The Role of Binders in the Prevention of Capping within a Tablet

Ken-ichi SUGIMORI,*,[a] Shoichi MORI[a] and Yoshiaki KAWASHIMA[b]

Technology Development Laboratories, Takeda Chemical Industries, Ltd.,[a] 2-17-85, Juso-honmachi, Yodogawa, Osaka 532, Japan and Gifu Pharmaceutical University,[b] 5-6-1, Mitahora-higashi, Gifu 502, Japan. *Received November 1, 1988*

The role of a dry or wet binder in the prevention of capping within a tablet was evaluated by considering the binding strength of compacts and the residual die wall pressure during compression.

Capping of bucetin tablets was not prevented by adding dried colloidal silica, which increased the binding strength and the residual pressure. However, the addition of dried low-substituted hydroxypropyl cellulose, which increased the binding strength but decreased the residual pressure, prevented the capping.

The effect of addition methods of a low viscosity grade of hydroxypropyl cellulose and α-starch was also investigated for bucetin and ascorbic acid tablets. The compacts showed the greatest binding strength when the binders were added in a wet state. However, the residual die wall pressure did not depend on the addition method. These results suggest that the addition of a binder in the wet method is effective for the prevention of the capping.

Keywords tablet; capping; binder; binding strength; residual die wall pressure; capping index

When pharmaceutical powders are compacted into tablets, uniform tablets sometimes can not be obtained since cracks are generated within the tablet. This phenomenon is usually referred to as "capping". Prevention of capping has been a subject of studies for a long time.[1,2] Capping has been correlated to the die wall pressure during tableting,[3-7] or to the compressibility indices of powders.[8-12] However, much remains to be learned about these events.

The authors in this context have previously investigated the characteristics of the die wall pressure during the decompression process, and concluded that capping could be regarded as cracking of a powder compact by a high residual die wall pressure.[13] It was also found that capping occurred when the residual die wall pressure exceeded the binding strength of the compact.

The authors proposed an indicator, the capping ratio, to quantitatively evaluate cracking within a tablet[13];

$$\text{capping ratio} = (F_u - F)/F_u \quad (1)$$

where F is the diametrical crushing strength of the tablet compacted by an ordinary method and F_u is that of the tablet which is uniformly compacted by the loaded ejection method.[14,15] The capping ratio becomes zero for the tablet without capping, and becomes unity for the tablet with complete capping.

The authors further proposed another indicator, the capping index, to predict the capping tendency of tablets[13];

$$\text{capping index} = Q_r/P_c \quad (2)$$

where Q_r is the residual die wall pressure during compaction and P_c is the binding strength of the compacted powder. When the capping index exceeds unity, capping will occur.

The residual die wall pressure of a convex-faced tablet (Q_{rc}) is higher than that of a flat-faced one (Q_{rf}). These two residual pressures can be related by Eq. 3[13];

$$(Q_{rc} - Q_{rf})/Q_{rf} = 0.7\,(T_v - T_e)/T_e \quad (3)$$

where T_v is the thickness of the flat-faced tablet having the same volume as that of the convex-faced tablet and T_e is the edge thickness at the periphery of the convex-faced tablet.

In this study, the effect of added binders on the binding strength of compacts and on the residual die wall pressure was investigated, and the role of the binder in the prevention of capping was clarified.

Experimental

Materials Hydroxybutyl phenetidin (bucetin, Yamato Chemicals, Ltd., Japan) and ascorbic acid (Takeda Chemical Industries, Ltd., Japan) were used as drug powders. Bucetin is relatively insoluble in water, while ascorbic acid is soluble in water.

A colloidal silica (Syloid 266, Fuji Davison Chemicals Ltd., Japan), a low-substituted hydroxypropyl cellulose (L-HPC, Shin-etu Chemicals Ltd., Japan), a low viscosity grade of hydroxypropyl cellulose (HPC-L, Nippon Soda Co., Ltd., Japan) and α-starch (Nichiden Chemicals, Ltd., Japan) were used as binders. HPC-L (50—200 μm) and α-starch (50—200 μm) were micronized by a jet mill (Nihon Pneumatic Co., Ltd., Japan). The particle sizes of micronized HPC-L and micronized α-starch were 1—10 and 5—20 μm, respectively.

Dry Mixing and Wet Granulation Dry mixing of a binder was carried out using a mortar and pestle. The binder was mixed with the drug powder, carefully avoiding grinding.

Wet granulation was also performed using a mortar and pestle. The drug powder was massed by adding an aqueous solution containing the binder, dried in a vacuum dryer at 50 °C for 8 h, and sieved through a 500 μm screen. The dry-mixed powders were also dried under the same conditions to equalize moisture content.

