International Journal of Pharmaceutics 242 (2002) 147–153

international journal of pharmaceutics

www.elsevier.com/locate/ijpharm

Characterization of the structures of poly(urea–urethane) microcapsules

Yuki Matsunami, Kimio Ichikawa *

Fujinomiya Laboratory, Fuji Photo Film Co. Ltd, 200 Onakazato, Fujinomiya, Shizuoka 418-8666, Japan

Received 12 December 2001; received in revised form 25 December 2001; accepted 9 January 2002

Abstract

A series of poly(urea–urethane) microcapsules containing phthalate derivatives as a core material were prepared by an interfacial polymerization process in order to investigate the structural formation mechanism. Scanning electron microscopy (SEM) analysis for the cross sections of microcapsules revealed the systematic formations of porous structures followed by the formation of core/shell structures. Critical values of the core oil content for the formation of porous and core/shell structures were obtained from SEM results and the critical values were found to be proportional to the solubility parameters of core materials. Dynamic mechanical measurements indicated an amorphous structure of wall membrane and the glass transition temperature was found to decrease with increasing the core oil content suggesting a plasticizing effect. The surface amount of the core oils absorbed in the wall membrane was estimated using time of flight secondary ion spectroscopy analysis and found to increase with increasing the oil content before reaching constant. This tendency was interpreted in terms of the structural formation of the microcapsules. The results obtained in the present investigation were reasonably understood on the basis of swelling theory of wall membrane and the Flory–Huggins interaction parameters of the systems were discussed.

Keywords: Poly(urea–urethane); Core/shell structure; Glass transition temperature; ToF-SIMS; Swelling; Solubility parameter

1. Introduction

The morphology of microcapsules such as core/shell structures could be one of the major factors affecting the physicochemical properties of microcpasules such as in drug delivery systems, thermo sensitive recording papers, etc. The morphological characterization of micocapsules has been investigated on the basis of interfacial tension analysis (Berg et al., 1989; Loxley and Vincent, 1998), and an earlier study was made for the three-phase liquid system (Torza and Manson, 1970). Thermodynamically, creation of a new surface generated in emulsification processes requires work, and the surface free energy has to be minimum for morphological formations of the microencapsulation processes. For immiscible liquids system, in order to spread liquid a over

---

* Corresponding author. Tel.: +81-544-26-7617; fax: +81-544-26-7678

E-mail address: kimio-ichikawa@fujifilm.co.jp (K. Ichikawa).

0378-5173/02/$ - see front matter © 2002 Published by Elsevier Science B.V.
PII: S0378-5173(02)00138-2

liquid b, spreading coefficient must be always negative, and then,

$$\gamma_{ab} > |\gamma_a - \gamma_b| \tag{1}$$

where γ is surface tension of liquid a and b respectively, and γ_{ab} is interfacial tension between two liquids.

The microcapsule used in the present study is composed of a poly(urea–urethane) wall forming polymer, a core oil, and a protective colloidal polymer. The tri-functional isocyanate monomer is a wall forming material and the wall forming process is considered to be a process followed by a polymerization-induced phase separation mechanism. The swelling properties of the wall membrane by core oil compounds have been investigated by thermo-mechanical analysis (Ichikawa, 1994), light scattering analysis (Dobashi et al., 1995, 1996, 2001), and ultrasound measurements (Ichikawa, 1997; Ichikawa et al., in press), and found to be dominated by plasticizing effects of the core materials (swelling mechanism). The process dissolving the core oils in a wall polymer would be governed by the enthalpy change of mixing;

$$\Delta H_m = v_1 v_2 (\delta_1 - \delta_2)^2 \tag{2}$$

where ΔH_m is heat of mixing, v is volume fraction, and δ is solubility parameter of each phase, respectively. It could be expected that the morphologies of microcapsules containing oils would be explained by the solubility parameters of each component. In the present paper, phthalate compounds are employed as core oils and the compounds are thought to be absorbed in the poly(urea–urethane) membrane depending on the solubility of the materials. In order to investigate the structural formation mechanism mentioned above, morphological analysis, thermo-mechanical analysis, and surface analysis are employed for the poly(urea–urethane) microcapsules.

