

Improvement of Impact Toughness of Sugar-Coated Tablets Manufactured by the Dusting Method

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The purpose of this study was to improve the impact toughness of sugar-coated tablets manufactured by a dusting method. The effects of sugar-coating formulations, which were the sugar-coating suspension formulations and the dusting powder formulations, on impact toughness of sugar-coated tablets were investigated. Impact toughness of sugar-coated tablets was measured by the friability test. We found that the dusting powder formulation was a control factor in impact toughness of sugar-coated tablets manufactured by the dusting method. The dusting method using dusting powder containing 20% microcrystalline cellulose (MCC, Avicel PH-F20) was a useful method for improvement of the impact toughness of sugar-coated tablets. The mechanism of improvement of impact toughness was that MCC in the subcoating layer resulted in a tight bond between the subcoating layer and the smoothing layer and prevented separation of the two layers on impact, because MCC improved the wettability of the subcoating layer, increased the surface roughness of the subcoating layer, and played the role of a binder between the two layers. We confirmed that the MCC between the subcoating layer and the smoothing layer acts to prevent separation of the two layers by impact. We demonstrated that MCC is a suitable material for sugar-coating in order to improve the impact toughness of sugar-coated tablets.

Key words sugar-coated tablets; microcrystalline cellulose; impact toughness; friability; dusting powder; dusting method

Coating is a significant way to improve stability, appearance, easiness to swallow, and to mask unpleasant taste and odor of drugs in tablets.^{1,2)} Of the various kinds of coating, sugar coating has several advantages: masking of unpleasant taste and odor of drugs, elegant appearance, and excellent easiness to swallow.^{3,4)} Since a sugar-coating layer mainly consists of dense sucrose crystals, the sugar-coating layer has both low gas permeability and low water vapor permeability. Maekawa *et al.* have reported that the water vapor and gas permeability coefficients of hydroxypropylcellulose (HPC) were smaller than those of hydroxypropylmethylcellulose (HPMC). Furthermore, they reported that the water vapor and gas permeability coefficients of the sugar-coating layer were one fourth and one eleventh, respectively, those of HPC.⁵⁾ Therefore, when the drug in tablets has an unpleasant odor and taste, a sugar coating should be applied to the tablets in order to mask unpleasant odor and taste.

In contrast, sugar-coated tablets have had several disadvantages: time consuming processes, expert skills required to manufacture, and weakness against impact. In addition, sugar-coating formulations and manufacturing process conditions have been controlled by expert's decisions, relying on empirical knowledge based on past experience. However, due to great advances in pharmaceutical manufacturing technologies and machines, the problems of long manufacturing time and expert skills required to manufacture have been solved. We can manufacture two million sugar-coated tablets automatically by a dusting method in approximately 10 h. In addition, four million sugar-coated tablets can be manufactured automatically in a day in the plant.⁶⁾

Strong impact toughness is indispensable for sugar-coated tablets. If the impact toughness of sugar-coated tablets is weak, cracking or removal of the sugar-coating layer will occur and this will cause deterioration of the characteristics of sugar-coated tablets. Several studies on sugar coating had done,^{5,7–10)} and some characteristics of sugar-coated tablets such as water vapor permeability and gas permeability have

been clarified. However, the disadvantage of weakness against impact has still not been solved. The difficulty of solving this problem has been the complexity of sugar-coating methods, formulations and manufacturing process conditions.

Sugar-coating methods can be classified into two methods. One is the dusting method of sugar coating using a sugar-coating suspension and a dusting powder. The other is the suspension method of sugar coating using a sugar-coating suspension. The dusting method has several advantages compared with the suspension method in the pan. Firstly, the moisture content of sugar-coated tablets manufactured by the dusting method can be lower than that of sugar-coated tablets manufactured by the suspension method, because the dusting powder can expand the surface area for drying in the sugar coating. Secondly, the manufacturing time using the dusting method can be shorter than that using the suspension method, because the dusting powder can promote forming coating layers in the sugar coating. Finally, the dusting method can coat a thick core tablet band, because the dusting powder can expand the thick core tablet band in the sugar coating. Therefore, we have tried to establish a dusting coating formulation that can manufacture sugar-coated tablets which have improved impact toughness.

The purpose of this study was to improve the impact toughness of sugar-coated tablets manufactured using the dusting method. In this study, the effects of sugar-coating suspension formulations and dusting powder formulations on the impact toughness of sugar-coated tablets were investigated. Furthermore, this paper describes a new method for improving the impact toughness of sugar-coated tablets and its mechanism.

