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Preparation of Temperature and Water Responsive Microcapsules Containing Hydroquinone with Spray Drying Method

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ABSTRACT

It was tried to prepare temperature and water responsive microcapsules containing hydroquinone as a water soluble core material with the spray drying method. Microcapsules were composed of ethyl cellulose (EC), methyl cellulose (MC) and P-N-isopropylacrylamid (PNIPAM). P-N-isopropylacrylamid and methyl cellulose were used as a temperature responsive polymer and as a water responsive polymer, respectively. Ethyl cellulose was the main shell material of microcapsule. At the microencapsulation process, the core and shell materials were dissolved in ethyl alcohol dissolving water (20 wt%) and then, spray-dried to prepare microcapsules. In the fundamental operation, the concentration and molecular weight of methyl cellulose were mainly changed. The releasing rate of hydroquinone was repressed at 40˚C and increased at 20˚C due to temperature responsive PNIPAM. Furthermore, responsibility to water was increased with the concentration of methyl cellulose.

Keywords: Stimuli Responsive Microcapsule; Spray Drying Method; Hydroquinone; Controlled Release; Methyl Cellulose

1. Introduction

Stimuli-responsive microcapsules for controlled release of core material have been applied in many fields such as drug delivery systems (DDS), painting, self-healing agent, cosmetics, foods [1-9].

As stimuli, mechanical pressure, temperature, water, pH, specified enzyme and ultra violet ray have been utilized according to physical properties of shell materials.

Among these stimuli, temperature was utilized frequently for controlled release of core material.

As the temperature responsive shell materials, fatty acids, paraffin wax, fatty acid ester and polymer (poly-N-isopropylacryl-amid) have been applied to form the microcapsule shell.

On the other hand, as the water responsive shell materials, the water soluble materials such as methyl cellulose (MC), hydroxyl propyl methyl cellulose (HPMC), gelatin, starch, polyvinyl alcohol, pectin and chitosan have been applied to form the microcapsule shell.

Until now, the stimuli responsive microcapsules have been mainly prepared with the chemical methods such as the miniemulsion polymerization method, the suspension polymerization method, the interfacial reaction method and the physical chemistry methods such as the drying-in-liquid method, the coacervation method, the hetero-coagulation method and the spray drying method [10].

Among these preparation methods, the preparation method without the continuous water phase is desired to microencapsulate the water soluble core materials, because the core materials are easy to dissolve in the water phase during the microencapsulation process.

The spray drying method without the continuous water phase has been generally utilized to prepare various powdery composite particles and microcapsules, because the products with stable quality are able to be manufactured in large quantities [11-14].

However, there are few reports with respect to the

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preparation of the temperature and water responsive microcapsules with the spray drying method.

Taking these things into consideration, it is tried to microencapsulate hydroquinone as a water soluble core material with the spray drying method. It is well known that hydroquinone is used as an inhibitor for polymerization, a reduction agent and a bleaching agent and is easily deteriorated.

In this study, hydroquinone is designed to act as a bleaching agent in cosmetics.

Namely, it is designed that hydroquinone is released from the microcapsules responding to temperature and water by using P-N-isopropylacrylamid as the temperature responsive shell and methyl cellulose as the water responsive shell.

The purposes of this study are to investigate whether the microcapsules with the temperature and the water responsibility are able to be prepared with the spray drying method or not and how the release of hydroquinone is controlled by stimuli of temperature and water.

2. Experimental

2.1. Materials

Materials used to prepare the microcapsules are as follows.

Core material: hydroquinone (HQ, Tokyo Kasei, Co. Ltd.).

Shell materials:

- Ethyl cellulose (EC, Shinetsu Kagaku Kogyo, Ltd.);
- Methyl cellulose (MC, MC25, MC400, MC1500, Shinetsu Kagaku Kogyo, Co. Ltd.).

Here, MC25, MC400 and MC1500 mean the viscosity of aqueous solution of 1.0 wt% of MC, namely 25 cP, 400 cP and 1500 cP.

- P-N-isopropylacrylamid (MW: 150000, PNIPAM, Tokyo Kasei Co. Ltd.);
- Solvent for shell and core materials: Ethyl alcohol (EA: Tokyo Kasei Co. Ltd.).

2.2. Preparation of Microcapsules

Figure 1 shows the flow chart for preparing the microcapsules containing hydroquinone as a water soluble core material with the spray drying method.

