PERMEABILITY CONTROL OF ACTIVE AGENT FROM POLYMERIC MICROCAPSULES BY COATING OF GELATIN/GUM ARABIC MEMBRANE

HIDEKAZU YOSHIZAWA, YOSHIMITSU UEMURA, KAZUYA IJICHI, TADASHI HANO**, YOSHINOBU KAWANO*** AND YASUO HATATE

Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Kagoshima University, Kagoshima 890

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Introduction

A polymeric microcapsule is a small vessel in which an extremely active agent is encapsulated as core material, and is endowed with various functions. Sustained release is one of the consequent functions, and has been paid much attention in the field of drug delivery systems (Longo *et al.*, 1982; Tsai and Levy, 1984; Wada *et al.*, 1989).

Permeability of the active agent from the polymeric microcapsules is an important factor, and it is well known to be affected by the polymeric membrane characteristics such as membrane thickness and porosity (Hatate *et al.*, 1988; Yoshizawa *et al.*, 1993). The coating method of microcapsules with polymeric membrane, seems to be convenient to control the permeability of microcapsules.

In the present study, we investigated permeability control by coating the surface of poly (styrene-co-divinylbenzene) microcapsules (henceforce designated as poly (St-co-DVB) microcapsules) with crosslinked gelatin/gum arabic membrane via complex coacervation.

1. Experimental

1.1 Preparation procedure of polymeric microcapsules

Poly (St-co-DVB) microcapsules encapsulating biphenyl were prepared by *in situ* polymerization according to a conventional procedure (Hatate *et al.*, 1994). St and DVB were used as a monomer and a crosslinker, respectively, and were distilled under reduced pressure in a nitrogen atmosphere. The purity of DVB was ca. 55 %. The core material used in this study was biphenyl, which was in solid state at room temperature, so the preparation of O/W emulsion was carried out at a temperature above T_m of biphenyl (T_m = 344 K). Preparation conditions are listed in **Table 1**. The polymerization temperature and the revolution rate in polymerization were 353 K and 3.33 s^{-1}, respectively.

A prescribed amount of microcapsules prepared under a monomer concentration of 4.0 mol·dm^{-3} by *in situ* polymerization was dispersed in the aqueous gelatin solution at 313 K. The gum arabic solution of the equi-volume was added into this solution. The revolution rate in this stage was 5.0 s^{-1}. The solution pH was adjusted to 4.0 by the addition of aqueous acetic acid solution where the complex coacervation of gelatin-gum arabic mixture was induced. The temperature of the coacervated solution dropped slowly from 348 K to 278 K. After attaining the desired temperature, a 30 wt% aqueous formamide solution of 1×10^{-3} dm^3 was added and the solution pH was adjusted to 9.0 with aqueous sodium hydroxide solution. Subsequently, moderate stirring was continued for 3.6 ks at 323 K.

1.2 Measurement of sustained release rate

A weighted quantity of microcapsules was dispersed in 1-butanol at a given temperature and revolution rate. The temperature of the ambient solution was changed from 303 K to 333 K. Samples were withdrawn at appropriate intervals for analysis. Concentrations of the released biphenyl were determined by spectroscopy.

1.3 Characterization of microcapsules

The average diameter of the prepared microcapsules was determined by the microphotographic method mentioned previously (Yoshizawa *et al.*, 1993). The average diameter of the microcapsules was the arithmetic mean.

The morphologies of the polymeric microcapsules were observed using SEM (JEOL JSM-840) at an intensity of 15.0 kV under various magnifications.

2. Results and Discussion

2.1 Microphotographic and SEM observations of polymeric microcapsules

Figure 1 shows a SEM photograph of poly (St-co-DVB) microcapsules via *in situ* polymerization under monomer concentration of 4.0 mol·dm^{-3}. The shape is

* Received on October 9, 1995. Correspondence concerning this article should be addressed to H. Yoshizawa.

