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Efficient *In situ* Production of Monodisperse Polyurethane Microbeads in Microfluidic Device using Increase of Residence Time of Droplets

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Abstract

This study presents a simple method for the efficient generation of monodisperse polyurethane (PU) microbeads in microfluidic device integrating with downward outlet to increase the residence time of droplets on the UV irradiating area. Based on the mechanism of shear force-driven break-off, monodisperse droplets of acrylated urethane as an oil-in-water (O/W) emulsions are continuously generated in an immiscible continuous phase at the cross-shaped junction.The droplets of oligomeric PU as a dispersed phase are rapidly polymerized at downward outlet channel by *in situ* UV polymerization. The low coefficient of variance (CV, 1%) indicates that the produced microbeads have narrow size distribution. In addition, the size of microbeads produced can be controlled by important operating parameters such as flow rates of continuous and dispersed phase. Therefore, the proposed *in situ* microfluidic method provides a novel route for the synthesis of monodisperse microbeads via a one-pot synthetic approach.

Keywords: Microfluidics, Microbeads, UV-polymerization, Monodispersity, Droplets

Introduction

Polymeric microbeads in the size range from 10 μm to 100 μm have been attracted due to their versatile applications including bead based immunoassay, chromatography support, and biomedical microdevices[1,2]. Among them, polyurethane microbeads are widely used in industries such as toners, coatings, hot melt adhesives, and optical pigments. In these applications, there are great needs for the synthetic method having a capability of precise control of their size and narrow size distribution[3,4]. Generally, several methods including suspension, emulsion, precipitation and dispersion polymerization, and multistage process were widely used to synthesize micron-sized polymeric microbeads[4-7]. However, it is difficult to obtain monodisperse microbeads using conventional polymerization methods. Moreover, these methods are material specific or time and labor consuming. Thus, the novel synthetic method of micron sized beads having a narrow size distribution is still challenging area. One of the promising methods, membrane emulsification method using porous membrane, has been reported to produced monodisperse droplets[8,9]. However, this method also limited in the production of monodisperse microbeads because it crtically depends on the size distribution of pores of membrane. In addition, the membrane having narrow size distribution of pore size is another challenging topic.

Recently, microfluidic systems used to overcome conventional methods because they showed strong potentials for *in situ* production of uniform size of spherical beads[10-13], microcapsules[14], emulsions[15-18], and various shaped polymeric particles[19-22]. Especially, microfluidic flow-focusing device (MFFD) is one of the widely used devices for generation of monodisperse microemulsions because produced emulsions can be easily controlled by adjustment of driving pressures of two immiscible fluids[23,24]. Monodisperse monomer emulsions can be generated at the junction of the channels due to the shear force driven sheath flow of immiscible phase. Subsequently, these monomer emulsions is easily polymerized by exposure to UV irradiation in the channel. In case of *in situ* UV polymerization, it is important to ensure enough UV irradiation time to prevent adhesion of produced microbeads and maintain their spherical shapes. In order to increase residence time of droplets, the MFFD is devised with long wavy channel at the region of UV irradiation[23]. However, it is difficult to provide enough UV irradiation time with high flow rate of the fluids because the UV irradiation time is inverse proportion to flow rate of the fluids.

In this study, we report a simple and novel method to increase the UV irradiation time using novel design of downward outlet in microfluidic device. Firstly, based on the mechanism of shear force-driven break-

