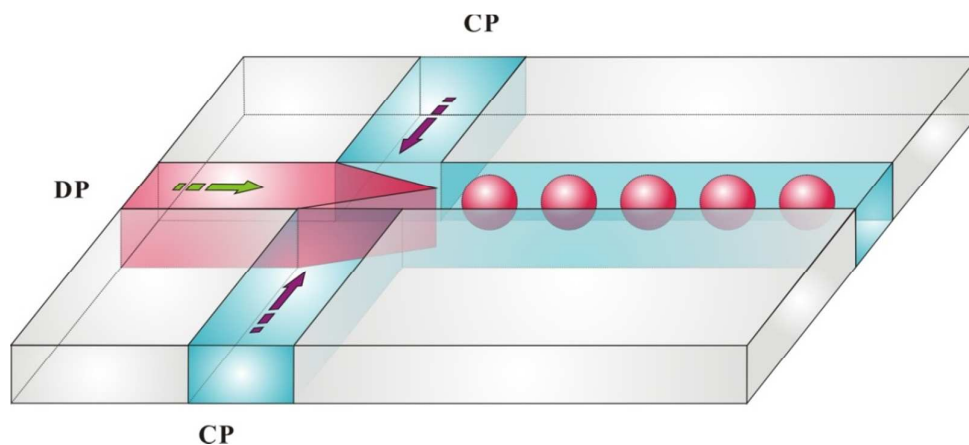


Figure S2. Schematic illustration of the microfluidic device used for synthesis of Janus and microcapsule particles. Fabrication and operation procedure is described in detail in experimental section. CP: continuous phase, DP: dispersed phase.

(3) Fabrication of PLGA/PCL particles using a mixture solvent containing dimethyl carbonate and dichloromethane

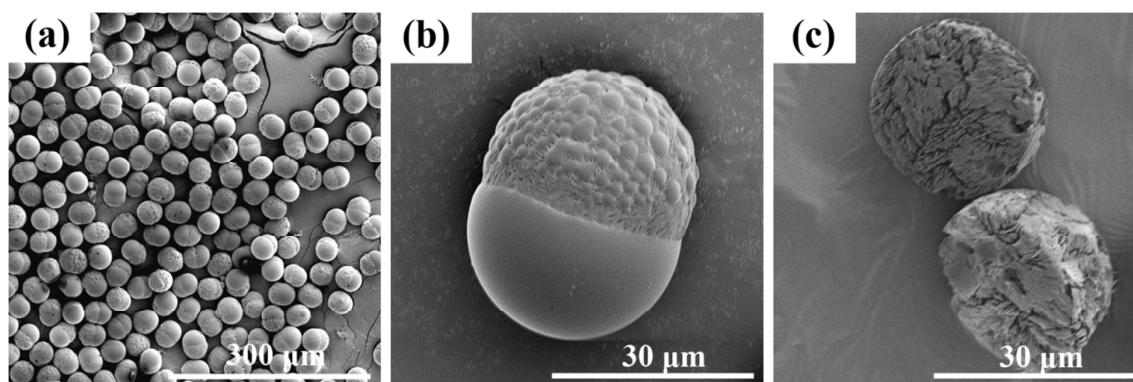


Figure S3. SEM images of PLGA/PCL microparticles prepared using the mixture of dimethyl carbonate and dichloromethane (5:1, v/v) as solvent for the dispersed phase. (a, b) microparticle without acetone treatment; (c) microparticle after treated with acetone.

(4) Calculation of interfacial tension between PLGA and PCL in dimethyl carbonate system

PLGA and PCL solutions were first spin-coated on clean glass slides to form a uniform film after solvent evaporation. Then, two standard probe liquids (pure water and diiodomethane) with well-known surface energy (γ_L), dispersive (γ_L^d) and polar component (γ_L^p), were dropped on the surface of polymer film for contact angle measurements (OCA15, Data Physics Instruments GmbH). According to the classic Owens-Wendt-Kaelble (OWK) equation,

$$\gamma_L(1 + \cos \theta) = 2\sqrt{\gamma_S^d \gamma_L^d} + 2\sqrt{\gamma_S^p \gamma_L^p}$$

The dispersive (γ_S^d) and the polar component (γ_S^p) of PLGA and PCL could be obtained, and their surface energy were calculated as $\gamma_S = \gamma_S^d + \gamma_S^p$. The interfacial tension between PLGA and PCL is the D-value between the surface energy of PLGA and PCL. These data were summarized in Table S1.

Table S1. Calculation of interfacial tension between PLGA and PCL in dimethyl carbonate system

Entry	Water-PLGA	Diiodomethane-PLGA	Water-PCL	Diiodomethane-PCL
Contact angle ($^\circ$)	85.5	44.5	102.7	38.8
Surface energy (mN/m)	37.28		44.76	
Interfacial tension (mN/m)	7.48			

- (5) SEM images of the sliced microcapsules prepared under the mass ratio of PLGA and PCL (7:3, w/w).

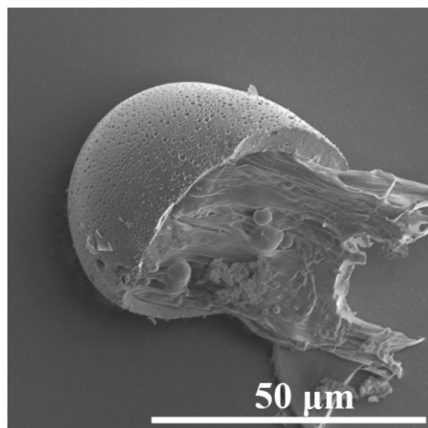


Figure S4. SEM images of the sliced microcapsules prepared under the mass ratio of PLGA and PCL (7:3, w/w).

Movie S1: Video of droplets generation for the synthesis of Janus particle in microfluidic device. The flow rates of disperse phase and continuous phase were 0.4 and 1.6 mL/h, respectively.

Movie S2: Video of droplets generation for the synthesis of microcapsule particle in microfluidic device. The flow rates of disperse phase and continuous phase were 0.25 and 0.45 mL/h, respectively.