

Preparation of Monodispersed Emulsion with Large Droplets Using Microchannel Emulsification

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ABSTRACT: Microchannel (MC) emulsification is a novel technique for producing monodispersed emulsions with coefficients of variation of less than 5%. To produce emulsions with large droplets, we designed three MC with large dimensions. The MC structure consists of two parts: a channel and a terrace. Terrace length was defined as the length from the exit of the MC to the end of the terrace. The MC plates used in this study have deeper channels and longer terraces. The size limit of droplets prepared by MC emulsification was studied. Monodispersed emulsions with droplets as large as 100 μm were prepared using an MC with a depth of 16 μm and a terrace length of 240 μm . The average diameter (coefficient of variation) of the emulsion droplets was 98.1 μm (2.5%). Emulsions with larger-diameter droplets were prepared using an MC with a longer terrace. The effect of the applied pressure on emulsification behavior was studied and discussed from the viewpoint of the droplet formation mechanism. At low applied pressures, droplet diameters were independent of the applied pressure, and monodispersed emulsions were produced. The pressure ranges of constant droplet diameter for large-droplet emulsions were narrower than those for the 5 to 30 μm droplet size emulsions because interfacial tension is more significant on a smaller scale compared with the other forces.

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Emulsions have been utilized in various industries, including food, cosmetics, and pharmaceuticals. In these applications, physical and qualitative stabilities are important, which depend on the size and size distribution of the dispersed droplets (1,2). Rheology, appearance, chemical reactivity, and physical properties are influenced by both the average size and size distribution of droplets (1,3). Monodispersed emulsions are useful for fundamental studies because interpreting experimental results is much simpler than for polydispersed emulsions (1). Monodispersed emulsions are also applicable to valuable materials, such as microcapsules for drug-delivery vehicles, microparticles, and packed beads for column chromatography. Microcapsules are prepared from emulsions by various methods, such as solvent evaporation (4), interfacial polycondensation (5), and internal gelation (6). Microparti-

cles can be prepared by solidifying emulsions, such as in suspension polymerization (7). Packed beads for a chromatographic column, which determine separation performance, should possess a uniform size distribution. Drug-release properties from microcapsules and their degradation rate depend on their size. Furthermore, the behavior of microcapsules *in vitro* is influenced by their size.

Various instruments have been used to produce emulsions on industrial and laboratory scales, including high-speed blenders, colloid mills, and high-pressure homogenizers (8,9). However, the emulsions made by these instruments exhibit considerable polydispersity, with typical droplet size distributions of 2 to 10 μm with high-speed blenders (1), 1 to 5 μm with colloid mills (1), and 0.05 to 1 μm with high-pressure homogenizers.

Membrane emulsification, in which the pressurized dispersed phase passes through a microporous membrane and forms emulsion droplets, is a promising technique for producing monodispersed emulsions with a coefficient of variation of approximately 10% (10–12). The emulsion droplet size is controlled by the membrane pore size. This technique can be used to produce emulsions without high mechanical stress.

Recently, we proposed a novel method for making supermonodispersed emulsion droplets from a microfabricated channel array (13–15). This emulsification technique is called microchannel (MC) emulsification. Emulsions with droplet sizes of 5 to 30 μm (16,17) and a coefficient of variation of approximately 5% have been successfully prepared by applying this technique (15). This emulsification technique exploits interfacial tension, which is the dominating force at micrometer scales, as the driving force for droplet formation (15). During droplet formation, the dispersed phase passed through the MC inflates into an elongated shape, and the elongated dispersed phase spontaneously transforms into spherical droplets due to interfacial tension. This spontaneous droplet formation leads to very low energy input during emulsification compared to conventional emulsification techniques (15). Therefore, this technique is promising for preparing not only emulsions but also various microspheres. We have applied it to preparing several types of oil-in-water emulsions, water-in-oil emulsions (18,19), lipid microparticles (16), polymer microparticles (20), and microcapsules.

In this study, we attempted to prepare monodispersed emulsions with larger droplet sizes using MC emulsification. Monodispersed emulsions with large droplets are useful as precursors of microcapsules and microparticles because

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monodispersed microcapsules, and microparticles with diameters of 10 to 300 μm are presently difficult to produce. They are expected to be applied in various industrial fields, such as fine chemicals, cosmetics, and pharmaceuticals. They are also useful for fundamental studies. In a previous study (15), we demonstrated that the droplet size is controlled by the MC shape. We designed an MC with large dimensions for producing emulsions with large droplets and studied the size limit of emulsion droplets prepared by MC emulsification. The effects of the pressure and MC shape on the emulsification behavior were studied with reference to the formation of 5- to 30- μm droplets.