First, ethyl cellulose (EC), methyl cellulose (MC) and P-N-isopropylacrylamid (PNIPAM) were dissolved in ethyl alcohol (EA) containing water of 20 wt% and then, hydroquinone (HQ) of a given weight was dissolved to prepare the uniform solution.

This solution was spray dried under the given conditions with Spray Drier (Yamato Seisakusho Co. Ltd.).

In this fundamental microencapsulation operation, the concentration and molecular weight of methyl cellulose were mainly changed.

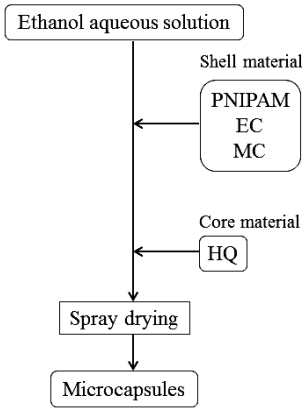


Figure 1. Flow chart for preparing microcapsules with spray drying method.

Experimental conditions adopted in this study are shown in **Table 1**.

2.3. Characterization

2.3.1. Content of HQ

The content of HQ in the microcapsule was measured as follows.

Namely, the microcapsules of a given weight were added and mechanically crushed in the water of 10 cm^3 to dissolve HQ. The amount of HQ dissolved was obtained by the spectrophotometer (Shimazu Co. Ltd.) and then, the concentration of HQ was determined by comparing the amount of HQ with the calibration curve which was obtained beforehand from the results correlating the concentration of hydroquinone with the absorption degree.

2.3.2. Measurement of Released Amount of HQ

The given weight of microcapsules was added in the water phase of 30 cm^3 at 20˚C and 40˚C, respectively. From this point, the change in the concentration of HQ in the water phase was measured at temperature of 20˚C and 40˚C, respectively.

The concentration of HQ in the water phase was measured as follows.

The water phase of 2 cm^3 was sampled out at the finite time interval and the amount of HQ dissolved was obtained by the spectrophotometer (Shimazu Co. Ltd.). The concentration of HQ was determined by comparing the amount of HQ with the calibration curve as stated above.

By using these results, the released rate was defined as the ratio of released amount to the microcapsulated amount of HQ.

2.3.3. Observation of Microcapsules

The surface and inner structure of microcapsules were

Table 1. Experimental conditions.

Solvent	
80 wt% Ethanol aqueous solution	50 g
Shell material	C_{PN} = 0, 2.0 wt% (Solvent × 100)
PNIPAM	
EC	2 g
MC	C_{MC} = 0.5 - 1.5 wt% (MC/Solvent × 100)
MC species	MC25, MC25, MC1500
Core material	
HQ 20 wt%	(HQ/(HQ + Shell Material) × 100)
Spray drying	
Velocity of dried air	0.42 m^3/min
Pressure of spray	0.15 MPa
Inlet Temp.	110˚C
Exit Temp.	50˚C
Nozzle diameter	3 mm

observed by scanning electron microscope (JSM-5800, JEOL Ltd.).

2.3.4. Diameter Distribution and Mean Diameter of Microcapsules

Diameter distribution and mean diameter (Sauter diameter) were obtained directly from the SEM photographs.

Namely, the diameters of microcapsules of 100 number were directly measured from the SEM photographs and the diameter distributions and mean diameters were obtained from these results.

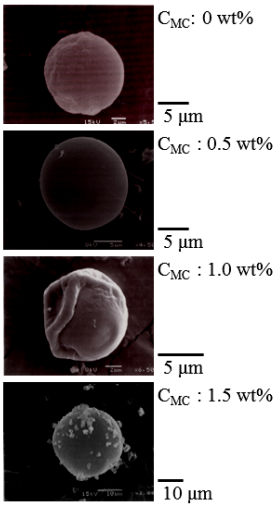
3. Results and Discussion

3.1. Observation of Microcapsules

Figure 2 shows the SEM photographs of microcapsules prepared with the various MC (MC25) concentrations. The microcapsules are spherical and the surfaces of microcapsule are smooth at C_{MC} = 0 and 0.5 wt%. However, the microcapsules become irregular and the surface becomes slightly rough at C_{MC} = 1.0 and 1.5 wt%. This is considered due to increase in the degree of shrinkage of polymeric chain with the MC concentration.

3.2. Effect of Temperature

First, in order to investigate the effect of temperature, the released rate was measured by preparing the microcapsules composed of PNIPAM and EC as the shell materials.



(MC25)

Figure 2. Observation of microcapsules (SEM photographs).

