CONTROLLED RELEASE OF STYRENE-DIVINYLBENZENE COPOLYMER MICROCAPSULES BY PHASE TRANSFORMATION OF ENCAPSULATED STEARIC ACID

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Functional microcapsules encapsulating stearic acid were prepared by *in situ* polymerization of styrene and divinylbenzene. Morphology and release rate were investigated by changing preparation conditions.

Total monomer concentration was found to be an important determinant of morphology while being a less dominant factor in average diameter of microcapsule. The sustained release of stearic acid was controlled by pore diffusion through porous microcapsule membrane. The permeability was dependent upon total monomer concentration and average diameter of microcapsule. The permeability coefficient increased with an increase of average diameter of microcapsules and decreased with increasing total monomer concentration.

The sustained release rate from microcapsules to ambient solution abruptly changed in the vicinity of melting point of stearic acid. This may indicate that functional microcapsules exhibiting temperature-dependent permeability can be prepared.

Introduction

Microencapsulation is a unique technique to enclose active agents in porous polymeric membrane, and has been extensively studied concerning the elongation of sustained release of core materials^{8, 9, 13, 14}), the protection of alterable compounds^{6, 12}), the immobilization of microorganisms^{5, 11}) and the separation^{15, 16, 17}). Especially, in the field related to sustained release, researches such as the amphiphile corking and the polyelectrolyte surface-coating have been worthy of remark for the application of a specific function to microcapsules^{7, 10}). Nevertheless, the optimization of such release system has not been carried out and has been left as future work.

Sustained release rate has been known to be significantly influenced by membrane thickness of microcapsule, polymeric materials for microcapsule membrane, which were strongly dependent on preparation conditions of microcapsules³). Thus, it seems to be one of the most important subjects to clarify the effect of preparation condition in order to bring into full potential of functional microcapsules.

In the present work, functional microcapsules exhibiting temperature-dependent release of active agent were prepared by *in situ* polymerization of styrene and divinylbenzene. The first object of this investigation is to

prepare microcapsules enclosing stearic acid as core material. Such microcapsules would be expected to show specific permeation characteristics in the vicinity of the melting point of stearic acid. The second aim is, furthermore, to clarify the effect of preparation conditions on sustained release rate.

1. Experimental

1.1 Materials

Styrene and divinylbenzene were used as monomer and crosslinker, respectively, which were purified according to the same procedure mentioned previously¹⁶). Benzoyl peroxide (hereafter called BPO), an initiator of radical polymerization, was prepared as follows. A given amount of unpurified BPO was dissolved into chloroform. Chloroform solution containing BPO was poured into a large amount of methanol in ice bath. The recrystallized BPO was filtrated and dried *in vacuo* at room temperature.

Stearic acid ($T_m = 343$ K) as core material was of reagent grade.

Distilled water was used as continuous phase. Arabic Gum, which works as stabilizer of dispersed droplets and microcapsules, was purchased from Wako Pure Chemical Industries, Ltd. and used without further purification.

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Table 1. Preparation conditions of microcapsules

	A_0 [mol·dm ⁻³]	ϕ [-]	W [-]	N [s ⁻¹]
MC-1	2.0	0.1	0.2	3.33
MC-2	4.0	0.1	0.2	3.33
MC-3	4.0	0.1	0.2	6.67
MC-4	4.0	0.1	0.2	10.0
MC-5	6.0	0.1	0.2	3.33

Fig. 1 Effect of total monomer concentration on average diameter of microcapsules

(a) Surface morphology

(b) Cross section

Fig. 2 SEM observation of microcapsules under $A_0 = 2.0$ mol·dm⁻³ (MC-1)

1.2 Preparation of St-DVB copolymer microcapsules containing stearic acid as core material

The experimental apparatus for the preparation of St-DVB copolymer microcapsules was the same as described in the previous paper¹⁶.

The experimental procedure is shown below. Prescribed amounts of St, DVB and BPO were first dissolved in stearic acid at 348 K. This solution was then

(a) Surface morphology

(b) Cross section

Fig. 3 SEM observation of microcapsules under $A_0 = 4.0$ mol·dm⁻³ (MC-2)

added into the aqueous solution dissolving Arabic Gum, and homogenized at 21.7 s⁻¹ for 10 s to obtain O/W emulsion. After that, O/W emulsion was quickly replaced to the reactor and was stirred at 3.33 s⁻¹. The polymerization experiments were conducted under nitrogen atmosphere at 353 K and the copolymerization of St and DVB was completed within 36 ks for each run.

Microcapsules having larger diameters than those from the above mentioned method were also prepared to investigate the effect of microcapsule size on the release properties. In this case, they were prepared without premixing by a homogenizer.

Preparation conditions are shown in **Table 1**. The regular conditions for the preparation of microcapsules were the following.

