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Volume change of microcapsules induced by solvent exchange

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We have measured volume change of microcapsules composed of dioctylphthalate inner core and polyethyleneglycol-grafted poly(ureaurethane) (PUU) wall membrane induced by solvent exchange in dispersing medium from water to ethanol. The time course of the process consisted of a lag phase, a swelling phase and a shrinking phase. The temperature dependence of the duration of the lag phase t_l was roughly described by the Arrhenius plot, and the slope for the logarithm of the time constant vs. the reciprocal of the absolute temperature was coincident with that of the viscosity coefficient of ethanol, suggesting that the permeation rate of ethanol into the core mainly determines the duration of the lag phase.
Key words: microcapsule, solvent exchange, swelling, lag phase, Arrhenius plot

1. INTRODUCTION

The immunoassays, analytic separations, and proteomics have become more and more important in biotechnology [1], and microcapsules are one of familiar devises in those systems. They are colloidal entities with a semi-permeable membrane, through which functional agents can be transported at controlled release rate [2]. If the inner core of microcapsules contains impermeable polymers and permeable solvent, the microcapsules are useful as controlled microreactors [3], since the reactivity of the polymers and the structure of the assembly are changed easily by solvent exchange and controlled by varying the size of the confined spacing. Indeed, switching of the direction of helix of polysilane in microcapsules has been reported recently [4]. Most of the wall membranes of microcapsules consist of semi-permeable polymer network gel. The dynamics of the characteristic properties of microcapsules is, however, often much different from those of bulk gels, when the thickness of the wall membrane is thin enough to show approximately two-dimensional elasticity and the core plays a role of a large reservoir [5]. Also, the transport properties of the microcapsule membrane from the inner core to the dispersing fluid through the wall membrane are much different depending on the size distributions of microcapsules [6-8]. It is expected that the mechanisms inducing relaxation phenomena of microcapsules including material transport could be varied depending on the interactions among the membrane and the inner and outer solvents (or solutions) in the process of solvent exchange. The first step to understand the mechanism is to observe the time course of microcapsule volume when the inner and outer materials are simple fluids.

In this study we report a unique response of microcapsules consisting of dioctylphthalate core and polyethyleneglycol-grafted polyureaurethane wall membrane (PUUMC) to solvent exchange in the dispersing medium from water to ethanol. PUUMC has been conventionally dispersed with the aid of protective colloid such as polyvinylalchohol [6]. The advantage to use the present polyethyleneglycol-grafted PUUMCs is that they can be dispersed in water as well as polar solvents, which enables us to use various pairs of inner and outer solvents in application [9].

2. EXPERIMENT

2.1 Preparation of Microcapsule

An adduct of trimethylolpropane carbamate with xylylene diisocyanate (TCXDI) and polyethylene glycol monomethyl ether (PEGME) was obtained as follows [10]. 35 g of PEGME (average molecular weight: 5,000, Polyscience) dried in vacuum overnight was dissolved in 35 cm^3 of dried acetonitrile (Kanto Chemical Co.) adding 4 g of molecular sieves 4A. After the mixture had been stirred for 3 hrs under dry nitrogen, 40 g of Takenate D110N (70 ~ 80% ethyl acetate solution of TCXDI, Mitsui Takeda Chemical Co.) and 0.16 cm^3 of Tin(II) 2-ethylhexanoate (Wako) were added to the mixture. The resultant mixture was stirred at room temperature for 1 hr and at 50 °C for 3 hrs in order to complete the reaction.

Then 0.5 g of the mixture obtained and 0.5 g of Takenate D110N were added to 1.5 g of ethyl acetate (Wako Pure Chemical Co.) with 1.85 g of di-2-

ethylhexyl phthalate (DOP, Wako Pure Chemical Co.). After stirring on ice, we added 13.5 g of pure water and immersed the solution vigorously at 1,000 rpm for 2 min by using an emulsifier (Excel Auto, Nihon Seiki Co.) at room temperature. The emulsion was further stirred at room temperature for 4 hrs to complete microencapsulation. It was confirmed that acetonitrile and ethyl acetate were evaporated throughout in this process to make a final microcapsule suspension. Microscopic image of the microcapsules is shown in Fig. 1. The cross-sectional area of the microcapsules is distributed in the range from 20 μm^2 to 400 μm^2.