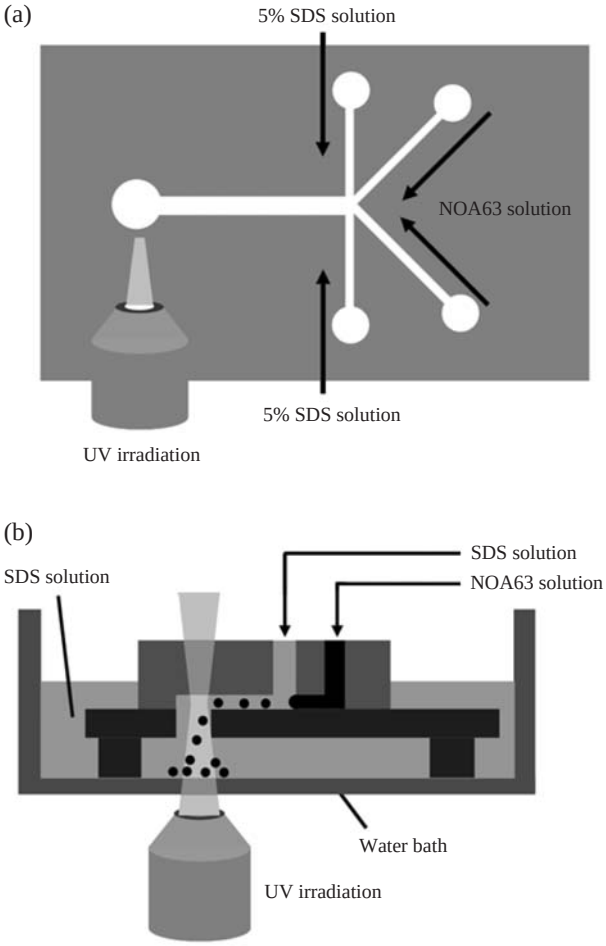

Figure 1. Schematic diagram of microfluidic system for the generation of monodisperse microbeads. (a) Top view and (b) side view of the microfluidic device.

off, monodisperse monomer emulsions can be formed continuously in immiscible aqueous phase at junction in the MFFD. The emulsions are moved to the downward outlet through the main channel and dropped to the water bath containing continuous phase due to the gravity. During the process, the emulsions can be fully polymerized by *in situ* UV irradiation due to the increased UV irradiation time to the emulsions in the irradiation region. In addition, the size of microbeads could be manipulated according to the flow rate of continuous and dispersed phase.

Results and Discussion

Generation of Monodisperse PU Microbeads

The design of microfluidic device is shown in Figure 1. Two immiscible fluids containing the hydrophobic and hydrophilic solution are injected into the microfluidic device using microsyringe pumps. NOA63 and 5% SDS solution are used as dispersed and continuous phase, respectively.

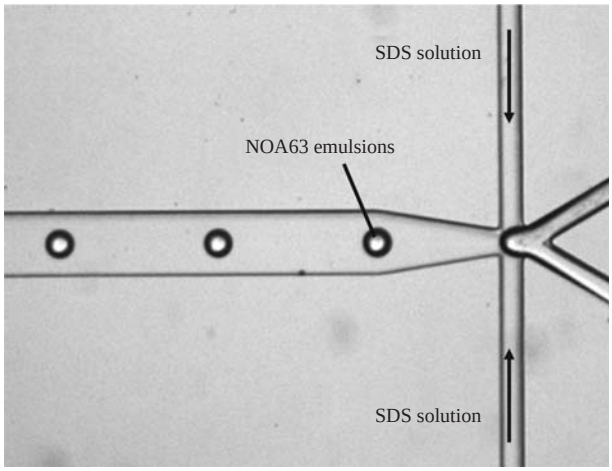

Figure 2. Optical image of continuous generation of monodisperse NOA 63 droplets in the microfluidic device.

High viscosity of NOA63 (2,000 cps) can cause the jetting formation at the junction of the microchannel. The jetting regime is quite irregular, resulting in polydisperse emulsions. To generate stable monodisperse droplets of NOA63, the elegant force-balance between dispersed and continuous phase is adjusted by the decrease of viscosity of NOA63 via addition of acetone (30% v/v). The dispersed phase containing the 70% of NOA63 is slowly injected into inlet and the second immiscible liquid. And the hydrophilic phase containing SDS, is also introduced into the other inlets as a continuous phase. UV irradiation at the region of downward outlet triggers the photopolymerization of NOA63 droplets. As shown in Figure 2, the uniform size of droplets of NOA63 at the junction of the microchannel could be easily obtained by the control of flow rate of aqueous and monomer phase.