- The concentration of BPO in dispersed droplets, I_0 , was kept at 0.20 mol·dm⁻³.
- The holdup of dispersed droplets was 0.10.
- DVB/St weight ratio was 0.20.

1.3 Sustained release rate measurement of encapsulated stearic acid in ethanol

The agitated vessel used in the experiments was a 0.50 dm³ separable flask with an agitator having two baffles. The temperature of ambient solution was varied from 293 K to 348 K.

A weighted quantity of St-DVB copolymer microcapsules containing stearic acid was dispersed in ethanol at a given temperature and revolution rate. Samples were

(a) Surface morphology

(b) Cross section

Fig. 4 SEM observation of microcapsules under $A_0 = 6.0$ mol·dm⁻³ (MC-5)

withdrawn at appropriate intervals for analysis. The specific concentrations of stearic acid released into ethanol were determined from the concentration of released BPO, which was easily detected by spectroscopy.

1.4 Dissolution rate measurement of stearic acid into ethanol

The dissolution process of stearic acid may play an important role in the release of stearic acid through the microcapsule membrane. Thus, the dissolution rate of stearic acid into ethanol should be measured. The following experiments were carried out from 298 K to 333 K. Molten stearic acid was poured into a cylindrical holder of 25.4 mm in inner diameter and 27.2 mm in depth. After stearic acid was solidified, the holder was immersed in 0.50 dm³ ethanol in a separable flask at a given temperature and revolution rate. The concentration of stearic acid dissolving into ethanol across one circular surface of the holder was measured by spectroscopy.

1.5 Characterization of microcapsules

Average diameter and diameter distribution of the prepared microcapsules were determined by the microphotographic method mentioned previously¹⁶. The average diameter of microcapsules was the arithmetic mean.

The morphologies of cross sections and internal structures were observed using SEM (JEOL JSM-840) at the intensity of 15.0 kV under various magnifications.

(a) Surface morphology

(b) Cross section

Fig. 5 SEM observation of microcapsules, MC-3

2. Results and Discussion

2.1 Morphology of St-DVB copolymer microcapsule

1) Effect of total monomer concentration on average diameter of microcapsule **Figure 1** illustrates the effect of total monomer concentration on the average diameter and diameter distribution of microcapsules. Φ in this figure represents the average diameter and the standard deviation for diameter distribution. As can be seen in Fig. 1, total monomer concentration was found to be a minor parameter to determine microcapsule diameter. Average diameter of microcapsules slightly decreased with an increase in total monomer concentration. This suggests that microcapsule diameter may be altered by change of physical property of the dispersed liquid, and that polymer clusters, which have a certain degree of polymerization, induce the phase separation and subsequently form the shell of microcapsules covering the surface of dispersed droplets in an initial polymerization stage².

2) Scanning electron microscopic observation of microcapsule

• Effect of total monomer concentration

SEM observation of microcapsules was carried out to investigate the surface morphology and the internal structure.

SEM photographs are shown in **Figs. 2, 3 and 4** which represent (a) the surface morphologies and (b) the cross section of MC-1, 2 and 5, respectively.

From these photographs, diameters of microcapsules

(a) Surface morphology

(b) Cross section

Fig. 6 SEM observation of microcapsules, MC-4

are substantially between 40 and 100 μm . In the case of MC-1, many wrinkles were observed on the surface of microcapsules. For the microcapsules prepared under the condition of $A_0 = 4.0 \text{ mol}\cdot\text{dm}^{-3}$ (MC-2), a few crater like wrinkles were observed (Fig. 3 (a)). No wrinkle was observed for MC-5 as shown in Figs. 4 (a).

The results above mentioned permit the following explanation. Stearic acid is transformed into solid state at room temperature from liquid state during polymerization. This phase transformation of stearic acid would be accompanied with the volume shrinkage and be considered to be a trigger for wrinkling. The membrane thickness of microcapsule is expected to increase with increasing total monomer concentration¹⁶⁾. Hence the wrinkles were more remarkable for microcapsules prepared at lower concentrations.

From the observation of the cross section of microcapsules, it is obvious that a lot of 10 μm microspheres were produced for MC-1 and MC-2. These microspheres would be formed by dispersion polymerization in the core solution with the formation of microcapsule membrane¹⁶⁾.

• Effect of average diameter

Figures 5 and 6 are SEM photographs of MC-3 and MC-4, respectively. As shown in these figures, many wrinkles are recognized on the surface of microcapsules. Many minute microspheres are also observed in the microcapsules. The degree of wrinkling was increased with

Fig. 7 Time course of C_B in ethanol with MC-2

Fig. 8 Relation between $\ln \Theta$ and duration time

increasing average diameter of microcapsules. This change of wrinkling is probably due that the ratio of average diameter to membrane thickness of microcapsules would be varied.