** Department of Applied Chemistry, Faculty of Engineering, Oita University, Oita 870-11

*** Department of Materials Science, Faculty of Engineering, Miyazaki University, Miyazaki 889-21

Table 1. Preparation conditions of polymeric microcapsules

Poly (St-co-DVB) microcapsules via *in situ* polymerization					
MC No.	C_m[mol Dm^{-3}]	I_0[mol dm^{-3}]	ϕ[—]	W[–]	d_p[mm]
MC-1	4.0	0.2	0.1	0.2	42.6
MC-2	6.0	0.2	0.1	0.2	67.8

(St-co-DVB) polymer and Ge/AG duplicated membrane microcapsules							
MC No	C_m[mol dm^{-3}]	I_0[mol dm^{-3}]	ϕ [–]	W[–]	C_{AG}[wt%]	C_{Ge}[wt%]	d_p[μm]
MC-3	4.0	0.2	0.1	0.2	0.5	0.5	42.6

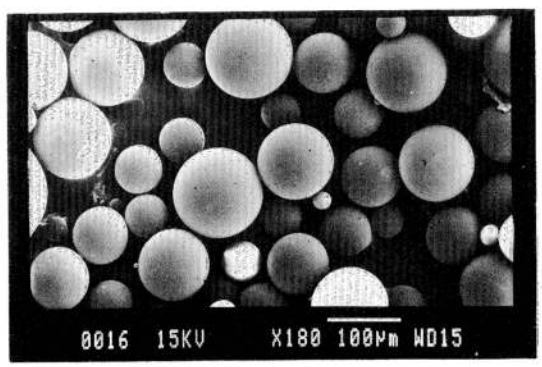

Fig. 1 SEM photograph of poly (St-co-DVB) microcapsules

shperical and no dent was observed. The average diameter of the microcapsules was found to be 42.6 μm.

Figure 2 represents optical photographs of crosslinked gelatin-gum arabic membrane coated poly (St-co-DVB) microcapsules. In the complex coacervation method used as a microencapsulation technique, induced coacervates are adsorbed on the surface of the core material to form a microcapsule membrane. As can be seen from Fig. 2, gelatin-gum arabic coacervates, not encapsulating poly (St-co-DVB) microcapsules, were also observed. This indicates that all of the gelatin-gum arabic coacervate was not used to cover the surface of the poly (St-co-DVB) microcapsules. However, it was clearly found from this figure that poly (St-co-DVB) microcapsules encapsulating biphenyl were covered with transparent thin crosslinked gelatin-gum arabic membranes.

2.2 Sustained release of biphenyl from polymeric microcapsules

The permeability coefficient for the biphenyl release from polymeric microcapsules was calculated from the following equation (Hatate *et al.*, 1994).

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

where Θ represents dimensionless concentration of biphenyl in 1-butanol and can be shown as follows.

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

Furthermore, ε in Eq. (1) is initial holdup of biphenyl in polymeric microcapsules, which is 0.52 for MC-1 and MC-3, and 0.20 for MC-2.

Figure 3 illustrates the dependency of the permeability coefficient on ambient solution temperature as an Arrhenius plot. At a constant temperature, the permeability coefficient of crosslinked gelatin-gum arabic membrane coated poly (St-co-DVB) microcapsules was reduced to

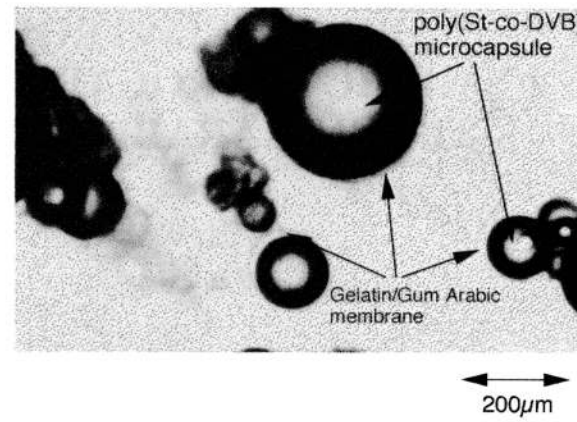

Fig. 2 Optical photograph of crosslinked gelatin-gum arabic coated poly (St-co-DVB) microcapsules