Experimental

Materials Core tablets containing fursultiamine hydrochloride, vitamin B₆, vitamin B₁₂, vitamin E were used. The weight, diameter, radius of curvature and thickness of core tablets were 180 mg, 8 mm, 6.5 mm, 4.25 mm, respectively. Sucrose (Ensuiko Sugar Refining Co.) with a mean particle diam-

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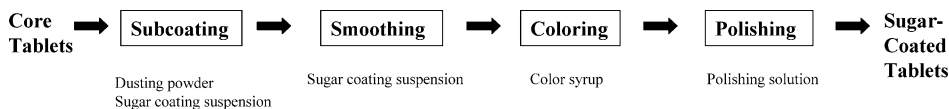


Fig. 1. Manufacturing Flow of Sugar-Coated Tablets

eter measured by laser particle analyzer (Helos & Rodes, Sympatec) of 16.5 μm, talc (Matsumura Sangyo Co.), precipitated calcium carbonate (Nitto Funka Kougyo Co.), titanium dioxide (Ishihara Sangyo), powdered acacia (San-ei Yakuhin Boueki Co.), pullulan (Hayashibara), hydroxypropylmethylcellulose 2208 (HPMC 2208) (SB-4, Shin-Etsu Chemical Co.), lactose (Sorbolac 400, Meggle), microcrystalline cellulose (MCC) (Avicel PH-F20, Avicel PH-101, Ceolus KG-801, Asahi Kasei Co.), and low-substituted hydroxypropylcellulose (L-HPC) (LH-31, Shin-Etsu Chemical Co.) were used for sugar coating.

Manufacturing of Sugar-Coated Tablets by Dusting Method Sugar coating was performed manually in a 12-inch onion pan (Kikusui Seisakusyo). Five thousand tablets were loaded in the pan. The manufacturing flow of sugar coating is described in Fig. 1.

A dusting method can be divided into 4 steps: (1) subcoating, (2) smoothing, (3) coloring, (4) polishing. The feature of the dusting method is the subcoating. The subcoating is applied to round the edges to build up the tablet size. The subcoating step consists of alternately applying a sugar-coating suspension to the tablets followed by dusting with the powders and then drying. Firstly, the sugar-coating suspension is added to the core tablets. Secondly, the tablets are stirred by hand to distribute the suspension. Thirdly, the dusting powder is dusted onto the tablets until no wet tablets show and the tablets again tumble freely. Finally, the tablets are dried by the hot air at 55 °C and the exhaust. The excess dusting powder is removed by the exhaust. The subcoating step was repeated 13 times. The weight of final subcoated tablet was 298 mg. The smoothing step is to smooth out the tablet surface further prior to application of the coloring. The smoothing step consists of alternately applying a sugar-coating suspension to the tablets and then drying. The drying temperature was 55 °C. The weight of final smoothed tablet was 345 mg. The coloring step is to impart the desired color to the tablets. The coloring step consists of alternately applying a coloring syrup to the tablets and then drying. The drying temperature was initially 50 °C, and was gradually reduced to 25 °C. The weight of final colored tablet was 370 mg. The polishing step is to achieve a final gloss. Polishing was achieved by applying a mixture of waxes (carnauba wax and white beeswax) to the tablets in a polishing pan.

Formulations of sugar-coating suspensions and dusting powders are shown in Tables 1 and 2, respectively. The amount of each binder in sugar-coating suspensions was determined to be the upper manufacturing limit from the viewpoint of the viscosity of coating suspensions. A conventional dusting powder mainly consists of talc,¹¹⁾ and dusting powder A listed in Table 2 is a standard dusting powder. Unless otherwise specified, suspension A and dusting powder A were used for the sugar coating. Equilibrium relative humidity (ERH),¹²⁾ as an indicator of moisture content of sugar-coated tablets, was 50 ± 3% in this study.

Manufacturing of Sugar-Coated Tablets by Suspension Method The suspension method can be divided into 3 steps: (1) smoothing, (2) coloring, (3) polishing. Smoothing and coloring were achieved as for the suspension method. The weights of smoothed and colored tablets were 345 and 370 mg, respectively. Polishing was also achieved as for the suspension method. Unless otherwise specified, ERH¹²⁾ of sugar-coated tablets was 50 ± 3% in this study.