2. Materials and methods

2.1. Microencapsulation

Takenate D-110N (Triisocyanate monomer (75%) in ethyl acetate) was purchased from Takeda Chemical Co. Ltd and used as a wall forming material as received. Dimethyl phthalate (DMP), diethyl phthalate (DEP), dipropyl phthalate (DPP), dibuthyl phthalate (DBP), and di-*n*-octhyl phthalate (DOP) were purchased from Wako Chemical Co. Ltd as core materials. Phthalated gelatin (MGP gelatin) was purchased from Nippi Gelatin Co. Ltd and used as a protective colloid. Ethyl acetate purchased from Wako Chemical Co. Ltd was used as a solvent to control the viscosity of the hydrophobic phase. All materials were used without further purification. A given weight of a core oil compound and 8.47 g of Takenate D-110 N with 10 g of additional ethyl acetate were mixed to form a clear organic solution. The organic phase was pored into 5.8% gelatin aqueous solution at 40 °C and immersed vigorously using an emulsifying apparatus (Toyo Seiki Co. Ltd). The resultant emulsion was stirred under the atmospheric pressure at 40 °C for 3 h. The microcapsules with given ratio of the core materials were prepared.

The microcapsule film for Fourier Transform IR measurements was obtained to dry the suspension on a polyethylene film, and no residual isocyanate peak was observed in the spectra. The average diameter of the microcapsule was evaluated by a light scattering technique using LA-910 (Horiba Seisakusyo Co. Ltd) assuming the refractive index is 1.18. The mean diameters of samples were from 0.9 to 1.2 μm with almost the same distribution.

2.2. Scanning electron microscopy analysis

Scanning electron microscopy (SEM) photos were taken using ISI-DS130 (Topkon Co. Ltd). Samples were prepared by cutting the microcpasules under liquid nitrogen temperature.

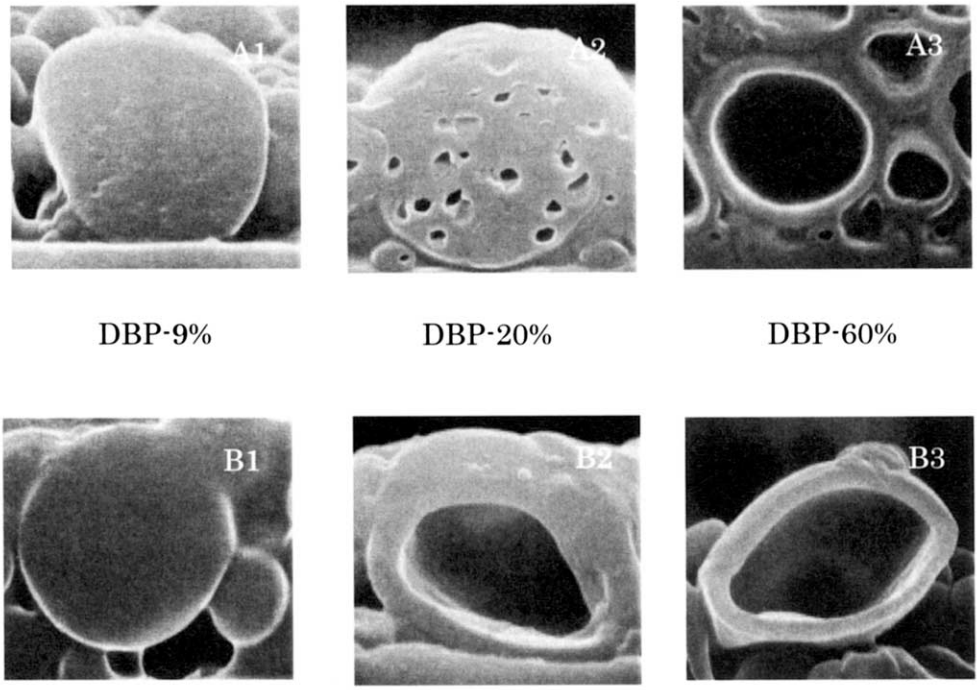
2.3. Dynamic mechanical thermal analysis

Diluted microcpasule suspensions by ultra pure water were centrifuged to remove colloidal gelatin and the resultant slurry were coated on the plane paper. Dynamic mechanical thermal measurements were performed using DMA8000 (Seiko Instruments Co. Ltd) and the ramp rate for the temperature scan was 5 °C/min at 1 Hz. The details were published elsewhere (Ichikawa, 1994).

