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Effect of Affinity between Core Medium and Wall Membrane on Permeability of Dye through Microcapsule Membrane

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Transfer of azo-dyes from a series of phthalate compound core to dispersing medium of methanol through poly(ureaurethane) microcapsule membrane has been measured. The release curves were expressed well by a stretched exponential equation $C(t) = C^{eq}\{1-\exp[-(t/\tau_{eff})^{\alpha}]\}$, where $C(t)$ is the concentration of the dye in methanol as a function of the elution time t, C^{eq} that at the equilibrium state, τ_{eff} an effective time constant and α an exponent related to the size distribution of microcapsules. C^{eq} and τ_{eff} are functions of the chemical potentials and the diffusion constant of the dye, based on a simple theoretical model. τ_{eff} was determined as 17.0, 1.6 and 0.57 min, respectively, for the core of di(2-ethylhexyl) phthalate, dibutyl phthalate and diethyl phthalate using an azo-dye with a large molar volume, whereas no difference in τ_{eff} was observed for different core media using an azo-dye with a small molar volume. The difference of the release properties was attributed to the relative size of the pore in the membrane network and the azo-dye, and the affinity between the wall membrane and the core medium.

Key words: microcapsule, permeability, dye, affinity

I. INTRODUCTION

Recent development in biotechnology and pharmaceutical science requires more and more intelligent and controllable drug delivery systems [1-4]. Superior release rate control and target detecting device are of special importance in the applications. In a previous paper, we reported that the structure of poly(ureaurethane) (PUU) microcapsules could be controlled with the use of an interfacial polymerization method through a coupling of chemical cross-linking, swelling and phase separation during the microencapsulation [5-8]. Atomic, electron and optical microscopies as well as glass transition temperature measurements suggested that one of the most important factors for determining the structure of microcapsule walls was the affinity of the core solvent with the wall-forming materials [7]. When di(2-ethylhexyl) phthalate (DOP), the compound with low affinity for the membrane, is used as the core medium, the PUU microcapsule membrane has a two-phase domain structure and it is mechanically brittle. When diethylphthalate (DEP), the compound with high affinity for the membrane, is used as the core medium, the membrane has a homogeneous swollen structure and it is elastic. Thus, it is expected that the release rate of chemical compounds from the inside the microcapsule to the outside should be highly correlated with the affinity of the core compound for the membrane due to the membrane structure formed in the microencapsulation.

In this paper we tried to study the relationship between the membrane structure and the permeability of azo-dyes by using a triisocyanate wall-forming monomer and plasticizing agents of a series of phthalate core medium.

2. EXPERIMENTAL

2.1 Materials

1.66 g of Takenate D110N (75% triisocyanate monomer in ethyl acetate) purchased from Takeda Chem. Co. was mixed with 1.25 g of a series of phthalate compounds, DEP (System A), dibutylphthalate DBP (System B) and DOP (System C), containing 0.065 g of azo-dye, N-[2,5-bis(heptyloxy)phenyl]-2-[(2,5-dibutoxy-4-p-tolylthio phenyl) hydrazono]-3-oxobutylamide, 3 g of ethyl acetate and 10 g of 5 % Copoly(vinyl acetate-vinyl alcohol) aqueous solution. The azo-dye was produced by Fuji Photo Film Co. Ltd. The copolymer used as a protective colloid was a gift from Klare Co. Ltd.

The solutions were homogenized on ice at 5,000 rpm for 10 min by an emulsifier (Excel Auto, Nihon Seiki Co.). The resultant suspension was stirred at 40 °C for 4 h [9]. A smaller compound of Sudan IV was also used as the dye and encapsulated with the same procedure using DEP (System D) and DOP (System E) as the core media. Sudan IV and reagent grade core media were purchased from Tokyo Kasei Co. Ltd. and Aldrich Co., respectively. The reagents were used without further purification. The chemical structure of azo-dyes and an illustration of poly(ureaurethane) membrane network are shown in Figs. 1 and 2, respectively.

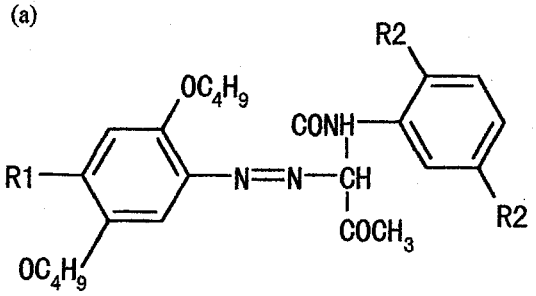
2.2 Method

One milli litter of the microcapsule suspension with the percentage weight of 20 % was dipped on a polyethylene terephthalate sheet, spread on it homogeneously by a spin coater and dried completely by a dryer. The film was cut into squares (1 cm x 1 cm). Ten sheets of the square films were put into a glass vessel containing 20 ml of methanol, which was gently stirred and thermally controlled at 40 °C.