The formation of droplets at the junction is changed by the competition between the viscous stress and the surface tension stress. The capillary number ($Ca = U\mu/\gamma$) is a representative value showing the relative importance of these two effects, where U is the flow rate of continuous phase, μ is the viscosity of the continuous phase, and γ is the interfacial tension between the dispersed and continuous phases. *Ca* can be modified by varying Q_c, the flow rate of the SDS solution continuous phase, which results from a change in U through the relationship, $U = Q_c/A$, where A is the cross-sectional area of the microchannel. Previous works on droplet formation have used a phase diagram

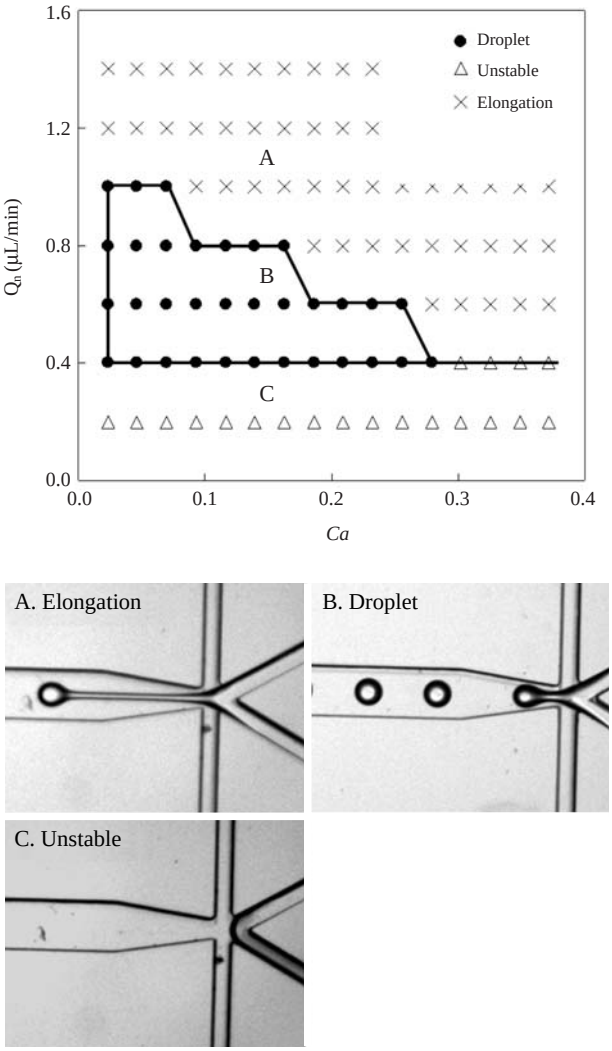

Figure 3. Phase diagram for the formation of droplets as a function of Q_n (flow rate of NOA63) and *Ca* (capillary number).

to describe the different regimes observed as a function of the experimental factors[3,25]. Using a similar method, the flow patterns of our system are described in *Ca* and Q_n (flow rate of NOA63). Figure 3 shows three typical regimes observed after the junction: elongation flow (A), stable droplets (B), and unstable droplets pattern (C). Firstly, we found that it is difficult to generate stable droplets at very low flow rate of NOA63 ($Q_n < 0.4$ μL/min). In this case, there is a back-flow of NOA63 because relatively fast flow rate of SDS solution overflows (regime C). In the regime B, monodisperse droplets are formed only within a limited range of *Ca* (2.3×10^{-2}-2.8×10^{-1}) and flow rate of NOA63 ($0.4 < Q_n < 1.0$ μL/min). When the flow rate of NOA63 is increased from 0.4 to 1.0 μL/min, *Ca* range in the stable formation of droplet is decreased because the elongation of NOA63 thread is occurred according to relatively fast flow rate of NOA63. Increase of *Ca* induced the long thread formation as elongation phase at above 0.4 μL/min of Qn. At higher flow rate of NOA63 phase ($Q_n > 1.0$ μL/min), droplets does not separated by immiscible SDS solution and flow formation is changed to cylindrical elongated thread along the microchannel because the shear force of SDS solution phase is not high enough to induce monomer phase to break off as droplets at the junction (regime A).