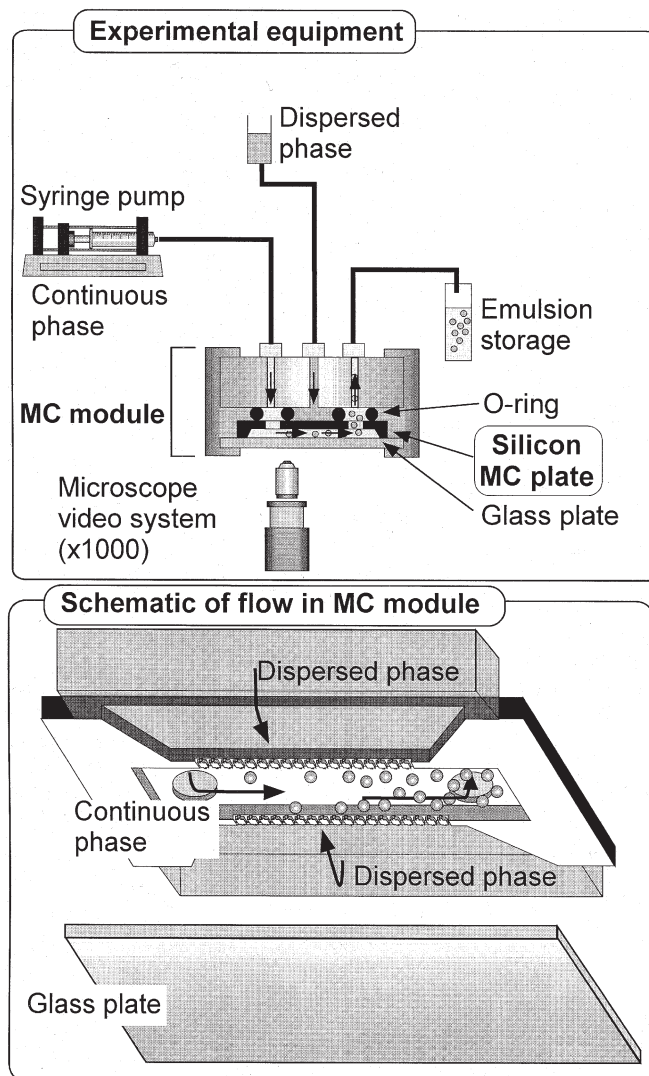
MATERIALS AND METHODS

Materials. Triolein (purity >90%) obtained from Nippon Lever B.V. (Tokyo, Japan) was used as the dispersed oil phase. MilliQ water (Millipore, Milford, MA) was used as the continuous water phase. SDS was purchased from Wako Pure Chemical Ind. (Osaka, Japan) and used as the surfactant for emulsification.

MC emulsification. The laboratory-scale apparatus for MC emulsification was described previously (13,14). Scheme 1 shows the experimental setup and MC plate used in this study. A crossflow-type MC plate was adopted for continuous emulsification (14). The emulsification behavior was observed through a glass plate using a microscope video system. The observed images were realized with an inverted metallographic microscope (MS-511B; Seiwa Optical Industrial Co., Saitama, Japan), detected by using a charge-coupled device (CCD) camera (HV-C20M; Hitachi, Tokyo, Japan), and recorded by a VHS video recorder (WV-ST1; Sony Corporation, Tokyo, Japan) with a total magnification of 1000 \times .

New crossflow silicon MC plates were designed for continuous emulsification. They were fabricated by a process of photolithography and orientation-dependent etching. Figure 1A shows schematics of the MC plates used in this study. The MC structure consists of two parts: a channel and a terrace. Over the terrace end, there is a deeply etched well. The terrace length is defined as the length from the exit of the channel to the end of the terrace as shown in Figure 1C. In the present study, three MC plates (MC-A, MC-B, and MC-C) were used for preparing emulsions with different size droplets. The MC module was initially filled with the continuous phase. The dispersed phase was pressurized and caused to flow into the module by lifting the liquid chamber filled with the dispersed phase. The dispersed phase supplied from the liquid chamber entered the space between the silicon MC plate and the glass plate, and droplets were formed from the MC. The prepared emulsions were recovered by a continuous phase flow.