2.4. ToF-SIMS analysis

0.1 g of protease powder (Actinase E, Kaken-Seiyaku Co.Ltd) was added to 1 g of microcapsule suspension and then kept at 40 °C for 4 h to decompose the gelatin polymers, the resultant slurry was diluted by ultra pure water and then centrifuged six times. 1 g of ion exchange resin (MB-3, Orugano Co. Ltd) was added and kept for 1 h to remove ionic species. Filtrated samples were coated on Si wafer and dried at room temperature.

Time of flight secondary ion spectroscopy (ToF-SIMS) analysis was performed using a PHI ToF-SIMS TRIFT II instrument equipped with a 15 kV Ga^+ pulsed liquid metal ion source (pulse width 11 ns, repetition rate 11.3 kHz, primary ion current of 600 pA measured as a DC beam). The secondary ions were accelerated into a ToF analyzer with 3 kV extraction voltage in both positive and negative ion polarity mode. All the spectra were acquired for 300 s and rastered over a surface area of 80×80 μm^2. SIMS operating conditions were maintained within the static limits. Charge neutralization was achieved with a pulsed low-energy electron flooding. The mass resolution $m/\Delta m$ was ~ 5000 as measured at $m/z = 28$ on a Si wafer in the case of using a bunching mode. The sample and the sample stage were cooled to -135–145 °C for preventing from vaporization of sample's oil.



DBP-9% DBP-20% DBP-60%

DOP-5% DOP-9% DOP-33%

Fig. 1. SEM photographs of microcapsules containing (A) DBP and (B) DOP with different rate of oils (cross-sectional view).