Therefore, three types of regime can be clearly distinguished in the phase diagram. In region B, stable droplets are always generated with reproducible size, whereas region A and C, elongated thread and unstable droplets are consistently produced. In the stable droplet formation (regime B), introduced monomer phase rapidly becomes unstable after a short distance from the junction, breaking up into droplets, while the SDS solution begins to wrap around the monomer solution due to the difference in wettability between two fluids with the PDMS wall. Thus, we can generate monodisperse PU microbeads in only region B.

Characterization of the PU Microbeads

In general, UV polymerization has been developed to produce monodisperse microbeads or polymeric particles in microfluidic system. Microemulsions generated from the junction of microchannel is polymerized by UV irradiation while they move through UV irradiation region. In these systems, UV irradiation time is critical factor for the successful synthesis of polymerization and mainly depended on the flow rate. UV irradiation time is decreased as increasing the flow rate of two liquids in the channel although the channel in UV irradiation region has wavy shape to increase the UV irradiation time. If the UV irradiation time is not enough, products can not be fully cured in the microchannel. Some parts of microbeads are not fully polymerized but still liquid. This unsuccessful polymerization can induce collapse or aggregation of products.

To overcome this problem, we designed outlet channel to downward for increase the UV irradiation time. The downward outlet has two major advantages. Firstly, it provides enough UV irradiation time to get fully cured microbeads without any post curing process. Monodisperse NOA63 emulsions generated at the junction of the microchannel are moved to outlet and exposed with UV. During the UV irradiation, the droplets of NOA63 migrate downward due to gravity. This downward migration of the droplets offers enough time to produce fully cured PU microbeads. Secondly, stable UV polymerization at outlet area produces solid-

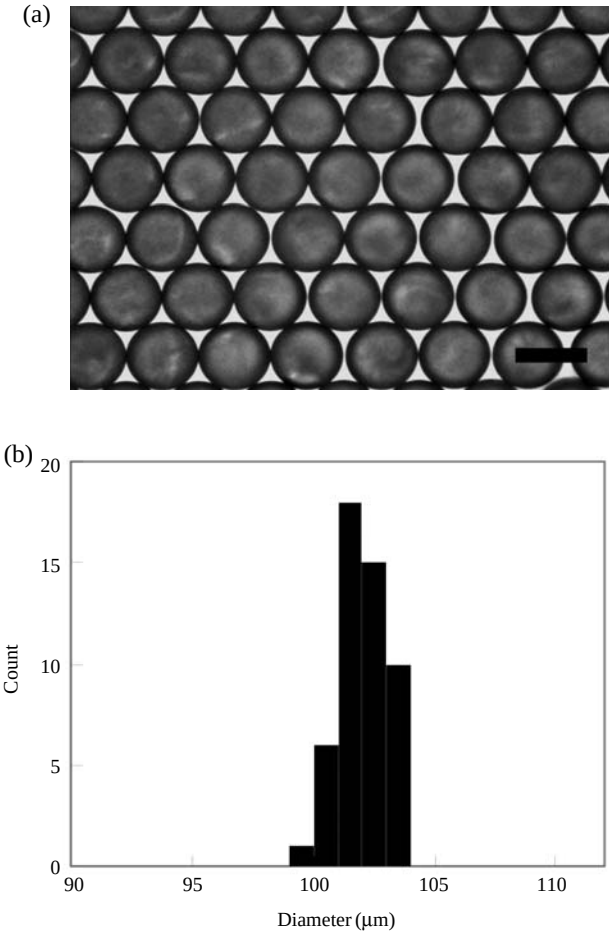

Figure 4. (a) Optical image of produced microbeads and (b) their size distribution of monodisperse PU microbeads. scale bar indicates 100 μm and measured average diameter of fully cured microbeads is about 101 μm with 1% CV.

ified microbeads continuously, which result in the prevention of back pressure or channel clogging problem in the microchannel.