Evaluation of Impact Toughness of Sugar-Coated Tablets We used the special friability tester to evaluate the impact toughness of sugar-coated tablets. The friability test is an easy method to measure impact toughness. The friability tester is shown in Fig. 2. The tester consists of a drum and a motor. The diameter of the drum was 50 cm. A stainless steel sheet where tablets were dropped in the test was attached to the inner side of the drum. The friability test was conducted at 30 rpm for 10 min. Twenty tablets were used for the test. Weight loss percentage was calculated as friability. Lower friability means stronger impact toughness. Sugar-coated tablets at 14 d after manufacture were used for the evaluation of impact toughness.

Effect of MCC Level in the Dusting Powder on Friability of Sugar-Coated Tablets MCC level was varied from 5 to 30% in dusting powder D in Table 2. The quantity of talc was reduced with increasing MCC level in order to maintain the weight percentage in dusting powder D. Avicel PH-F20 was used as MCC.

Table 1. Sugar-Coating Suspension Formulations (w/w%)

	Suspension A	Suspension B	Suspension C
Sucrose	41.8	43.5	41.8
Talc	11.5	11.5	11.5
Precipitated calcium carbonate	18.9	18.9	18.9
Titanium dioxide	1.7	1.7	1.7
Powdered acacia	4.9	—	4.3
Pullulan	—	1.6	—
MCC	—	1.6	—
HPMC 2208	—	—	0.6
Purified water	21.2	21.2	21.2

Table 2. Dusting Powder Formulations (w/w%)

	Dusting powder A	Dusting powder B	Dusting powder C	Dusting powder D	Dusting powder E
Talc	98	78	78	78	78
Powdered acacia	2	2	2	2	2
Sucrose	—	20	—	—	—
Lactose	—	—	20	—	—
MCC	—	—	—	20	—
L-HPC	—	—	—	—	20

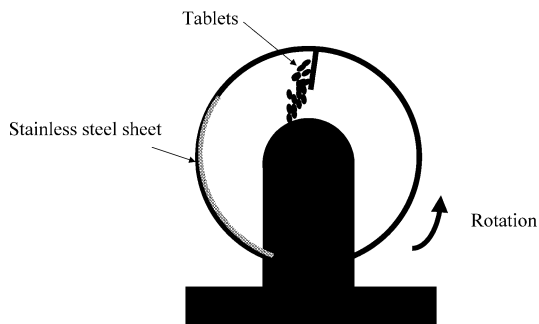


Fig. 2. Schematic Diagram of the Friability Tester

Effect of MCC Grade in the Dusting Powder on Friability of Sugar-Coated Tablets Ceolus KG801, Avicel PH101, and Avicel PH-F20 were used as MCC in dusting powder D in Table 2. MCC level in the dusting powder was 20%.

Effect of Dusting Powder between Subcoating Layer and Smoothing Layer on Friability of Sugar-Coated Tablets The subcoating step was performed 13 times. We manufactured four different kinds of sugar-coated tablets: (1) subcoated tablets manufactured by the dusting method using the dusting powder A from 1st to 13th step in the subcoating, (2) subcoated tablets manufactured by the dusting method using the dusting powder D from 1st to 9th step and the dusting powder A from 10th to 13th step in the subcoating, (3) subcoated tablets manufactured by the dusting method using the dusting powder A from 1st to 9th step and the dusting powder D from 10th to 13th step in the subcoating, and (4) subcoated tablets manufactured by the dusting method using the dusting powder D from 1st to 13th step in the subcoating. Smoothing, coloring, and polishing were performed identically. Impact toughness of these four kinds of sugar-coated tablets was measured.

Wettability The wettabilities of powder beds of sucrose : talc = 1 : 1 and sucrose : talc : MCC (Avicel PH-F20) = 1 : 0.8 : 0.2 were measured by a liquid penetration method.¹³⁾ The specific volume of each powder bed in the exper-

iment was 2.2 ml/g. In this experiment, L , the height of the wetted powder bed, was measured with the time, t .

Surface Roughness of Subcoated Tablets The subcoated tablets manufactured using dusting powder A and the subcoated tablets manufactured using dusting powder D were used for measurement of surface roughness. Surface roughness of subcoated tablets was expressed as an arithmetic average surface roughness (Ra). Ra was calculated from measurements using a color laser microscope (VK-8500, Keyence). Ra was calculated using the following equation:

$$Ra = \frac{1}{n} \sum_{i=1}^n |Z_i - Z| \quad (1)$$

where n is number, Z_i is height, and Z is average height.