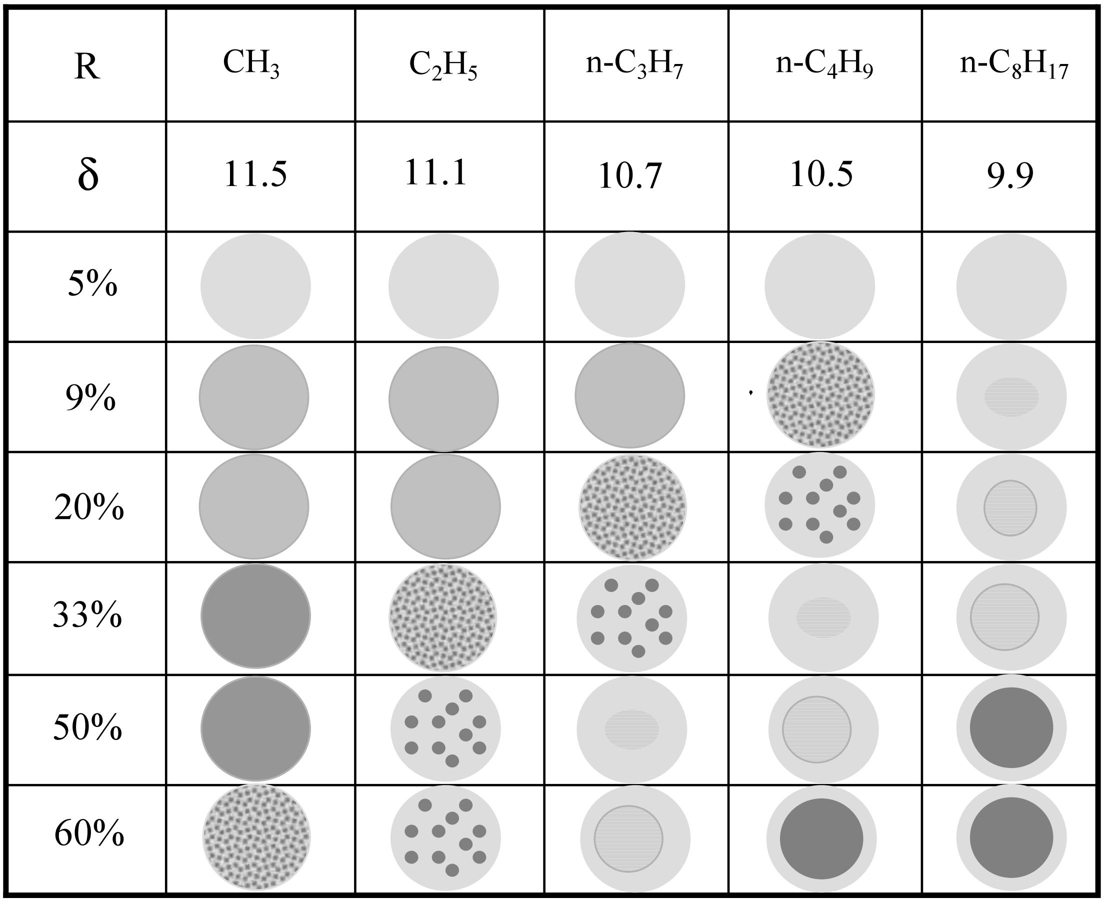


Fig. 2. Schematic representation of SEM results obtained for the microcapsules. (bright gray: homogeneous phase, dark particle in bright gray: porous structure with a diameter of ≈ 100 nm. R denotes derivatives of carboxyl ester moiety of phthalate compounds. Insert photographs: cross section of microcapsules typically shown the structures).

3. Results and discussion

3.1. Morphological analysis

SEM microphotographs using freeze-fracture method are typically shown for the microcapsules containing DBP in Fig. 1(A) and DOP in Fig. 1(B) with different ratios of oils respectively. In the case of microcapsules containing DBP, the small pore with a diameter of approximate 100 nm was observed at the ratio of 9%, and at the ratio of 33% the core/shell structure was formed. The critical value for the formation of small pore is defined as φc, and the value for the core/shell structure is defined as ψc in the present study. From Fig. 1(B), φc is 20% and ψc is 33% for the DBP case. Fig. 2 schematically represents the summarized results obtained by SEM observation. The solubility parameter for the materials was calculated using Fedors equation (Fedors, 1974) and the critical ratios φc and ψc obtained from Fig. 2 were plotted against the difference of solubility parameter of wall membrane from the phthalate compounds as shown in Fig. 3. The critical values were found to be the increasing factors on the solubility parameter of core oil indicating the swelling mechanism mentioned above is the major mechanism dominating the structural formation of microcapsules. In the present study the solubility parameter of

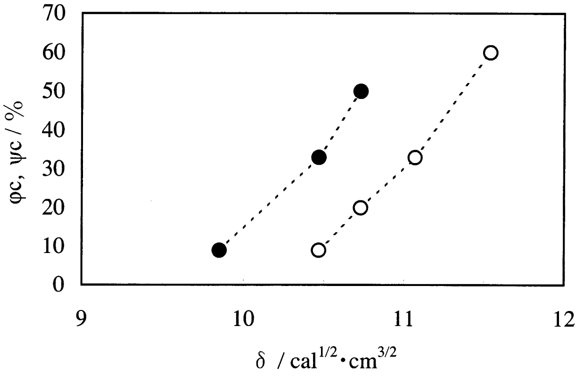


Fig. 3. Dependences of critical rates, ϕc and ψc, on the solubility parameter of core materials. (ϕc (○), ψc (●)).

poly(urea–urethane) is obtained as 12.8 $\mathrm{cal}^{1/2}/\mathrm{cm}^{2/3}$ assuming the urea structure for the reacted isocyanate group.