Figure 4a shows optical microscopy images of the resulting microbeads. Monodisperse PU microbeads are easily obtained without any channel clogging or back pressure. The generated PU microbeads have very narrow size distribution (Figure 4b). The coefficient of variance (CV) is about 1%, which shows that the microbeads are highly monodispersed, which proves that the microbeads are monodisperse according to the US National Institute of Standards and Technology (NIST) definition of monodispersity as a narrow size distribution having a $CV < 5\%$[26]. Figure 5. shows a typical SEM image of the resulting microbeads. The microbeads were formed at $Q_c = 3.0\,\mu L/min$ with continuous phase and $Q_n = 0.5\,\mu L/min$ with disperse phase. The SEM image confirms that our proposed method

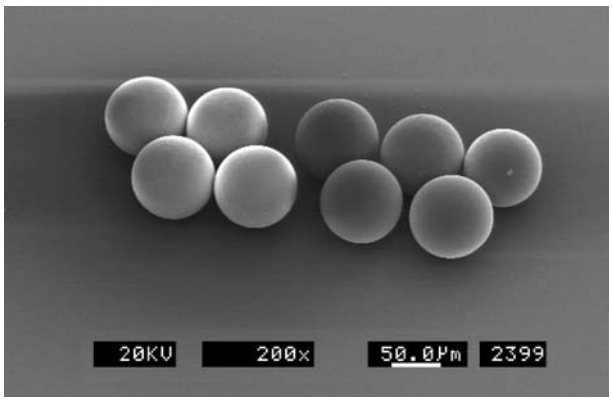

Figure 5. SEM image of fully cured PU microbeads.

can be applied to *in situ* generate polymeric particles. And the generated microbeads can retain their spherical structure without any deformations, collapse and aggregation each other. This presents the microbeads produced using our proposed method are fully polymerized due to the enough UV irradiation time in the microfluidic device.

Effect of Flow Rate on the Microbead Size

The strong advantage of microfluidic system is the simple control of microbead size. Previous studies using flow-focusing microfluidic system reported that the control of produced droplets size could be manipulated by experimental factors such as viscosity, interfacial tension, and flow rate[26-28]. The formation of NOA63 droplets is similar to previously studied droplet formation process using the flow-focusing technique. Thus, the details of the effect of flow rate were investigated.

To investigate the influence of flow rate of NOA63 and continuous phase in the pinch-off process between the two phases, we investigate the average diameter of generated microbeads as a function of flow rate of NOA63 and continuous phase. Figure 6 clearly shows the effect of the flow rate, both flow rate of Q_n (0.4-0.6 μL/min) and Q_c (1.0-8.0 μL/min) on the size of microbead at fixed concentration of surfactant (SDS, 5 wt%). A higher flow rate of Q_c produces smaller microbead at a constant flow rate of monomer phase because viscous force is in proportion to flow rate. When the flow rate of the continuous phase increased from 1 to 8 μL/min, the average diameters of microbeads reduced from 120 to 90 μm at constant flow rate of monomer phase (0.6 μL/min). Whereas increasing flow rate of disperse phase (NOA63) at constant continuous phase generates bigger microbeads. The increase of flow rate of disperse phase causes the increasing volume of NOA63 droplets in the emulsions at specific