2.2 Permeation of stearic acid from St-DVB copolymer microcapsules

1) Effects of total monomer concentration and ambient temperature The experiments were carried out to investigate the temperature-dependent release of stearic acid enclosed in microcapsules under various total monomer concentrations.

Figure 7 shows the time course of C_B at 313 K and 343 K. It is obvious from Fig. 7 that the equilibrium at a higher ambient temperature 343 K was attained in a shorter period. This drastic change of release rate is owed to the phase transformation of stearic acid at about 343 K. Generally, the following equation derived by taking mass balance for stearic acid is used to quantitatively investigate the release rate⁴⁾.

$$\ln \Theta = -k_p \cdot (6/(\varepsilon \cdot d_p)) \cdot t \quad (1)$$

where Θ represents dimensionless specific concentration of stearic acid in ethanol and can be shown as follows.

$$\Theta = (C_{B,e} - C_B) / (C_{B,e} - C_{B,0}) \quad (2)$$

Figure 8 illustrates the relation between Θ and duration time for a series of experiments at $A_0 = 4.0 \text{ mol}\cdot\text{dm}^{-3}$.

Fig. 9 Effect of total monomer concentration on initial permeability coefficient

Fig. 10 Arrhenius plot of initial permeability coefficient

The experimental values of Θ obviously lie on a straight line for each ambient temperature in a short duration time. The initial permeability coefficient was determined from the slope of straight line using the least squares method.

Figure 9 represents the effect of total monomer concentration on the initial permeability coefficient. Permeability coefficient significantly decreased with increasing total monomer concentration. The dependency of release rate on total monomer concentration at 313 K was the same as that at 348 K, although melting point of stearic acid lies between 313 K and 348 K. Decrease of k_p with total monomer concentration is probably due to the change of microcapsule membrane thickness. The larger dependency on total monomer concentration was observed than that obtained with the extraction microcapsules¹⁶.

Figure 10 shows the influence of ambient temperature on permeability coefficient as an Arrhenius plot above 323 K. This figure indicates a discontinuity of k_p value at about 343 K, which corresponds to the melting point of stearic acid. The activation energy calculated from the slope of two straight lines was found to be 25.4 kJ·mol⁻¹. So, it is suggested that the rate-determining step is probably the pore diffusion of stearic acid through porous microcapsule membrane. Mass transfer coefficients of solid stearic acid

Table 2. Mass transfer coefficient of stearic acid in ethanol

T [K]	$k_s \times 10^5$ [m·s ⁻¹]
323	3.46
308	2.33
293	0.04

Fig. 11 Effect of average diameter of microcapsules on initial permeability coefficient

into the ambient solution were measured and the results calculated by using Eq. (3) are listed in **Table 2**.

$$C_s / C_{s,0} = (k_s \cdot S / V) \cdot t \quad (3)$$

The initial permeability coefficients in **Fig. 11** are much smaller than mass transfer coefficients of stearic acid in Table 2. This also indicates that pore diffusion through porous microcapsule membrane is dominant process in release of stearic acid from microcapsules.

2) Effect of average diameter The initial permeability coefficients calculated from Eqs. (1) and (2) are represented in Fig. 11. It is obvious from the figure that the initial permeability coefficients increase with increasing average diameter of microcapsules. Many macropores having diameters of several μm could be detected on the surface of MC-4 by scanning electron microscopic observation. Macropores are likely to result from stress concentration due to buckling at relatively large micropores which were formed with phase separated polymer clusters.

Conclusion

Styrene-divinylbenzene copolymer microcapsules enclosing stearic acid as core material were prepared by *in situ* polymerization to offer a new microcapsule showing specific temperature-dependent release of active agent. Morphological and release rate changes were investigated by varying the relevant parameters to draw the following results.

1) Spherical microcapsules enclosing stearic acid as core material were successfully prepared by *in situ* polymerization. More wrinkles were observed on the surface of microcapsules prepared under lower concentrations of total

monomer. However, no wrinkles were observed on the surface of microcapsules at $A_0 = 6.0 \text{ mol} \cdot \text{dm}^{-3}$.

2) A lot of minute microspheres were produced by dispersion polymerization in microcapsules under low concentrations of total monomer.

3) The increase in total monomer concentration leads to the decrease in average diameter of microcapsules.

4) The rate-determining step was found to be pore diffusion of dissolved stearic acid through porous microcapsule membrane. The permeability coefficients decreased with increasing total monomer concentration.

5) Release rate in the vicinity of melting point of stearic acid showed discontinuous change, indicating that an active agent dissolved in stearic acid in the microcapsule would be released abruptly near that temperature.