Figure 3 shows the transient feature of released rate, in which the transient feature of released rate for the microcapsules prepared with only EC is shown for comparison. Here, the effect of temperature on the released rate was investigated at 20˚C and 40˚C, because P-N-isopropylacrylamid becomes hydrophilic at 20˚C and hydrophobic at 40˚C.

In the case of microcapsules composed of only EC, the released rate at 40˚C is larger than that at 20˚C. This is considered to be due to increase in the solubility and diffusion velocity of HQ in the water phase.

Contrary to this, in the case of microcapsules composed of EC and PNIPAM, the released rate at 40˚C is smaller than that at 20˚C.

This result is considered to be due to the following reason.

Namely, as PNIPAM becomes hydrophobic at 40˚C, swelling of microcapsules by absorption of water and diffusion of water through the microcapsule shell have to be repressed as shown by an illustration in **Figure 3**. As a result, the release of HQ may be prevented. From these results, it is found that PNIPAM is responsive to temperature for release of HQ.

3.3. Effect of Water Due to MC Concentration

Next, in order to investigate the effect of water, the released rate was measured by using the microcapsules prepared with EC, PNIPAM and MC, in which the concentration of MC (MC25) was changed.

Figure 4 shows the transient features of the released rate measured by using the microcapsules prepared with the various concentrations of MC and C_{PN} = 2.0 wt%.

At C_{MC} = 0.5 wt%, the released rates at 20˚C are larger

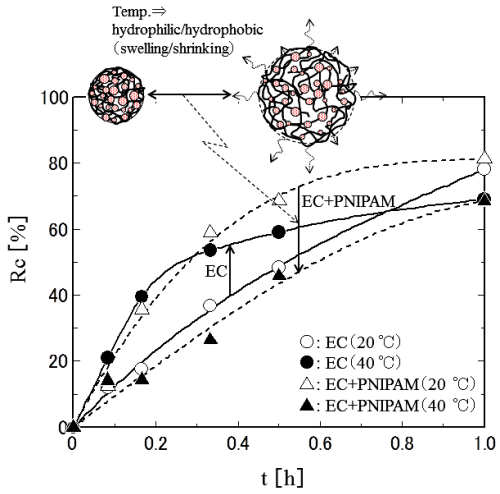


Figure 3. Effect of temperature on released rate.

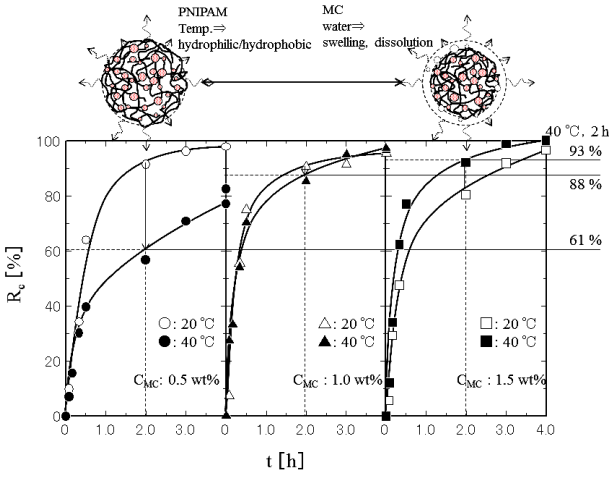


Figure 4. Effects of temperature and water on released rate.

than those at 40˚C. This result may be due to the effect of PNIPAM as shown by an illustration in **Figure 4**.

At C_{MC} = 1.0 wt%, the released rates at 20˚C and 40˚C are almost the same each other.

However, at C_{MC} = 1.5 wt%, the released rates at 40˚C become larger than those at 20˚C.

This result may be considered to be attributable to the fact that responsibility to water due to larger MC exceeds that to temperature due to PNIPAM.

Namely, as the concentration of MC increases, swelling of microcapsules by absorption of water and dissolution of HQ by water have to be superior to both repression of diffusion of water and non swelling of microcapsules due to PNIPAM. From these results, it is found that MC is responsive to water.

Figure 5 shows the dependences of the mean diameters (d_p) of microcapsules and content (F_C) of HQ on the MC concentration, where MC is MC25 and C_{PN} is 2.0 wt%.