Compression Apparatus A compression test apparatus (Autograph, Shimadzu Corporation, Ltd., Japan) was utilized for the compaction of powder, and for the measurements of the die wall pressure and the crushing strength of compacts or tablets.

The loaded ejection type compaction apparatus[14,15] was used for the uniform compaction of powder. This apparatus enabled the powder to be compacted without capping.

Measurement of the Binding Strength of Compacts The powder was compacted into a cylindrical compact without cracks using the loaded-ejection-type compaction apparatus. Conditions for the compaction were as follows: diameter of die, 8 mm; shape of punch, flat-faced; weight of powder, 400 mg; compaction pressure, 2000 kg/cm^2; compression and decompression speeds, 0.5 mm/min; ejection load, 50 kg; loaded ejection speed, 0.5 mm/min. The die was lubricated before each compaction with a very small amount of magnesium stearate.

These compacts were compressed in an axial direction at 0.5 mm/min using the compression test apparatus, and their crushing strengths (P_c, kg/cm^2) were determined. These crushing strengths were regarded as the binding strength of the compacted powder.[13]

Measurement of the Residual Die Wall Pressure A die with a constricted center section was used for the measurement of the die wall pressure. The die wall pressure was detected with a strain gauge attached to the outer surface of the die. The output of the gauge was connected to a strain meter and a recorder. The values obtained were calibrated by compressing paraffin wax and silicone rubber, which behave like liquids under compressive pressure. The residual die wall pressure (Q_r, kg/cm^2) was determined by extrapolating the die wall pressure in a decompression

process to the intercept.[13]

Measurements were carried out under the following condition: diameter of die, 8.5 mm; shape of punch, flat-faced; weight of powder, 200 mg; compaction pressure, 2000 kg/cm^2; compression speed, 5 mm/min; decompression speed, 0.5 mm/min. The die was lubricated before each measurement with a very small amount of magnesium stearate.

Tablet Preparation and Measurement of Its Strength Tablets were prepared by using the ordinary press and the loaded-ejection-type compaction apparatus. Conditions adopted were as follows: diameter of die, 10 mm; radius of curvature of punch, 7.5 mm; weight of powder, 350 mg; compaction pressure, 2000 kg/cm^2; compression speed, 5 mm/min; decompression speed, 25 mm/min. In the ordinary method tablets were ejected from the die at 100 mm/min, and in the loaded ejection method they were ejected at 25 mm/min under 44 kg ejection load. The die was lubricated before each compaction with a very small amount of magnesium stearate.

These tablets were compressed in a diametrical direction using the compression test apparatus, and their crushing strengths (F or F_u, kg) were determined. The values from several runs were averaged.

Results and Discussion

The Role of Colloidal Silica as a Dry Binder in Preventing Capping The addition of binders is the simplest method for increasing the binding strength of tableted powders. The binder which is added by a dry mixing method is referred to as a dry binder. Colloidal silica is an extremely fine silicic anhydride and is one of the dry binders. In this section, the effect of colloidal silica on the uniform compaction of powders is discussed. Bucetin, which has low binding strength and strong capping tendency, was used as a drug powder. Colloidal silica was added to bucetin by the dry mixing method, and the compaction characteristics of the mixed powders were evaluated.

The binding strength and the residual die wall pressure of the mixture are shown in Fig. 1. Bucetin exhibited low binding strength and high residual pressure. The addition of colloidal silica remarkably increased the binding strength of the mixture, and slightly increased the residual die wall pressure.

These powders were compacted into convex-faced tablets and the capping ratio was determined. The results are presented in Table I. The addition of colloidal silica did not lower the capping ratio. Thus, the capping tendency of the tablets was not reduced by the addition of colloidal silica.

This phenomenon was analyzed with respect to the capping index. The residual die wall pressures of the convex-faced tablets (Q_{rc}) were calculated using Eq. 3, and are listed in Table I. The resultant capping index and capping ratio are illustrated in Fig. 2.

The value of capping index was decreased slightly as colloidal silica was added, but was not lowered to a level below unity. This indicated that the capping tendency of the powder was not sufficiently improved by the addition of colloidal silica. Actually, their capping ratios were near unity and capping was not prevented.

These results suggest that the addition of a binder is ineffective in the prevention of capping unless it reduces the residual die wall pressure, even if it increases binding strength.