3.2. Dynamic mechanical analysis

The temperature scan data for loss tangent (tan δ) of microcapsules with different loading were shown in Fig. 4 and the glass transition temperature (T_g) of the wall membrane could be defined as the temperature of peak position. Fig. 4 shows the structure of wall membrane is considered to be amorphous and the phthalate compounds as core materials are thought to de dispersed as compatible. The T_g's were found to decrease with increasing the ratio and then reach almost constant. This result is consistent with the results reported before (Ichikawa, 1994), and the decrease of T_g could indicate a plasticizing effect of core oil in the wall membrane. The decrease of T_g is plotted against the solubility parameters of oils as shown in Fig. 5 and the result suggests the decrease of T_g is due to the plasticizing effect of phthalate compounds absorbed in the wall membrane.

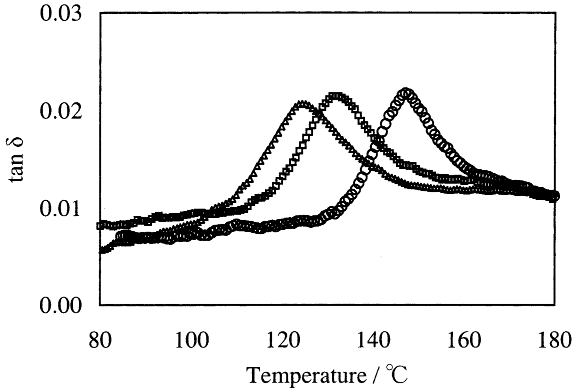


Fig. 4. Temperature dependences of tan δ at 1 Hz obtained by dynamic mechanical measurements of microcapsules containing DPP. (0% (○), 5% (□), 20% (△)).

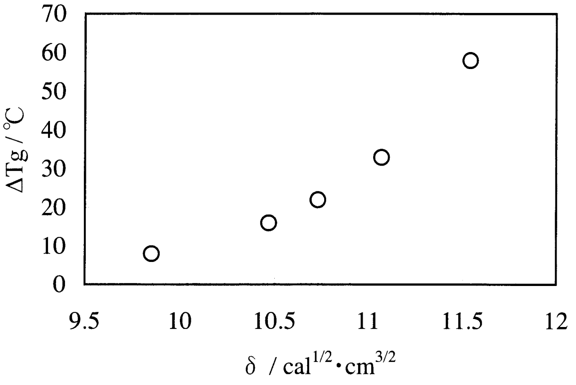


Fig. 5. Dependence of ΔT_g (decrease of T_g of microcapsules) on the solubility parameter of core materials.

3.3. ToF-SIMS analysis

In order to evaluate the amount of phthalate compound absorbed in the wall membrane, ToF-SIMS measurements were carried out for the microcapsule samples. The positive ion ToF-SIMS spectra in the region of m/z 0–400 of the microcapsules containing DEP and DOP at the ratio of 50% were shown in Fig. 6 and it can be seen that the ion at m/z 149 is diagnostic. The ion at m/z 149 can be assigned to the cationic molecule as shown in Fig. 6. Additional ions were observed and assigned. The ions due to the ionization of gelatin molecules were not observed in the present study indicating no residual gelatin molecules on the microcapsule surface. The ion count of m/z 149 for DEP is significantly larger than that of DOP indicating the rich concentration of the compound at the top surface of the microcapsules. The results were obtained by calibrating the differences of ionization rate of each compound. Fig. 7 typically shows the amount of phthalate