The optical density of the outer dispersing medium of methanol was measured as a function of time at the wavelength of 430 nm for System A-C and of 516 nm for System D and E. The concentration of azo-dyes in methanol, C, was estimated from calibration curves. The size distribution of microcapsules measured by the dynamic light scattering did not depend on the system. A typical example is shown in Fig. 3.

The solubility parameter of the chemical compounds, DOP, DBP, DEP and PUU network is 9.56, 10.07, 10.54 and 12.03 $(cal/cm^3)^{1/2}$, respectively [10]. From the solubility parameter difference, PUU network is considered to have the highest affinity with DEP and the lowest affinity with DOP.

(a)



R_1= -p-tolylthiophenyl
R_2= -heptyloxy

(b)

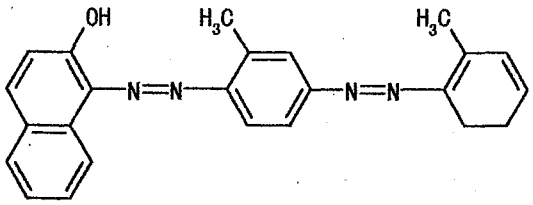


Fig. 1 Chemical structure of azo-dyes of N-[2,5-bis(heptyloxy)phenyl]-2-[(2,5-dibutoxy-4-p-tolylthio phenyl)hydrazono]-3-oxobutylamide (a) and Sudan IV (b).

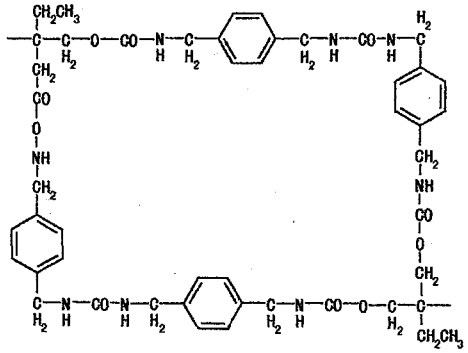


Fig. 2 Illustration of poly(urea-urethane) network in the microcapsule membrane.

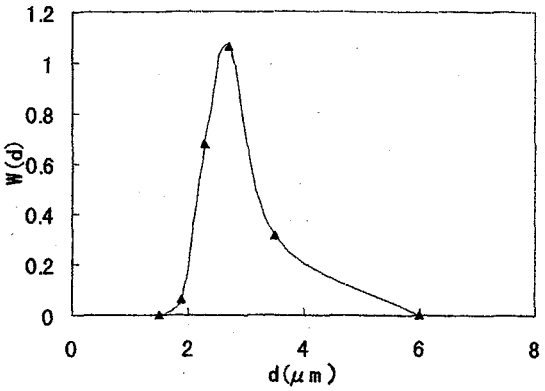


Fig. 3 Size distribution of microcapsules of System C.

2.3 Data Analysis

For monodisperse microcapsules, the profile of dye release from microcapsules is expressed by an exponential equation based on Fick's law:

$$C(t) = C^{eq}(1 - e^{-t/\tau}) \quad (1)$$

where $C(t)$ is the concentration of the dye in the dispersing medium as a function of the elution time t, C^{eq} that at the equilibrium state. The time constant for the dye release τ is given by [12]

$$\tau = \frac{Rl}{3}\frac{1}{D_m}\frac{\mu'_m}{\mu'_c}. \quad (2)$$

Equation (2) shows that τ is proportional to the thickness l of the microcapsule membrane, the outer radius R of the microcapsule and the ratio of the concentration derivative of the chemical potential of the dye in the membrane μ'_m to that in the core μ'_c, and inversely proportional to the diffusion constant of the dye in the wall membrane D_m. In the case of microencapsulation by using the interfacial suspension polymerization, the membrane thickness is usually proportional to the radius of the microcapsule. Thus, introducing a numerical factor k, we have $l = kR$. Using this relationship, τ is expressed as

$$\tau = c_0 R^2 \quad (3)$$

where c_0 is a constant which does not depend on the size of microcapsules and is expressed as

$$c_0 = \frac{k}{3D_m \mu'_c / \mu'_m} \quad (4)$$

For a collection of microcapsules with various characteristic times resulting from the size distribution, introducing an effective time constant τ_{eff}, we have [11,13]