The Role of L-HPC as a Dry Binder in Preventing Capping L-HPC behaves as a binder and disintegrant. Hence. L-HPC is used as a dry binder for a drug which is relatively insoluble in water. L-HPC was mixed with bucetin in a dry state, and its compaction characteristics were estimated.

The binding strength of the compacts and the residual die wall pressure of the tablets are shown in Fig. 3. The binding

TABLE I. Capping Ratio and Calculated Residual Die Wall Pressure of Convex-Faced Tablets Composed of Bucetin and Colloidal Silica

Silica (%)	F_u (kg)	F (kg)	Capping ratio	Q_{rc} (kg/cm^2)
0	6.0	0	1.00	335
3	12.2	0.2	0.98	400
5	12.0	0.4	0.96	415
10	15.6	0.6	0.96	390

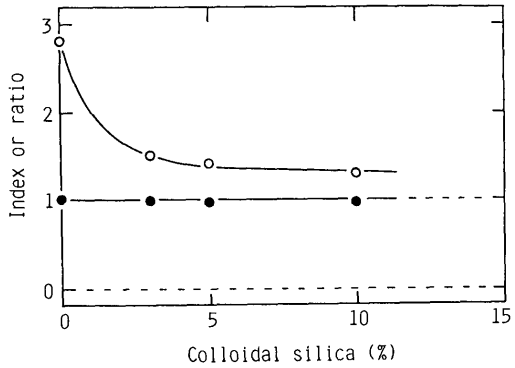

Fig. 2. Capping Index and Capping Ratio of Convex-Faced Tablets Composed of Bucetin and Colloidal Silica

○, capping index; ●, capping ratio.

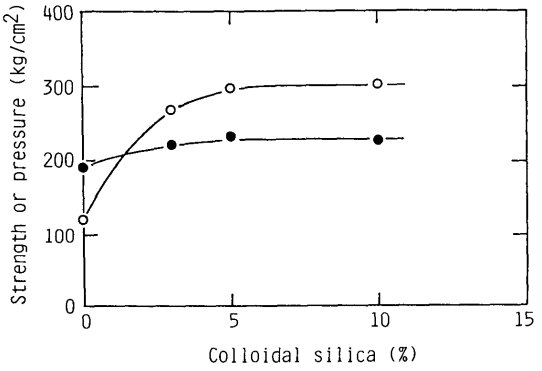

Fig. 1. Binding Strength and Residual Die Wall Pressure of Compacts Composed of Bucetin and Colloidal Silica

○, binding strength; ●, residual pressure.

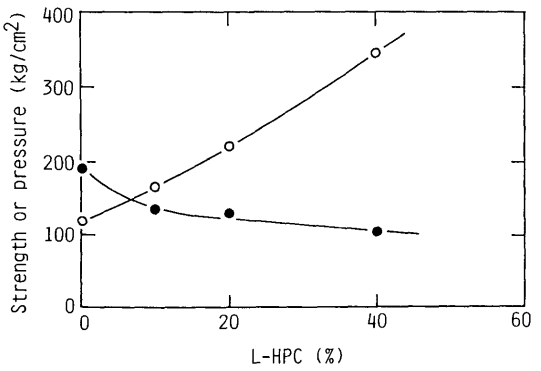

Fig. 3. Binding Strength and Residual Die Wall Pressure of Compacts Composed of Bucetin and L-HPC

○, binding strength; ●, residual pressure.

strength increased linearly with the addition of L-HPC. However, the extent of the effect was significantly smaller than that in the case of colloidal silica. On the other hand, the residual die wall pressure was lowered by the addition of L-HPC.

The capping ratios of convex-faced tablets made of these powders are shown in Table II. Capping was prevented by adding 40% L-HPC.

These results were also analyzed in terms of the capping index. The calculated residual die wall pressures of the convex-faced tablets are shown in Table II. The resultant capping index and capping ratio are illustrated in Fig. 4. The capping index was lowered by the addition of L-HPC, and decreased to below unity. The capping ratio decreased as the capping index decreased to a level below unity, and reached zero when the capping index was about 0.5.

These facts indicate that the decrease in the residual die wall pressure with the addition of L-HPC was effective to prevent capping. However, a large amount of L-HPC, *e.g.* 40%, was required for the complete prevention of capping. This is because the binding strength of the powder is not greatly increased by the addition of L-HPC.

The Role of HPC-L as a Wet Binder in Preventing Capping In a tableting process, powders are often granulated with a solution containing a binder. The binder used in this method is referred to as a wet binder. The main purpose of wet granulation is to increase the particle size by aggregation and to improve the flowability of the powder. In addition, this procedure also increases the binding strength of the powder. In this section, the effect of wet binders on the uniform compaction of powder is discussed.