Analytical methods. The number-average diameters and coefficients of variation of the prepared emulsions were determined from pictures of 100 droplets taken with the microscope video system described previously. The coefficient of variation (CV, %) is defined as follows:



SCHEME 1

$$CV = (\sigma/D_A) \times 100 \quad [1]$$

D_A is the number-average diameter (μm) and σ is the SD of the diameter (μm). Winroof (Mitani Corporation, Fukui, Japan) software was used to analyze the captured pictures. The interfacial tension in each system was measured using a Fully Automatic Interfacial Tensiometer (PD-W; Kyowa Interface Science Co., Ltd., Saitama, Japan).

RESULTS AND DISCUSSION

The droplet size in the MC emulsification is affected by the MC shape (16,20). In this study, MC plates with deep MC and long terraces were designed to produce larger emulsion droplets. MC emulsification was performed using the three MC plates (Fig. 1). Triolein was used as the dispersed oil phase. SDS (1% aqueous solution) was used as the continuous phase. Interfacial tension of the system was 4.5 mN/m. MC emulsification was performed at 25°C. The continuous phase was supplied by the microfeeder at a flow rate of 2.0 mL/h. The dispersed phase

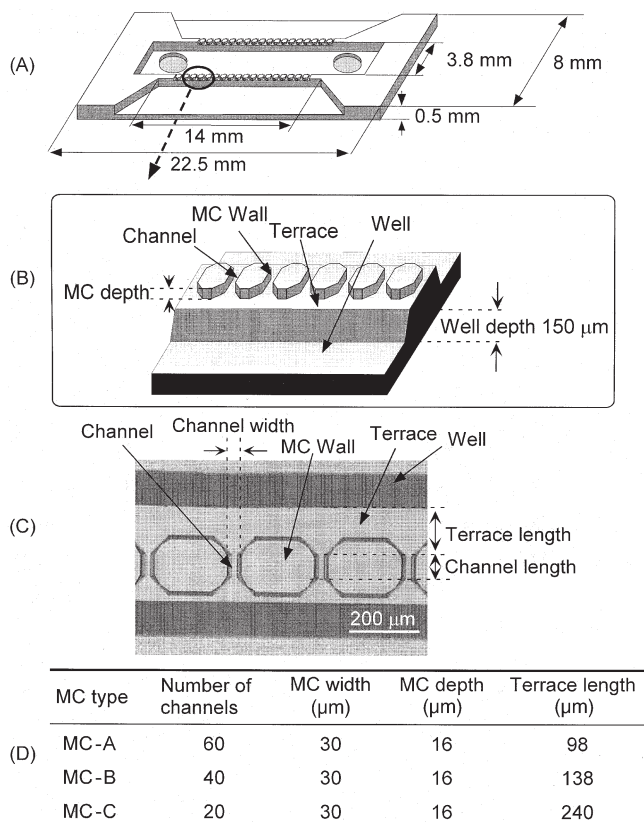


FIG. 1. Crossflow silicon microchannel (MC) plate. (A) Schematic of MC plate. (B) Enlargement of MC. (C) Photomicrograph of MC. (D) Dimensions of the three MC plates.

was pressurized and caused to flow into the MC module by lifting the liquid chamber filled with the dispersed phase. The applied pressure was calculated from the head difference between the liquid chamber and the emulsion outlet.

Figure 2 shows photomicrographs of the MC emulsification process at low (1.12 to 1.43 kPa) and high applied pressure (1.87 to 2.68 kPa) for each MC plate. The average diameters and the CV of the emulsions are shown in Table 1. Monodispersed emulsions were prepared at 1.12 to 1.43 kPa applied pressure. Polydispersed emulsions with larger droplets were prepared at 1.87 to 2.68 kPa applied pressure.

In comparing the three MC plates, the larger droplet emulsions were prepared using the MC with the longer terrace. Monodispersed emulsions with droplets as large as 100 μm

TABLE 1
Diameter Distributions of Prepared Emulsions

MC ^a type	Applied pressure (kPa)	Average diameter (μm)	CV ^b (%)
MC-A	1.16	64.4	3.4
MC-A	1.87	108.8	11.3
MC-B	1.12	74.6	2.1
MC-B	2.41	138	10.6
MC-C	1.43	98.1	2.5
MC-C	2.68	179	23.1

^aMC, microchannel.