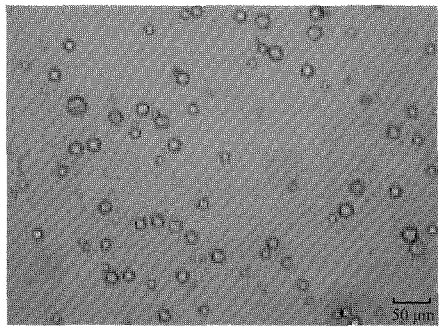

Figure 1. Optical micrographs of microcapsules observed at room temperature.

2.2 Measurements

We used an inverted microscope equipped with a temperature-controlled stage, on which a Pyrex Petri dish with a diameter of 10 cm was placed. A stainless steel mesh filter with a mesh size more than 100 times of the microcapsule diameter, was settled in the Petri dish for immobilizing microcapsules in size measurements. 10 ml of pure ethanol or ethanol-DOP mixture with different compositions was poured in the Petri dish and equilibrated at desired temperatures. Then 10 μl of the microcapsule suspension was dropped in ethanol in the Petri dish. Microcapsules trapped in each mesh of the stainless steel filter were observed without being disturbed by a convective flow caused by a small temperature gradient and a slow evaporation of dispersing ethanol. The microscopic image was taken into a video camera and stored in a computer. The cross-sectional area of each microcapsule observed at each time and each temperature was measured from the recorded image on a monitor by using software (Image Pro Plus, Media Cybernetics). The temperature of the sample was measured with a calibrated thermistor.

3. RESULTS

Figure 2 shows typical time courses of cross-sectional area S (converted into volume $V=S^{3/2}$) of microcapsules dispersed in ethanol-DOP mixture with various ethanol compositions. At high concentration of ethanol, S has a maximum and the time for the maximum decreases with increasing ethanol concentration. The shoulder observed for 70% ethanol in the swelling process could be attributed to the inhomogeneous network structure of PUU microcapsule membranes resulted from phase separation of DOP and PUU. Figure 3 shows a typical time course of reduced cross-sectional area $(S-S_0)/(S_p-S_0)$ of microcapsules dispersed in pure ethanol observed at 50.2 °C.

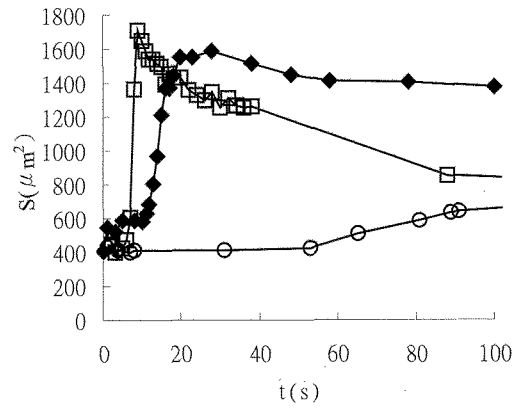

Figure 2. Time courses of cross-sectional area of microcapsules dispersed in ethanol-DOP mixture with various ethanol compositions of ○: 30%,◆: 70%,□: 100% at 25°C.

Here, S_0 and S_p are the cross-sectional areas at the initial state and at the time for the maximum of S, respectively. The time course is clearly divided into three phases; lag phase, swelling phase and shrinking phase. The time courses observed at different temperatures are essentially the same, although a shoulder is observed in the shrinking phase and the duration of each phase is smaller at higher temperatures (not shown).