$$C(t) = C^{eq}\{1 - \exp[-(t/\tau_{eff})^{\alpha}]\} \quad (5)$$

where τ_{eff} is expressed as

$$\tau_{eff} = \frac{c_0}{\kappa(\alpha)} < R^2 >. \quad (6)$$

and α $(1 \geq \alpha \geq 0.5)$ an exponent relating to the size

distribution of microcapsules, $< R^2 >$ the mean square outer radius of microcapsules, and the function $\kappa(\alpha)$ is given by[11]

$$k(\alpha) = \frac{1}{\pi} \int_0^\infty d\lambda \int_0^\infty dr \exp[-\lambda^\alpha r^\alpha \cos(\alpha\pi/2)] \times \cos[r - \lambda^\alpha r^\alpha \sin\frac{\alpha\pi}{2}] \quad (7)$$

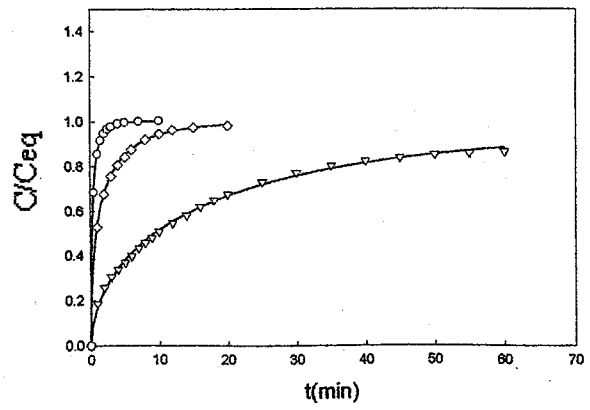
The function $\kappa(\alpha)$ is a downward-convex decrease function; it decreases rapidly up to the order of $\alpha \approx 0.6$ but slowly in the larger α region (See Fig.1 in ref.11). For the system with a wider size distribution, the value of α is smaller.

3. RESULTS

Figure 4(a) shows the observed release curves for System A (○), B (◇) and C (▽). All the curves were expressed well by the stretched exponential equation (5). The parameters C^{eq}, τ_{eff} and α were determined by a least-squares fit. The equilibrium value of the concentration C^{eq} for different core solvents agreed within experimental error. The magnitude of the time constant τ_{eff} was in the order of the affinity between the core medium and the wall-forming membrane; 0.57, 1.6 and 17.0 min for System A, B and C, respectively. The non-linearity index α was roughly constant and independent of the core medium; 0.60, 0.57 and 0.69 for System A, B and C, respectively.

In contrast, the observed release curve for System D coincides with that for System E, as shown in Fig. 4(b). The average values of the exponent α and the time constant τ_{eff} were 0.6 and 1.3 min, respectively. This result shows that the microcapsule form factor k and the size distribution are independent of core media. The difference in the effective time constant τ_{eff} for System A, B and C is due to the difference in diffusion length of the dye in the wall membrane.

(a)



(b)

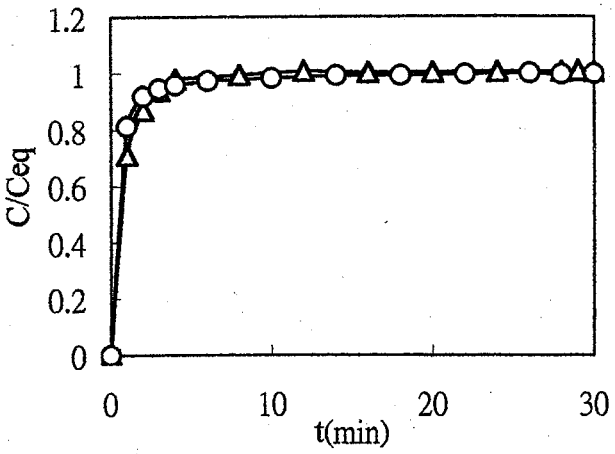
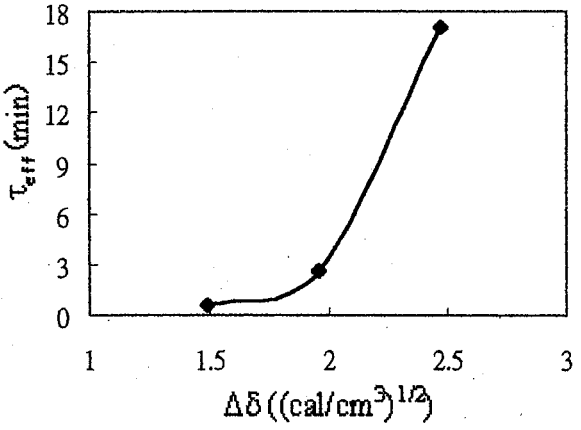
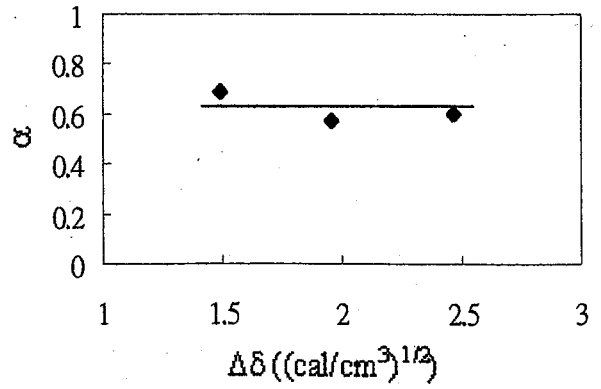