Disintegration Test The sugar-coated tablets were subjected to JP XIV disintegration test using an apparatus (disintegration tester, Toyama Sangyo Co.) in water maintained at 37 °C.

Six sugar-coated tablets were used for each disintegration test.

Dissolution Test The sugar-coated tablets were subjected to JP XIV dissolution test using a paddle apparatus (dissolution tester, Toyama Sangyo Co.) in 900 ml of water maintained at 37 °C, which the paddle rotating at 50 rpm. Measurement of fursultiamine hydrochloride release was performed HPLC (model 2690, Waters) with UV detection at 275 nm (model 2487, Waters). The mobile phase used was an aqueous solution of phosphoric acid (1→10000) containing 0.008 M sodium 1-octanesulfonate : methanol (3 : 2) at flow rate of 1.0 ml/min through a column (YMC-Pack ODS AM-303) at 50 °C. Six sugar-coated tablets were used for each dissolution test.

Results and Discussion

Effects of Sugar-Coating Formulation and Manufacturing Method on Impact Toughness of Sugar-Coated Tablets Impact toughness of sugar-coated tablets manufactured by a dusting method and a suspension method was measured. In general, the kinds of binders in sugar-coating formulations affect the impact toughness of sugar-coated tablets. Therefore, the effect of the binder in sugar-coating suspensions on impact toughness of sugar-coated tablets was also investigated. This is shown in Fig. 3. Although pullulan and HPMC 2208 are well known as stronger binders in sugar coating compared with powdered acacia,^{14,15)} the friabilities of the sugar-coated tablets manufactured using sugar-coating suspensions containing pullulan or HPMC 2208 (Suspension B or Suspension C) were not significantly lower than those manufactured using the sugar-coating suspension containing powdered acacia (Suspension A). For the dusting method, the kinds of binders in the sugar-coating suspension did not affect the friability of sugar-coated tablets. The friability of sugar-coated tablets manufactured by the suspension method was lower than that of tablets manufactured by the dusting method even though powdered acacia was used as the binder in the sugar-coating suspension. This finding suggested that the dusting powder plays a more important role in the impact toughness of sugar-coated tablets compared with binders in sugar-coating suspensions.

Effect of Dusting Powder Formulation on Impact Toughness of Sugar-Coated Tablets In order to improve the impact toughness of sugar-coated tablets, we changed the dusting powder formulation. Formulation change was achieved by addition of a binder to the dusting powder. To avoid increased disintegration time of the sugar-coated tablets, sugars or celluloses were chosen as the binder in the dusting powder. In this study, sucrose and lactose were chosen as sugars, and MCC and L-HPC were chosen as celluloses. Figure 4 shows the effect of dusting powder formulation on friability of sugar-coated tablets. Changing the

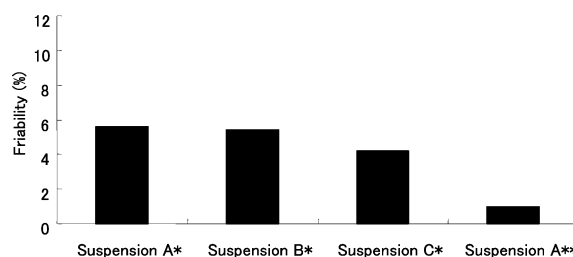


Fig. 3. Effects of Sugar-Coating Formulation and Manufacturing Method on Friability of Sugar-Coated Tablets

*, dusting method; **, suspension method.

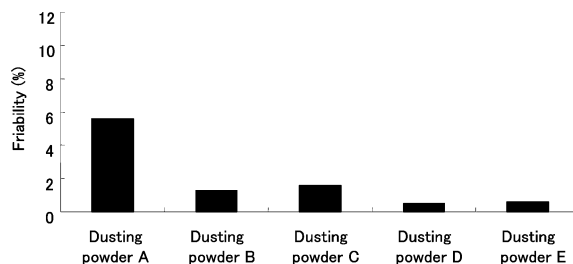


Fig. 4. Effect of Dusting Powder Formulation on Friability of Sugar-Coated Tablets

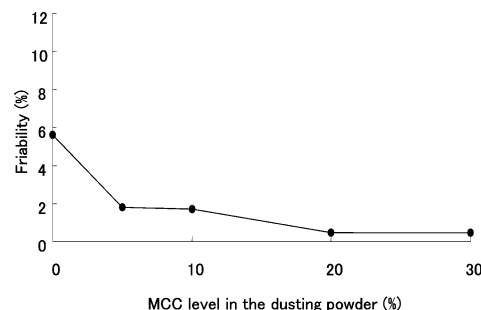


Fig. 5. Effect of MCC Level in the Dusting Powder on Friability of Sugar-Coated Tablets

dusting powder formulation resulted in a decrease of friability of sugar-coated tablets. Impact toughnesses of sugar-coated tablets manufactured with the dusting powder containing celluloses were stronger than those of sugar-coated tablets manufactured with the dusting powder containing sugars. Among the celluloses, we chose MCC as the binder in the dusting powder, because the appearance of tablets made with MCC was better than those made with L-HPC.