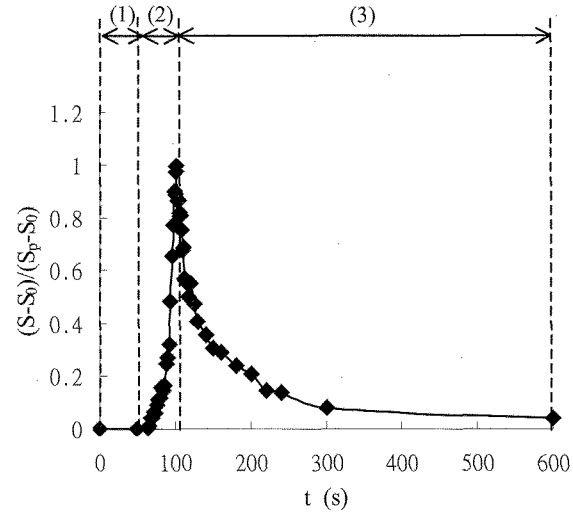

Figure 3. Typical time course of reduced cross-sectional area of microcapsules dispersed in pure ethanol observed at 50.2 °C and the definition of (1) lag phase, (2) swelling phase and (3) shrinking phase.

Figure 4 shows the duration of lag phase t_l observed at temperatures of 13.6 °C and 47.7 °C for microcapsules with different initial sizes S_0. t_l slightly increases with increasing S_0. The value of t_l extrapolated to $S_0=0$ is finite and depends on temperature. Figure 5 shows the logarithm of t_l at constant $S_0=200$ μm^2 as a function of reciprocal of absolute temperature. The relationship is expressed as a line except for the point observed at the lowest temperature of 10.9 °C. We note that no change of S was observed below 10 °C for more than 1 hr; the microcapsules do not change their volume below a

critical temperature around 10 °C, suggesting that the minimum energy required for swelling is around $283k$ (J), where k is the Boltzmann constant. In Fig. 5, the logarithm of viscosity coefficient of pure ethanol is also given for a comparison. The slope almost coincides with that of t_l.

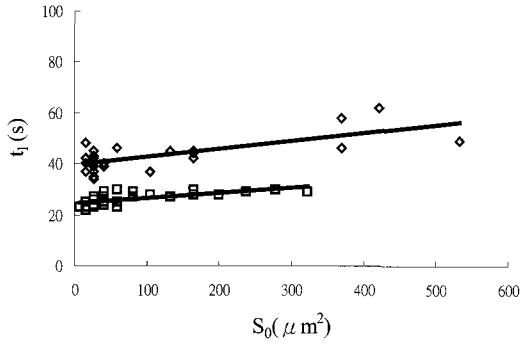

Figure 4. Durations of lag phase t_l at temperatures of 13.6 °C (◇) and 47.7 °C (□) for microcapsules with different initial sizes S_0.

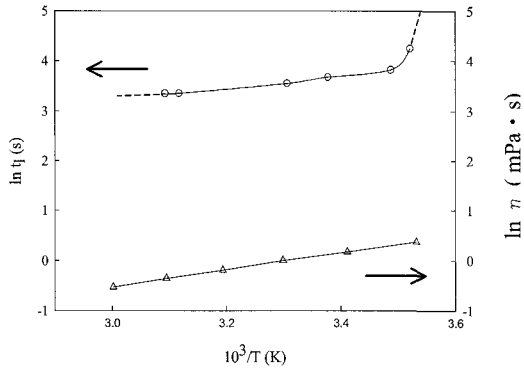

Figure 5. Logarithms of t_l and viscosity coefficient η of ethanol as a function of reciprocal of absolute temperature.

4. DISCUSSION

The molar volumes of the core DOP and the outer dispersing ethanol are 401.3 ml/mol and 58.0 ml/mol, respectively. They correspond to diameters of ca. 1.1 nm and 0.6 nm, respectively. On the other hand, the distance between cross-linking points in microcapsule membranes are roughly estimated as the diameter of the trifunctional TCXDI 1.1 nm at the initial state from the density of PUU membrane 1.255 g/cm^3 [11], that of DOP 0.9861 g/cm^3, the molar mass of TCXDI 690 and the volume ratio of DOP in the membrane 0.25 [12]. Here we used the values for PUU membrane with no PEG graft. This estimate indicates that the pore size of the microcapsule membrane is close to the size of DOP and much larger than the size of ethanol at the initial state.