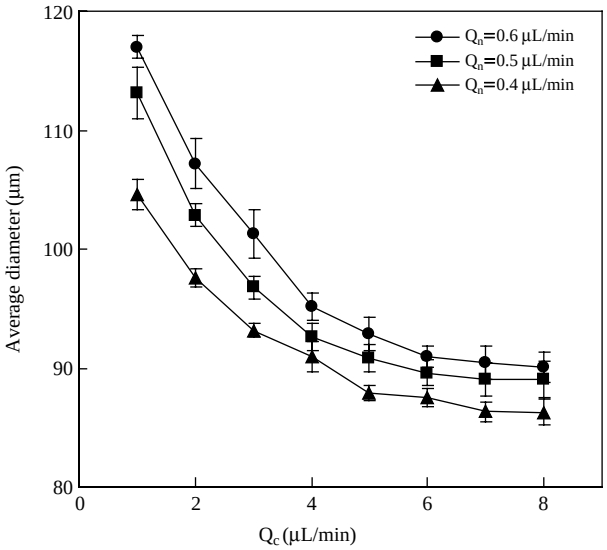

Figure 6. The control of size of microbead with function of the relative Q_n (flow rate of NOA63) and Q_c (flow rate of continuous phase).

time during the pinch-off process. While the flow rate of the disperse phase increased from 0.4 to 0.6 μL/min, the average diameters of microbeads increased from 105 to 120 μm at constant flow rate of continuous phase (1 μL/min). Thus, we found that flow rate is significant factor for the control of produced microbeads size which ranged from 80 to 120 μm in our experiments.

Conclusions

In this study, we have demonstrated a simple approach for the stable generation of polymeric microbeads with photopolymerization in microfluidic device. To increase residence time of droplets, we designed the microfluidic device having downward outlet. We can generate highly monodispered polymeric microbeads without clogging problem and back-pressure in the microfluidic device. In addition, droplet-based microfluidic approach shows easy control of the size of microbeads with the simple change of flow rate of disperse and continuous phase.

Novel design of microfluidic device offers some advantages such as enough UV irradiation time for fully cured products and prevention of back pressure and clogging problem in the microchannel. Although the experimental results were focused on PU, it can be applied to other polymer even required long UV irradiation time. We believe that our system has strong potentials in various chemical and biological applications.

Materials and Methods

Materials

Norland Optical Adhesives (NOA) 63 as UV curable polyurethane oligomeric resin and sodium dodecyl sulfate (SDS) were purchased from Norland Products (NJ, USA) and Sigma-Aldrich Chemicals (MO, USA), respectively. The SU-8 photoresist and developer solution were purchased from Microchem (MA, USA). The poly (dimethylsiloxane) (PDMS) was obtained from Dow Corning (MI, USA).

Fabrication of the Microfluidic Device

The mold masters were fabricated using SU-8 photoresist on a silicon wafer using conventional photolithography. A mixture of PDMS prepolymer and curing agent (10 : 1 ratio) was thoroughly stirred, and then degassed in a vacuum oven. The degassed PDMS mixture was then poured onto the silicon master and cured at 65°C. After curing, the PDMS replica containing the microchannel pattern was lifted off from the silicon master. After cooling the replica, holes were punched to the replica to supplement the reagent lines. The PDMS replica was then exposed to oxygen plasma for 20 s, and then bonded to a glass slide. To fabricate microchip has downward outlet for increasing the UV irradiation time, the glass slide was punched with hand drill before bonding process. The dimensions of the final assembled microfluidic channels were 50 μm × 100 μm (width × height) as injection line and 200 μm × 100 μm (width × height) as main reaction microchannel.

A schematic diagram of the microfluidic devices is shown in Figure 1. The microfluidic device has consisted of two inlets of dispersed phase and continuous phase, main channel, and downward outlet (Figure 1a). The finally assembled microfluidic device was placed into the water bath filled with 5% SDS solution (Figure 1b). Glass spacers were located under the bottom of assembled microfluidic device and UV irradiation area was adjusted at the downward outlet to ensure UV irradiation time.

Analytical Instruments

The inverted fluorescence microscopy (Nikon, TE2000, Japan) equipped with CCD camera (Photometrics, Coolsnap cf, USA) was used to observe the formation of microbeads. The distribution of the beads was analyzed using Image J (http://rsb.info.nih.gov/ij/) and Image Pro (Media Cybernetics) software. The size distributions of the microbeads along with their coefficients of variation (CV, defined as the standard deviation in the measured diameter divided by the average

diameter) were calculated from the measured value of total 5 photographs taken of 50 microbeads per an image.

Acknowledgements

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