Figure 5 shows the effect of MCC level in the dusting powder on friability of sugar-coated tablets. Friability of sugar-coated tablets decreased with increasing level of MCC. Sugar-coated tablets manufactured using dusting powder containing 20% or more MCC had sufficient impact toughness. The optimum MCC level in the dusting powder was 20%, because the percentage of dusting powder adhesion to tablets decreased with increasing MCC level in the dusting powder.

The effect of MCC grade on impact toughness of sugar-coated tablets was investigated. The results are shown in Fig. 6. Sugar-coated tablets manufactured with the dusting powder containing fine MCC (Avicel PH-F20) had strong impact toughness.

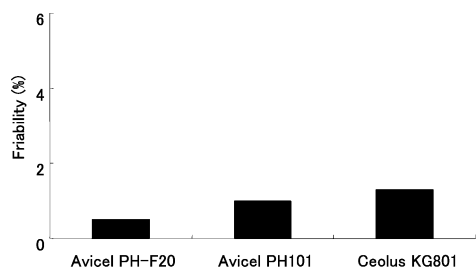


Fig. 6. Effect of MCC Grade in the Dusting Powder on Friability of Sugar-Coated Tablets

Avicel PH-F20 (mean particle size: 16.4 μm); Avicel PH-101 (mean particle size: 57.9 μm); Ceolus KG-801 (mean particle size: 58.5 μm).

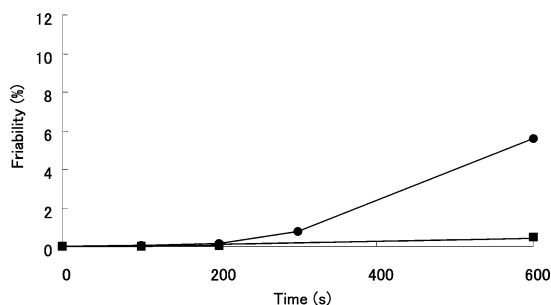


Fig. 7. Relationship between Time and Friability of Sugar-Coated Tablets

●, dusting powder A; ■, dusting powder D.

Ceolus KG-801 is a special grade for compression. In production of tablets, the compactibility of Ceolus KG-801 is superior to that of Avicel PH-101 due to the morphology of Ceolus KG-801.¹⁶⁾ However, in sugar coating, the impact toughness of sugar-coated tablets made with Ceolus KG-801 was almost the same as those made with Avicel PH-101. Furthermore, the impact toughness of sugar-coated tablets made with Avicel PH-F20 was superior to that of tablets made with Ceolus KG-801. It was interesting that this finding differed from the compactibility results of MCC.

The friability of sugar-coated tablets decreased with decreasing MCC mean particle size in the dusting powder. We assumed that the uniformity of MCC in the dusting powder would increase with decreasing MCC mean particle size in the dusting powder. The good distribution of MCC in the dusting powder could lead to good distribution in the subcoating layer, and good distribution in the subcoating layer could cause good impact toughness of sugar-coated tablets.

Mechanism of Improvement of Impact Toughness of Sugar-Coated Tablets In order to clarify the mechanism of improvement of impact toughness of sugar-coated tablets, impact toughness of sugar-coated tablets *versus* time and impact toughnesses of subcoated tablets and smoothed tablets were measured. Figure 7 shows the relationship between time and friability of sugar-coated tablets. The friability of sugar-coated tablets manufactured by the dusting method using dusting powder A increased significantly with time, due to cracking and removal of both the coloring layer and the smoothing layer from the tablets. After the friability test, the separation between the subcoating layer and the smoothing layer on sugar-coated tablets manufactured by the dusting method using dusting powder A was observed. Interestingly, the friability of sugar-coated tablets manufactured by the dusting method using dusting powder D increased slightly

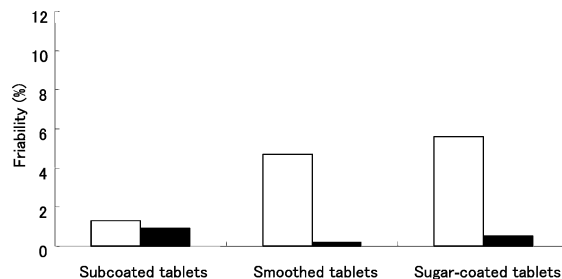


Fig. 8. Effect of Dusting Powder Formulation on Friability of Subcoated Tablets, Smoothed Tablets, and Sugar-Coated Tablets

□, dusting powder A; ■, dusting powder D.