Fig. 4 Dye release curves for System A (○), B (◇) and C (▽) (a), and System D (△) and E(○) (b). The solid lines are the ones calculated using Eq. (6) with the parameters τ_{eff} and α determined by a least squares fit.

(a)



(b)



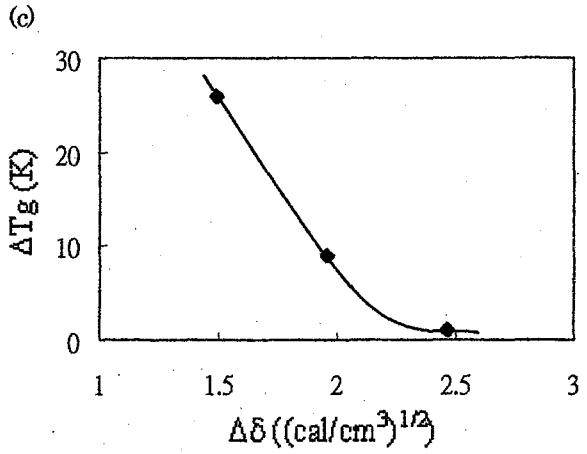


Fig. 5 Time constant τ_{eff} (a), the exponent α (b) in Eq. (6) and the glass transition temperature difference ΔT_g (c) as a function of solubility parameter difference

4. DISCUSSION

According to the theoretical consideration, the exponent α is determined by the width of the size distribution of microcapsules. Thus, the constant value of α obtained from the release curve is consistent with the constant size distribution determined from the dynamic light scattering.

According to Eqs. (4) and (6), the effective time constant depends on D_m and μ_c'/μ_m', since the average size of microcapsules R and the membrane thickness l are the same for System A-C. We have no information about the concentration derivatives, but the ratio μ_c'/μ_m' might not be strongly dependent on the core medium. The diffusion constant D_m could be expressed as $D_m \approx k_B T/f$ with $f \approx f_0 a$, where $k_B T$ has the usual meaning, f is the friction coefficient of the dye, a the radius of the dye and f_0 the "viscosity" of the "fluid" composed of the membrane network and the solution. In other words, D_m and the time constant τ_{eff} depend on the "micro-viscosity" in the membrane relating to the relative magnitude of the dye and the pore size in the wall membrane polymer network. Thus, the observed constant and small values of τ_{eff} for System D and E may be attributed to the size of the dye, Sudan IV, much smaller than the pore size of the membrane network when it is plasticized by methanol.

For the considerable difference of τ_{eff} for System A-C where the large azo-dye was used for the experiment, we need to look into the structure of the membrane more in detail. The pore size of the wall membrane depends on the polymer network structure. According to microscopic observations and glass transition measurements [8], the wall membrane is swollen for a high affinity core medium of DEP, whereas it has a domain structure by phase separation for a low affinity medium of DOP. Thus, the effective pore size should be in the order of DOP, DBP and DEP. In Fig. 5, the release curve parameters as well as the glass transition temperature of the microcapsule wall membrane were plotted as a function of solubility parameter difference $\Delta\delta$ of the core medium and the microcapsule wall membrane, which is an index for the affinity between the membrane polymer network and the core media. τ_{eff} increases considerably by increasing $\Delta\delta$. Correspondingly, the glass transition temperature decreases with increasing $\Delta\delta$, which symbolically indicates the strong relationship among the affinity of the chemical compounds consisting of microcapsules and dispersing media, the membrane structure and the dye release behavior. This suggests that the considerable difference of τ_{eff} for System A-C is attributed to the difference in the affinity of the core media and polymer membrane of the microcapsule through the difference of the membrane structure.

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