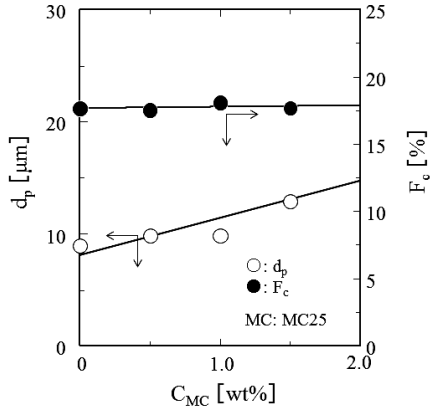


Figure 5. Dependences of diameter and content on MC concentration.

The content of HQ is found to be almost constant (18.0 wt%) and the mean diameters increase with the MC concentration. As the content of HQ on the basis of the feed is 20 wt%, the microencapsulation efficiency of HQ is estimated to be ca. 90%.

The dependence of mean diameter on the MC concentration is described as Equation (1).

$$d_p \sim C_{MC}^{1.2} \quad (1)$$

As the cohesive energy for droplet formation increases with the viscosity of shell solution, the diameter of liquid droplet of shell solution may be increased with the MC concentration. It is natural that the diameters of droplets atomized through the nozzle are strongly depended by the physical properties of liquids such as viscosity, surface tension and density.

3.4. Effect of MC Species

Figure 6 shows the transient features of released rate for the microcapsules prepared with the various MC species, where the MC concentration is 1.0 wt% and C_{MC} = 0 means that MC is not added.

From this figure, it is found that the released rate becomes smaller with the molecular weight of MC.

This result is considered to be attributable to the fact that the microcapsule shell becomes denser with the molecular weigh of MC. As a result, the released rate of HQ is decreased with the molecular weight of MC.

Figure 7 shows the dependences of the mean diameters of microcapsules and content of HQ on the MC species.

The mean diameters are found to be larger than that at C_{MC} = 0 and almost constant (d_p = 18 μm) irrespective the MC species.

On the other hand, the content of HQ is slightly larger than that at C_{MC} = 0 and almost constant (F_C = 18 wt%).

From these results, the microcapsules are found to be

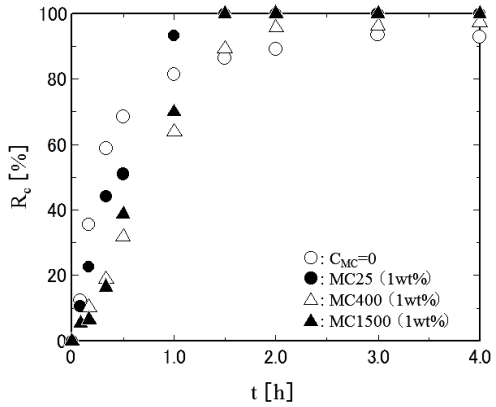


Figure 6. Transient feature of released rate.

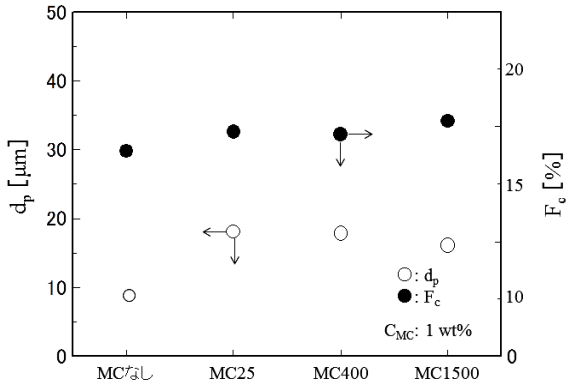


Figure 7. Dependences of mean diameter and content on MC species.

able to be stably prepared under the conditions adopted here.

Figure 8 shows the SEM photographs of microcapsules prepared with the various MC species.

The Microcapsules becomes more irregular with the molecular weight.

This is considered to be due to increase in the degree of shrinkage of polymeric chain with the molecular weight. As the irregular form results in the larger surface area of microcapsules, the irregular microcapsules may be better than the spherical microcapsules on releasing the core material.

3.5. Effects of MC Concentration and MC Species on Initial Release Velocity

The **Figure 9** shows the dependence of the initial release velocity on the MC concentration and the MC species. Also, responsibility to temperature and water of microcapsules prepared in this study is able to be summarized as shown in **Figure 10**.

The effects of MC concentration and MC species and the mechanism of controlled release may be explained according to **Figures 9** and **10** as follows.