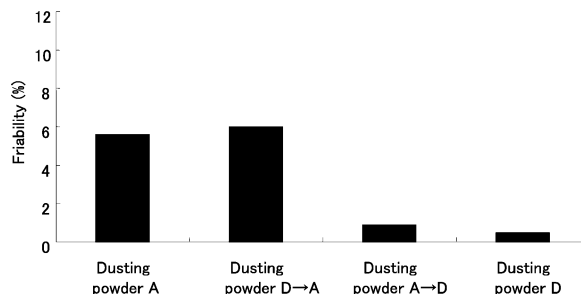


Fig. 9. Effect of Dusting Powder Formulation between Subcoating Layer and Smoothing Layer on Friability of Sugar-Coated Tablets

Dusting powder A, dusting powder of subcoating step from 1st to 13th is dusting powder A; dusting powder D→A, dusting powder of subcoating step from 1st to 9th is dusting powder D and dusting powder of subcoating step from 10th to 13th is dusting powder A; dusting powder A→D, dusting powder of subcoating step from 1st to 9th is dusting powder A and dusting powder of subcoating step from 10th to 13th is dusting powder D; dusting powder D, dusting powder of subcoating step from 1st to 13th is dusting powder D.

with time.

Figure 8 shows the friabilities of subcoated tablets, smoothed tablets, and sugar-coated tablets. The friability of subcoated tablets was not significantly affected by the dusting powder formulation. In contrast, the friability of smoothed tablets was significantly affected by the dusting powder formulation. The friability of smoothed tablets manufactured by the dusting method using dusting powder D was lower than that of tablets manufactured by the dusting method using dusting powder A. Furthermore, no separation between the subcoating layer and the smoothing layer by impact was observed when using dusting powder D.

In order to confirm our assumption that the bonding between these two layers is a critical factor in impact toughness of sugar-coated tablets manufactured by the dusting method, we changed the dusting powder in the process of subcoating. Figure 9 shows the effect of the dusting powder between the subcoating layer and the smoothing layer on the friability of sugar-coated tablets. The sugar-coated tablets with dusting powder A in the later steps in the subcoating did not show good impact toughness even though dusting powder D was used in the early steps in the subcoating. In contrast, the sugar-coated tablets with dusting powder D in the later steps in the subcoating showed good impact toughness even though dusting powder A was used in the early steps. We confirmed that MCC in the entire subcoating layer is not essential for the prevention of separation of the two layers by impact and MCC between the subcoating layer and the smoothing layer can act to prevent separation of the two layers by impact. In other words, MCC between the subcoating

layer and the smoothing layer played an important role in improving the impact toughness of sugar-coated tablets.

Felton and McGinity reported that the wettability of the tablet surface was one of the most important factors in adhesion of polymeric films to the tablets in coating.¹⁷⁾ Nadkarni *et al.* suggested that the better the wetting of the tablet by film coating solution, the better was the film adhesion.¹⁸⁾ Fisher and Rowe found that the adhesion with low-viscosity coating solution was higher than that with high-viscosity coating solution, because the rate of penetration of the low-viscosity coating solution into the tablets would be much faster than that of the high-viscosity coating solution.¹⁹⁾ Lehtola *et al.* suggested that uniform wetting of tablet cores with coating solution and good adhesion between a coating film and the surface are desirable properties in a film coating process. They reported that film adhesion to tablet surface increased with a decrease in contact angle between the coating solution and tablets.²⁰⁾ Therefore, we assumed that an im-

provement of wettability of the subcoating layer would result in improved bonding between the subcoating layer and the smoothed coated layer. Figure 10 shows wettability of sucrose-talc powder and sucrose-talc-MCC powder. Wettability of sucrose-talc-MCC powder was superior to wettability

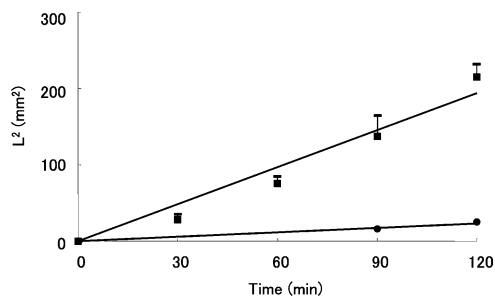


Fig. 10. Wettability
 ●, sucrose : talc = 1 : 1; ■, sucrose : talc : MCC = 1 : 0.8 : 0.2 (mean ± S.D.; n = 3).