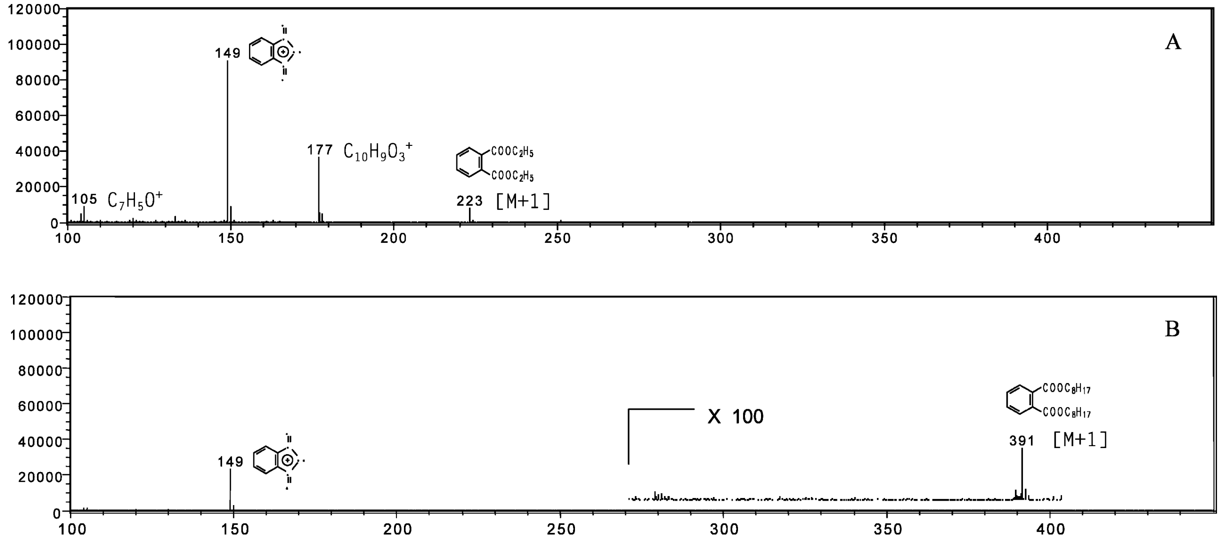


Fig. 6. Positive ion ToF-SIMS spectra of the microcapsules containing (A) DEP and (B) DOP; *m*/*z* 0-400.

compounds existing at the top surface of the wall membrane depends on the ratio of core oils and error bars were estimated to be within 10% of the observed count from the results performed twice. In the case of DBP, the surface amount increases in the range of ratio less than 20%, and then reaches almost constant. This dependence seems to be the same as the result obtained from T_g measurements mentioned above. However the surface amount of the oils is found to reach maximum for the cases of DMP, DEP, and DPP. The maximum values of the surface amount and the ratio giving the maximum are seemed to increase with increasing the solubility parameters of phthalate compounds.

3.4. Formation of the microcapsule structures

SEM results along with T_g analysis have clearly shown that the swelling mechanism is a major process dominating the formation of microcapsule structures in the present case. The ester moiety in the phthalate compounds is thought to be a plasticizer for the poly(urea–urethane) membrane because of its polarity. Dobashi et al. investigated the swelling ratio of poly(urea–urethane) microcapsules containing DOP as a core oil using a single-particle light scattering technique and found the swelling ratio in volume to be 1.2 (Dobashi et al., 2001). In the present study, the swelling ratio in weight is estimated approximately to be 1.1 from the results of SEM and T_g analysis and calculated to be 1.13 in volume assuming the density of materials (Ichikawa et al., in press). ToF-SIMS results for DOP samples as shown in Fig. 7 indicate the membrane could absorb DOP up to 20% in weight, then the swelling ratio in volume is estimated to be 1.25 for

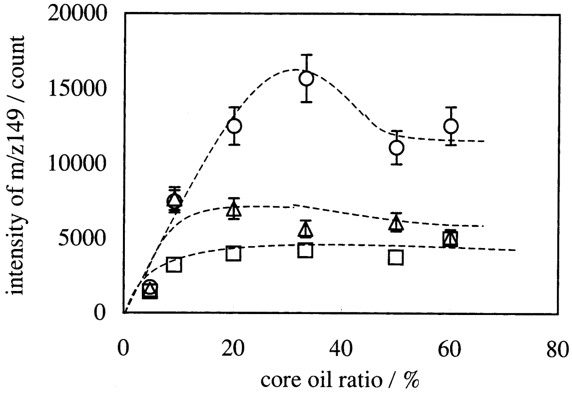


Fig. 7. Surface amount of phthalate compounds obtained from ToF-SIMS spectra for microcapsules containing DEP (○), DBP (△), and DOP (□), respectively. Dashed lines are drawn as a guide for eyes.

this case. The results obtained here are thought to be in good agreement with the results obtained by the light-scattering investigation.

The present SEM observation has clearly shown the small pore structure in the membrane and the critical content ψc was found to be a factor proportional to φc. It might be reasonable to assume that in the initial stage of the phase separation of core material the small pore structure is formed and then the number of the pore increases with increasing the loading. Finally, the pores would form the core in the microcapsule.