^bCV, coefficient of variation.

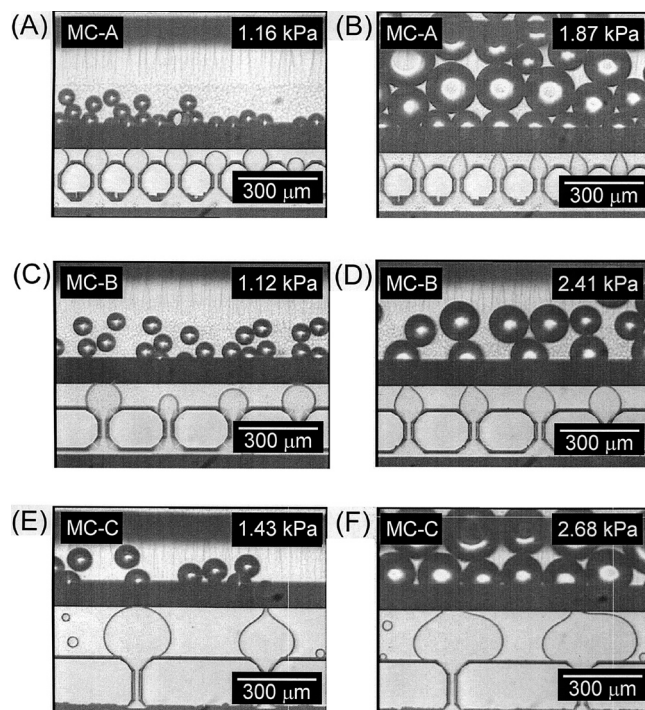


FIG. 2. Photomicrographs of MC emulsification process using three MC plates at low and high applied pressures. For abbreviation see Figure 1.

could be prepared using MC-C. It may be possible to prepare larger droplet emulsions using longer and deeper MC. However, it was difficult to fabricate an MC deeper than 16 μm and a terrace longer than 240 μm by the wet-etching process due to photoresist coating process limitations. Different etching processes, such as reactive-ion etching, may enable the fabrication of larger and deeper MC.

As shown in Figure 2, low applied pressures resulted in monodispersed emulsions, and high applied pressures in polydispersed emulsions. Figure 3 shows the effect of the applied pressure on the droplet diameter distribution for each

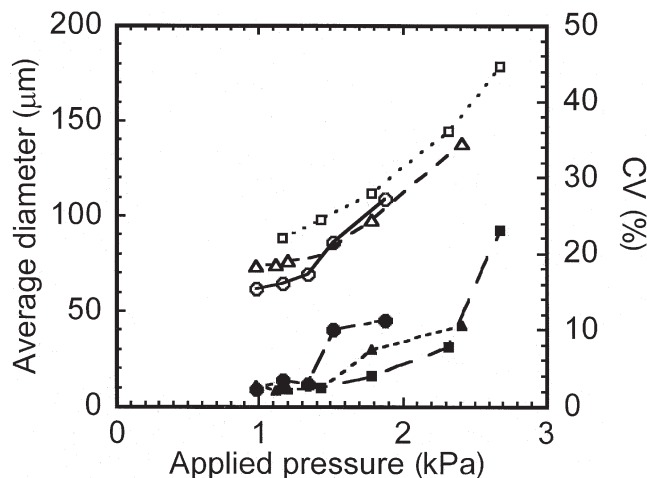


FIG. 3. Effect of applied pressure on the droplet diameter distribution using different MC plates. Average droplet diameter (μm), coefficient of variation (CV: %): MC-A (○,●); MC-B (△,▲); MC-C (□,■). For other abbreviation see Figure 1.