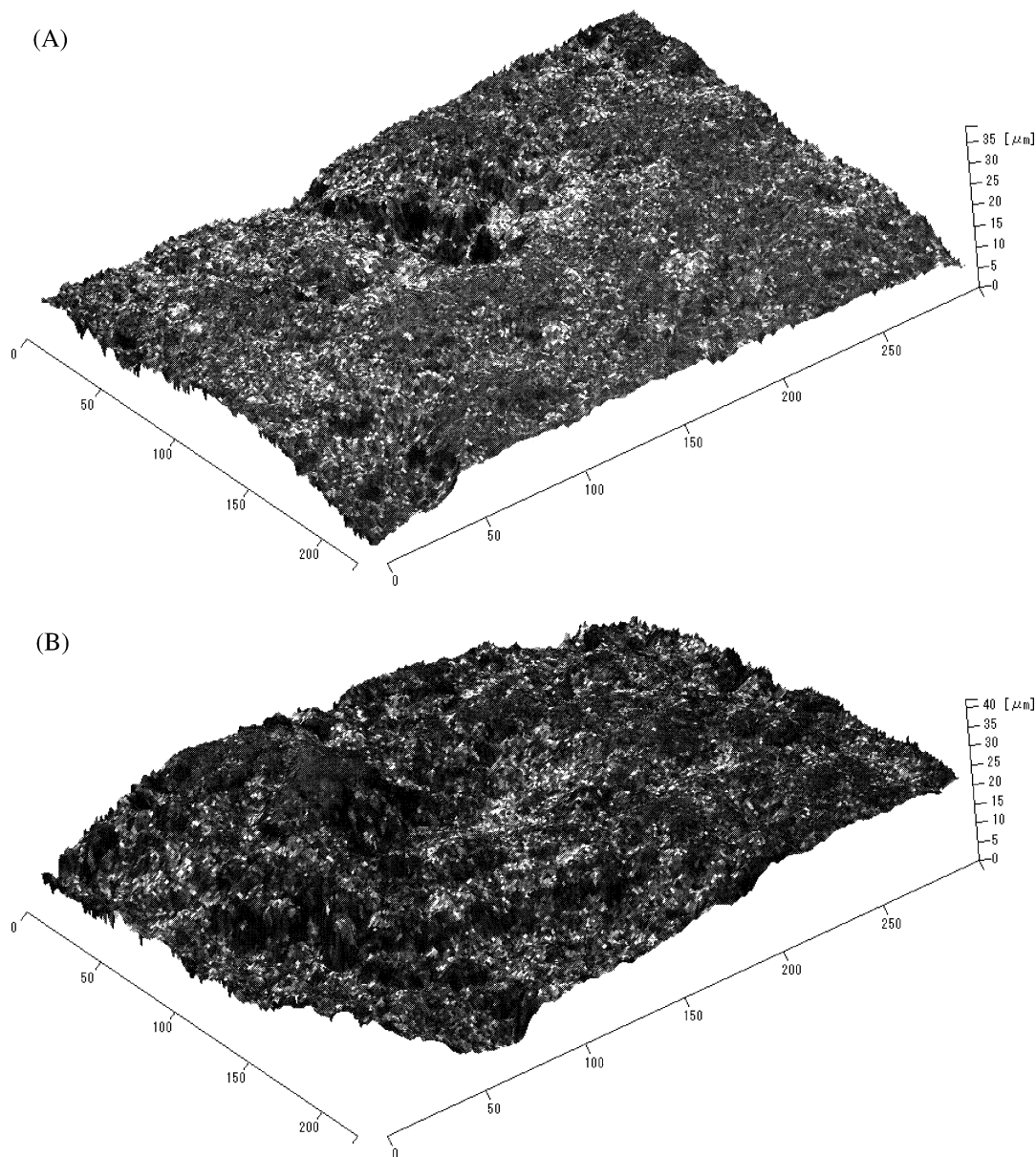


Fig. 11. Three Dimensional Diagrams of Surface Roughness of Subcoated Tablets

(A) Subcoated tablets manufactured by the dusting method using dusting powder A; (B) subcoated tablets manufactured by the dusting method using dusting powder D.

of sucrose-talc powder. Incorporating MCC in sucrose-talc powder improved the wettability. The improvement of wettability of subcoating layer would result in an improvement of impact toughness.