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Nomenclature

A_0	= total monomer concentration in dispersed droplet	$[\text{mol} \cdot \text{dm}^{-3}]$
C_B	= specific concentration of stearic acid in ambient solution at $t = t$	$[\text{mol} \cdot \text{dm}^{-3}]$
$C_{B,0}$	= specific concentration of stearic acid in ambient solution at $t = 0$	$[\text{mol} \cdot \text{dm}^{-3}]$
$C_{B,e}$	= specific concentration of stearic acid in ambient solution at $t = \infty$	$[\text{mol} \cdot \text{dm}^{-3}]$
C_s	= concentration of stearic acid in ethanol	$[\text{mol} \cdot \text{dm}^{-3}]$
$C_{s,e}$	= saturated concentration of stearic acid in ethanol	$[\text{mol} \cdot \text{dm}^{-3}]$
d_p	= average diameter of microcapsule	$[\text{m}]$
I_0	= concentration of initiator in dispersed droplet	$[\text{mol} \cdot \text{dm}^{-3}]$
k_p	= initial permeability coefficient	$[\text{m} \cdot \text{s}^{-1}]$
k_s	= mass transfer coefficient in ethanol	$[\text{m} \cdot \text{s}^{-1}]$
L	= membrane thickness of microcapsule	$[\text{m}]$
N	= revolution rate in polymerization	$[\text{s}^{-1}]$
S	= interfacial area of stearic acid fixed in the holder	$[\text{m}^2]$
T	= temperature of ambient solution	$[\text{K}]$
T_m	= melting point of stearic acid	$[\text{K}]$

t	= duration time	$[\text{s}]$
V	= volume of ethanol	$[\text{m}^3]$
W	= DVB/St weight ratio	$[-]$
Θ	= dimensionless specific concentration	$[-]$
ε	= holdup of stearic acid in dispersed droplet	$[-]$
σ	= surface tension of solution	$[\text{N} \cdot \text{m}^{-1}]$
ϕ	= holdup of dispersed droplets	$[-]$

Literature Cited

- 1) Barrett, K.E.J.: Dispersion Polymerization in Organic Media, John Wiley & Sons, London (1975)
- 2) Hatate, Y., H. Hamada, H. Nagata and T. Imafuku: *Kagaku Kogaku*, **51**, 519-522 (1987)
- 3) Hatate, Y., H. Hamada, H. Nagata, T. Sakaki, K. Kasamatsu, A. Ikari and F. Nakashio: *Reports of the Asahi Glass Foundation for Industrial Technology*, **52**, 247-253 (1988)
- 4) Hatate, Y., H. Nagata, K. Kasamatsu, A. Ikari and F. Nakashio: Preprints for Hiroshima Meeting of the Society of Chemical Engineers, Japan, 1988, B02
- 5) Iso, M., T. Shirahase, S. Hanamura, S. Urushiyama and S. Omi: *J. Microencapsulation*, **6**, 2, 165-176 (1989)
- 6) Kinugasa, N.: *Funtai to Kogyo*, **22**, 8, 29-39 (1990)
- 7) Kokufuta, E., N. Shimizu and I. Nakamura: *Biotech. Bioeng.*, **32**, 289-294 (1988)
- 8) Longo, W.E., H. Iwata, T.A. Lindheimer and E.P. Goldberg: *J. Pharm. Sci.*, **71**, 12, 1323-1328 (1982)
- 9) Ohtsu, T., Y. Uemura, T. Sakaguchi, Y. Kawano and Y. Hatate: Preprints for the 58th Annual Meeting of the Society of Chemical Engineers, Japan, 1993, E205
- 10) Okahata, Y., H.-J. Lim, G. Nakamura and S. Hachiya: *J. Am. Chem. Soc.*, **105**, 15, 4855-4859 (1983)
- 11) Kondo, T. and M. Koishi: "Shinpan Maikurokapuseru-Sono Seihō-Seishitsu-Oyo", 2nd Ed., Sankyo Shuppan Co., Tokyo (1989)
- 12) O'shea, G.M., M.F.A. Goosen and A.M. Sun: *Biochim. Biophys. Acta*, **804**, 133-136 (1984)
- 13) Tsai, M.F. and M. Levy: *J. Polym. Sci., Polym. Chem. Ed.*, **32**, 2523-2531 (1984)
- 14) Wada, R., S.-H. Hyon, Y. Kusanoi and Y. Ikada: *Polymer Preprints, Japan*, **38**, 11, 4048-4049 (1989)
- 15) Watarai, H. and S. Hatakeyama: *Analy. Sci.*, **7**, 487-488 (1991)
- 16) Yoshizawa, H., Y. Uemura, Y. Kawano and Y. Hatate: *J. Chem. Eng. Japan*, **26**, 2, 198-204 (1993)
- 17) Yoshizawa, H., Y. Uemura, Y. Kawano and Y. Hatate: Preprints for the 58th Annual Meeting of the Society of Chemical Engineers, Japan, 1993, E206