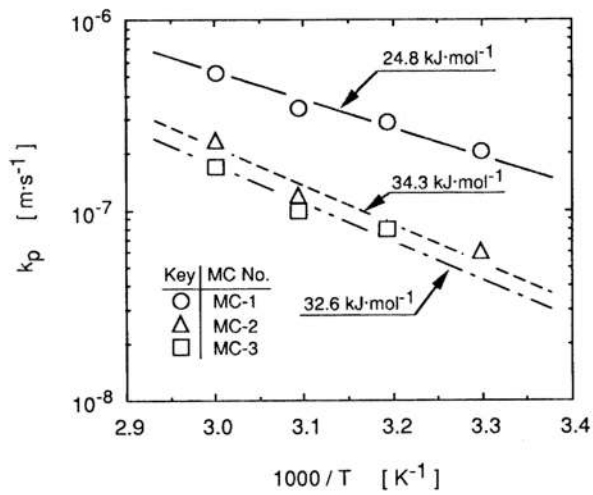

Fig. 3 Dependency of permeability coefficient on ambient solution

about one-third , compared with that of non-coated poly (St-co-DVB) microcapsules. It was furthermore mentioned that the permeability coefficient of crosslinked gelatin-gum arabic membrane-coated poly (St-co-DVB) microcapsules was almost the same as that of non-coated poly (St-co-DVB) microcapsules prepared under a monomer concentration of 6.0 mol·dm^{-3}. It has been clarified that monomer concentration in polymerization was a significant preparation parameter to determine the thickness of the microcapsule membrane, and that the thickness of the microcapsule membrane makes a considerable contribution to the permeability coefficient. The result illustrated in Fig. 3 suggests that the coating method, as is the preparation condition, is useful as the controlling technique of the permeation rate. In addition, coacervation can be recognized to be not only a preparation technique of microcapsules but also a useful coating procedure for water-soluble polymer.

The activation energy of each polymeric microcapsule was determined from the slope of the straight lines shown in Fig. 3. The values of activation energy ranged from 24.8 kJ·mol^{-1} to 34.3 kJ·mol^{-1}. It can therefore be presumed from these activation energies that the diffusion

of solute through a polymeric microcapsule membrane is a dominant step in the permeation kinetics. Especially, in MC-2 and MC-3, the contribution of diffusion to the permeation kinetics became more pronounced due to the higher concentration of St and DVB or crosslinked gelatin/gum arabic membrane.

Conclusion

This study was carried out in an atteptto control the permeability of polymeric microcapsules by complex coacervation of gelatin and gum arabic as a coating. Poly (St-co-DVB) microcapsules were prepared via *in situ* polymerization and crosslinked gelatin-gum arabic coated poly (St-co-DVB) microcapsules by complex coacervation, and the permeability coefficient of each microcapsule was measured. The crosslinked gelatin/gum arabic membrane significantly reduced the permeability coefficient of poly (St-co-DVB) microcapsules. Consequently, it was concluded that coacervation was applicable as a coating technique for water-soluble polymers and bio-compatible polymers such as protein, polysaccharide, nucleic acid and their derivatives.

Acknowledgment

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Nomenclature

C_m	=	monomer concentration in dispersed droplets	[mol·dm^{-3}]
C	=	concentration of chemical specie	[mol·dm^{-3}]
d_p	=	average diameter of microcapsule	[m]
E	=	activation energy	[kJ·mol^{-1}]
I_0	=	initiator concentration in dispersed droplet	[mol·dm^{-3}]
k_p	=	permeability coefficient	[m·s^{-1}]
T	=	temperature of ambient solution	[K]
W	=	DVB/St weight ratio	[-]
Θ	=	dimensionless specific concentration	[-]
ε	=	initial holdup of biphenyl in polymeric microcapsules	[-]
ϕ	=	holdup of dispersed droplets	[-]

<Subscript>

A	=	gum arabic
B	=	biphenyl
e	=	equilibrium value
G	=	gelatin
m	=	monomer
0	=	initial value

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