Beside wettability, the binding ability between the layers is one of the most important factors in coating. MCC is well known as a strong binder.^{21–23} MCC would act as a binder between the subcoating layer and the smoothing layer and promote strong binding between the two layers.

Nadkarni *et al.* suggested that an increase in tablet surface roughness also increased film adhesion to the tablet.¹⁸ Rowe suggested that the adhesion to the tablet was found to be influenced by tablet surface roughness.²⁴ Therefore, when considering the bonding between the layers, surface roughness would be one of the factors in controlling bonding between the layers. Figure 11 shows the difference in surface roughness of the subcoated tablets manufactured by the dusting method using dusting powder A and dusting powder D. *Ra* of the subcoated tablets manufactured by the dusting method using dusting powder A was 2.389 μm . On the other hand, *Ra* of the subcoated tablets manufactured by the dusting method using dusting powder D was 4.922 μm . An increase in surface roughness of the subcoating layer caused an increase in the surface area available for bonding between the two layers.

We clarified that the subcoating layer incorporating MCC had good wettability of the layer and good bonding ability. Therefore, bonding between the subcoating layer and the smoothing layer became tight and strong. This prevented separation between the subcoating layer and the smoothing layer by impact. In other words, the impact toughness of sugar-coated tablets was improved. An increase in roughness of the subcoating layer also plays a role in the improvement of impact toughness.

Disintegration Time and Dissolution Profiles on the Sugar-Coated Tablets Disintegration time of sugar-coated tablets manufactured using dusting powder A and that manufactured using dusting powder D were 22.0 and 21.2 min, respectively. We confirmed that MCC in the subcoating layer did not significantly affect disintegration time on the sugar-coated tablets. Dissolution profiles of fursultiamine hydrochloride from the sugar-coated tablets are shown in Fig. 12. Dissolution profiles of fursultiamine hydrochloride from sugar-coated tablets manufactured using dusting powder A and that manufactured using dusting powder D were similar. We also confirmed that MCC in the subcoating layer did not significantly affect dissolution characteristics on the sugar-coated tablets.

Conclusions

We found that dusting powder formulation played an important role in the impact toughness of sugar-coated tablets manufactured by the dusting method. The insufficient impact toughness of sugar-coated tablets manufactured by the standard dusting method was due to insufficient bonding between the subcoating layer and the smoothing layer. The dusting method using dusting powder containing microcrystalline cellulose (MCC) improved the impact toughness of sugar-coated tablets. The optimum MCC level in the dusting powder was 20% and optimum MCC grade was fine grade, Avicel PH-F20.

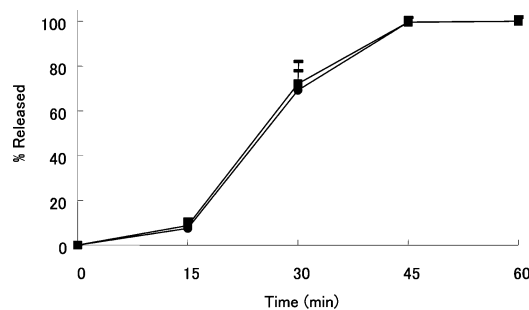


Fig. 12. Dissolution Profiles of Fursultiamine Hydrochloride from Sugar-Coated Tablets

●, dusting powder A; ■, dusting powder D (mean \pm S.D.; $n=6$).

MCC improved the wettability of the subcoating layer and played a role of binder between the subcoating layer and the smoothing layer. An increase in surface roughness of the subcoating layer incorporating MCC also played a role in ensuring tight bonding between the subcoating layer and the smoothing layer. Therefore, MCC in the subcoating layer resulted in a tight bond between the subcoating layer and the smoothing layer and prevented separation between the subcoating layer and the smoothing layer by impact. MCC between the subcoating layer and the smoothing layer is essential for the prevention of separation of the two layers by impact. Incorporating MCC in dusting powder is a useful manufacturing method for sugar coating in order to improve the impact toughness of sugar-coated tablets.

We confirmed that MCC in the subcoating layer did not significantly affect disintegration time and dissolution characteristics on the sugar-coated tablets.

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