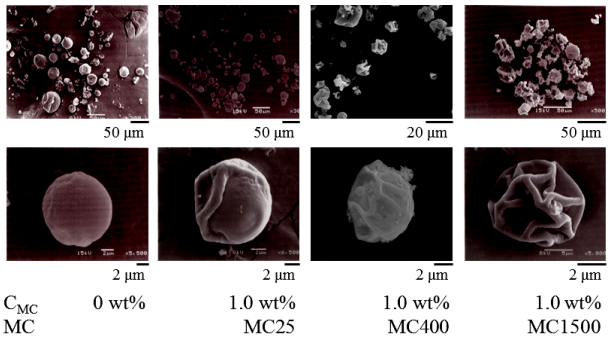


Figure 8. Observation of microcapsules (effect of MC species).

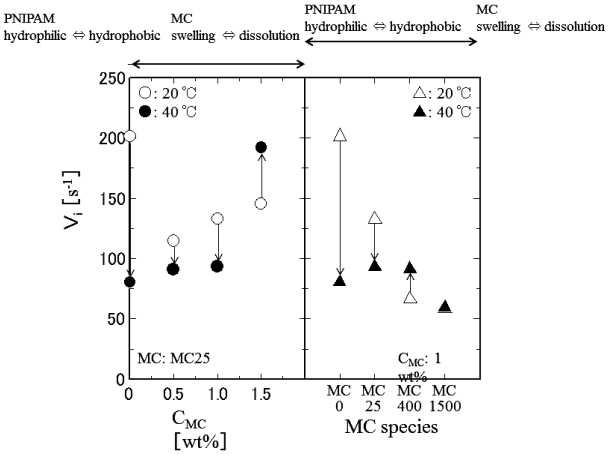


Figure 9. Dependence of initial release velocity on MC concentration and MC species.

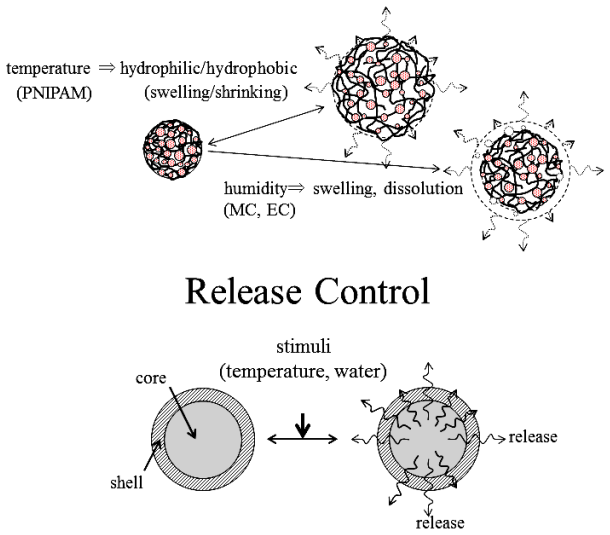


Figure 10. Mechanism of controlled release of core material.

Here, the initial release velocities are obtained from the slope of tangent line at $t = 0$ for the transient feature of released rate as shown in **Figures 3**, **4** and **8**.

In the case of MC25, the initial release velocities at

20˚C are larger than those at 40˚C in the range of MC concentration from C_{MC} = 0 to C_{MC} = 1.0 wt% because of repression of swelling of microcapsules and diffusion of water molecular due to PNIPAM.

However, at C_{MC} = 1.5 wt%, the initial release velocity at 40˚C is larger than that at 20˚C because of increase in swelling and dissolution of MC as stated above.

On the other hand, the initial release velocities at 20˚C are larger than those at 40˚C in the case of C_{MC} = 0 and MC25.

However, the initial release velocity at 40˚C is larger than that at 20˚C in the case of MC400 and the initial release velocities at 20˚C and 40˚C are almost the same in the case of MC1500, because the solubility of MC is decreased with molecular weight.

4. Conclusions

The microcapsules containing hydroquinone as the core material, which were composed of ethyl cellulose, methyl cellulose and P-N-isopropylacrylamid as the shell materials, were prepared with the spray drying method. The following results were obtained.

- Microcapsules were responsive to temperature due to P-N-isopropylacrylamid and water due to methyl cellulose.
- The released rate of HQ at 40˚C was smaller than that at 20˚C because of repression of swelling of microcapsules and diffusion of water molecule due to hydrophobic P-N-isopropylacrylamid.
- At the larger concentration of methyl cellulose, responsibility to water due to methyl cellulose was superior to that to temperature due to P-N-isopropylacrylamid.
- Responsibility to water due to methyl cellulose was decreased with molecular weight of methyl cellulose.

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