We can speculate the mechanism of change of membrane structure induced by the solvent exchange as follows: Dispersing ethanol permeates through the microcapsule membrane and the membrane swells with ethanol (lag phase). After ethanol reaches the core and the pore size increases up to the diameter of DOP (swelling phase), DOP permeates through the membrane into the dispersing fluid, and the size of microcapsules reduces to a new shrinking phase that determined by the equilibrium between the membrane and ethanol/DOP mixture, as shown in Fig. 3. The linear dependence of duration of the lag phase t_l on the initial size S_0 as shown in Fig. 4 suggests that the lag phase consists of S_0-independent main part and S_0-dependent additional part. At this stage we cannot identify the source of each part. In Fig. 5, the behavior of solvent exchange was well described by the Arrhenius plot in the temperature range between 13 °C and 50 °C. The similar slopes of $\ln t_l$ and $\ln \eta$ against the reciprocal of temperature suggest that the permeation rate of ethanol through the membrane into the core mainly determines the duration of the lag phase. The activation energy 1.54×10^3 K obtained by the slope could be regarded as the energy for ethanol permeation through the pores of the microcapsule membranes.

5.CONCLUSION

The time course of the size of PUU microcapsules in the process of solvent exchange from DOP to ethanol was divided into three phases: a lag phase, a swelling phase and a shrinking phase. From the temperature dependence of the duration of the lag phase, the activation energy for DOP permeation through the pores of the microcapsule membranes was estimated.

ACKNOWLEDGEMENTS

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REFERENCES

[1] Paper Symposium Miniaturization 2003. Ed. F. Foret, P. J. Landers, *Electrophoresis*, 24, 3521-3834 (2003).
[2] T. Kondo, "*In Surface and Colloid Science*" ; E. Matijevic, Ed.; Plenum: New York, 1978; Vol. 10, pp 1-43.
[3] W. Ehrfeld, V. Hessel,; H. Lowe, "*Microreactors: New Technology for Modern Chemistry*" , Wiley-VCH: Weinheim, 2000.
[4] K. Terao, Y. Mori, T. Dobashi, T. Sato, A. Teramoto, M. Fujiki, *Langmuir*, 2004, 20, 306-308.
[5] T. Narita, T. Yamamoto, D. Suzuki, T. Dobashi, *Langmuir*, 2003, 19, 4051-4054.
[6] T.Sato, S. Shibako, T. Yamamoto, K. Ichikawa, T. Dobashi, *J. Membr. Sci.*, 2003, 213, 25-31.
[7] C.P. Chang, T. Yamamoto, M. Kimura, T. Sato, K. Ichikawa, T. Dobashi, *J. Controlled Release*, 86, 207-211 (2003).
[8] T. Yamamoto, T. Dobashi, M. Kimura, C.P. Chang, *Colloids and Surfaces B: Biointerfaces*, 25, 305-311 (2002).
[9] K. Terao, A. Ohsawa, Y. Mori, T. Narita, K. Ichikawa and T. Dobashi, *Colloids and Surfaces B: Biointerfaces*, 37, 129-132 (2004).
[10] Y. Wakata, K. Ichikawa, (Fuji Film Co.). *Jpn. Kokai Tokkyo Koho* 10 114,153, May 6, 1998. (b) U. S. Patent 5,916,680, June 29, 1999.
[11] T. Dobashi, H. Ishimaru, A. Sakanishi, K. Ichikawa, *Langmuir*, 2003, 19, 3071-3073.
[12] T. Dobashi, T. Furukawa, T. Narita, K. Ichikawa, *Langmuir*, 2002, 18, 6031-6034.

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