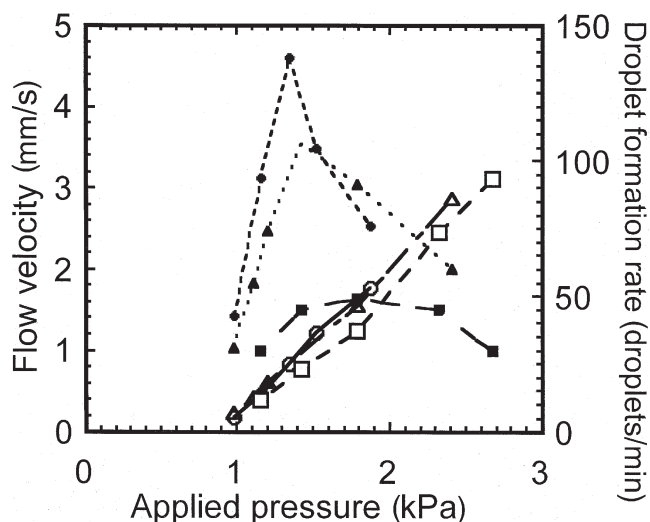


FIG. 4. Effect of applied pressure on productivity, expressed as flow velocity (mm/s), rate of droplet formation (droplets/min): MC-A (○,●); MC-B (△,▲); MC-C (□,■).

MC plate. Figure 4 shows the effect of the applied pressure on the flow velocity of the dispersed phase and the droplet formation rate of emulsions for each MC plate. We measured the number of droplets formed from each MC per minute.

The breakthrough pressure was 0.98 to 1.16 kPa for each MC plate, independent of terrace length. Breakthrough pressure corresponds to the Laplace pressure between the oil phase and water phase in an MC as shown in the following equation (16):

$$P_{bt} = \frac{4\gamma \cos\theta}{d} \quad [2]$$

where P_{bt} is the breakthrough pressure, γ is the interfacial tension, θ is the interface contact angle with the wall of the channel, and d is the channel diameter. Equation 2 means that breakthrough pressure depends on the MC width and depth and is independent of the terrace length, which is consistent with the experimental results.

In the pressure range from 0.98 to 1.34 kPa for MC-A and 0.98 to 1.43 kPa for MC-B, the applied pressure did not greatly affect the droplet diameter (Fig. 3). The CV were 2 to 3%, and monodispersed emulsions were prepared in these pressure ranges. In MC emulsification, droplets are formed by interfacial tension, which transforms the distorted dispersed oil phase on the terrace into spherical droplets (15). In these pressure ranges, the interfacial tension is dominant compared with the inertial force and the drag force of the continuous phase. The dispersed phase can thus be detached from the terrace at intervals. This dominant interfacial tension leads to monodispersed droplet formation even though the droplet formation rate increases with the applied pressure.

Over a certain pressure, the droplet diameter increases with increasing applied pressure. This pressure is critical for droplet formation by interfacial tension. Above the critical pressure, the interfacial tension force is not strong compared with the other forces. The droplet diameter is determined by the balance between the interfacial tension, the inertial force, and the

drag force of the continuous phase. At these pressure ranges, the emulsion droplets existing near the exit of MC affect the droplet formation, which leads to formation of a polydispersed emulsion. When a pressure exceeding 3 kPa was applied, the oil phase flowed out continuously from the channels. The pressure range resulting in a constant droplet diameter shown in this study was narrower than that for the 5- to 30- μm droplet emulsion (16). Interfacial tension, which is the shearing force for MC emulsification, dominates at smaller scales (15). This means that droplet formation caused by interfacial tension is effective for forming smaller emulsion droplets.

The flow velocity of the dispersed phase through the MC was proportional to the applied pressure (Fig. 4). This represents the pressure drop caused by the viscous force in laminar flow. The droplet formation rate increased at the pressure range of constant droplet diameter, and decreased over the critical applied pressures. This means that droplet formation behavior changed over the critical applied pressure.

For MC-C, the droplet diameter increased with increasing applied pressure because the shearing interfacial tension was not significant. Even though shearing interfacial tension was not a dominant force, a monodispersed emulsion was prepared at a low pressure range. The droplet diameter was determined by the balance between the interfacial tension, the inertial force, and the drag force of the continuous phase. At high pressure ranges, the emulsion droplets existing near the exit of the MC affected the droplet formation, which led to formation of a polydispersed emulsion. The experimental result shows that it may be possible to prepare an emulsion with droplets as large as 100 μm , but the pressure range for constant droplet diameter is narrow. Therefore, it may be difficult to prepare monodispersed emulsions with droplets exceeding 100 μm in diameter because interfacial tension is not dominant on such a large scale.

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