The equilibrium swelling theory of Flory and Rehner gives the following equation:

$$\chi_1 = -[\mathrm{Ln}(1 - v_2) + v_2 + V_1 n(v_2^{1/3} - v_2/2)]v_2^2 \qquad (3)$$

where χ_1 is the Flory–Huggins polymer-solvent interaction parameter, v_2 is the volume fraction of wall membrane swollen by the core oil, V_1 is the molar volume of the core oil, and n is the front factor representing the number of active network chain segments per unit volume of the wall membrane (Flory, 1953). The quantity n equals ρ/Mc, where ρ is the density and Mc the molecular weight between cross-links of the wall membrane. In the present case, the value of Mc is roughly estimated to be 460, which is 2/3 of the molecular weight of wall forming material. Dobashi et al. reported the swelling ratio of poly(urea–urethane) microcapsule containing DOP was 1.20 (Dobashi et al., 2001) and the result is consistent with the result obtained in the present paper. The Flory–Huggins χ parameter for the microcapsule containing DOP is obtained as 0.40 using the values mentioned above and 0.03 for the DBP sample. The χ_1 parameters obtained here suggest that DOP is a poor solvent and DBP is a good solvent for the wall membrane.

Finally the results obtained from ToF-SIMS analysis are discussed here. As shown in Fig. 7 the values which gives the maximum of the surface amount seem to increase with increasing the solubility parameter. The SEM results from Fig. 2 indicate that the maximum values occur along with the formation of the small core structure. It would be reasonable to consider that the porous structure gives some defects on the surface of the microcapsule with increasing the surface area. After reaching the maximum value the pores would form the core phase, and then the surface structure become uniform. The dependence on the solubility parameter of oil compounds could be understood on the basis of the swelling mechanism mentioned above. However, the fine structure of the wall membrane is not still clear, it should be pointed out that the swelling ratio might be over estimated from the results obtained from SEM analysis. Further investigations on detailed structures and physicochemical properties are needed.

Acknowledgements

One of the authors (K.I) is grateful to Professor T. Dobashi of Gunma University for his critical discussions.

References

Berg, J., Sundberg, D., Kronberg, B., 1989. Microencapsulation of emulsified oil droplets by in-situ vinyl polymerization. J. Microencapsulation 6, 327–337.

Dobashi, T., Yeh, F., Ying, Q., Ichikawa, K., Chu, B., 1995. An experimental investigation on the structure of microcpasules. Langmuir 11, 4278–7282.

Dobashi, T., Takenaka, M., Yeh, F., Wu, G., Ichikawa, K., Chu, B., 1996. Scattering studies of poly(urea–urethane) microcapsules in suspension. J. Colloid Interface Sci. 179, 640–642.

Dobashi, T., Furukawa, T., Narita, T., Shimofure, S., Ichikawa, K., Chu, B., 2001. Determination of the swelling ratio of poly(urea–urethane) microcapsules by single-particle light scattering. Langmuir 17, 4525–4528.

Fedors, F.F., 1974. A method for estimating both the solubility parameters and molar volumes of liquids. Polym. Eng. Sci. 14, 147–154.

Flory, P.J., 1953. Principles of Polymer Chemistry. Cornell University Press, Ithaca, New York.

Ichikawa, K., 1994. Dynamic mechanical properties of polyurethane–urea microcapsules on coated paper. J. Apply. Polym. Sci. 54, 1321–1327.

Ichikawa, K., 1997. Structure and physicochemical properties of poly(urea–urethane) microcapsules. Kobunshikako 46, 217–223 in Japanese.

Ichikawa, K., Ishimura, H., Sakanishi, A., Dobashi, T. An ultrasound study of poly(urea–urethane) microcapsules, in press.

Loxley, A., Vincent, B., 1998. Preparation of poly(methylmethacrylate) microcapsules with liquid cores. J. Colloid Interface Sci. 208, 49–62.

Torza, S., Manson, S.G., 1970. Three-phase interactions in shear and electrical field. J. Colloid Interface Sci. 33, 67–83.