Bucetin was granulated with HPC-L aqueous solution. For comparison, unmicronized or micronized HPC-L was added to bucetin by a dry mixing method.

The binding strengths of the compacts are shown in Fig. 5. The strength in the case of the wet granulation method was significantly higher than that obtained by the dry mixing method. However, the dry mixing of the micronized binder did produce a significant increase in the binding strength, although it was less than that achieved by the wet granulation method. These facts indicate that the strength of the compact is highly dependent on the particle size of the binder. It is assumed that the particles of HPC-L may be effectively micronized by the wet granulation process.

The residual die wall pressures of the tablets are shown in Fig. 6. They were reduced by the addition of HPC-L. However, they were independent of the particle size and type of the binder, and depended merely on the amount of the binder added. The residual die wall pressure may

TABLE II. Capping Ratio and Calculated Residual Die Wall Pressure of Convex-Faced Tablets Composed of Bucetin and L-HPC

L-HPC (%)	F_u (kg)	F (kg)	Capping ratio	Q_{rc} (kg/cm^2)
0	6.0	0	1.00	335
10	6.8	0.6	0.91	250
20	8.4	3.0	0.64	240
40	12.0	11.8	0.02	175

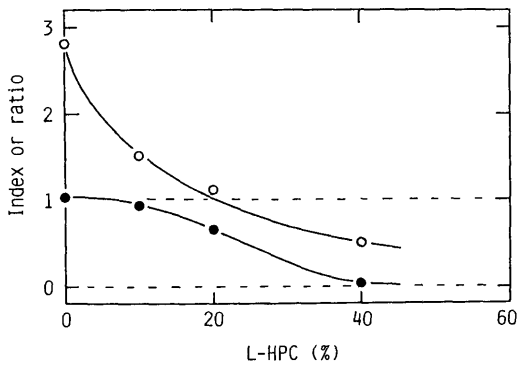

Fig. 4. Capping Index and Capping Ratio of Convex-Faced Tablets Composed of Bucetin and L-HPC

○, capping index; ●, capping ratio.

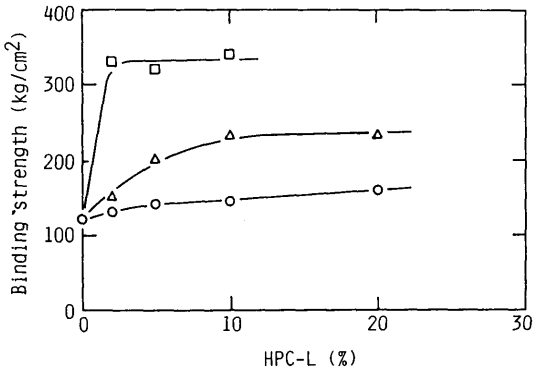

Fig. 5. Binding Strength of Compacts Composed of Bucetin and HPC-L

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

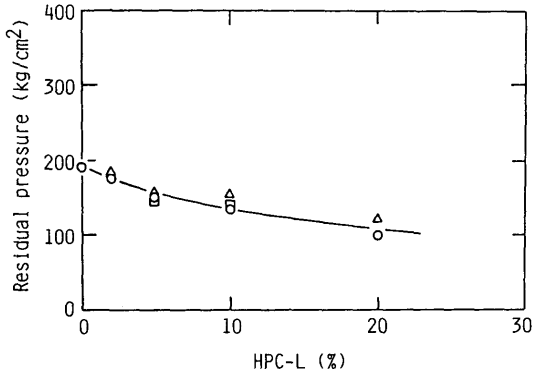

Fig. 6. Residual Die Wall Pressure of Tablets Composed of Bucetin and HPC-L

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

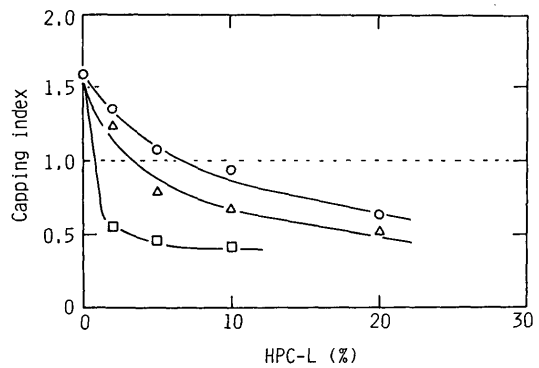

Fig. 7. Capping Index of Flat-Faced Tablets Composed of Bucetin and HPC-L

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

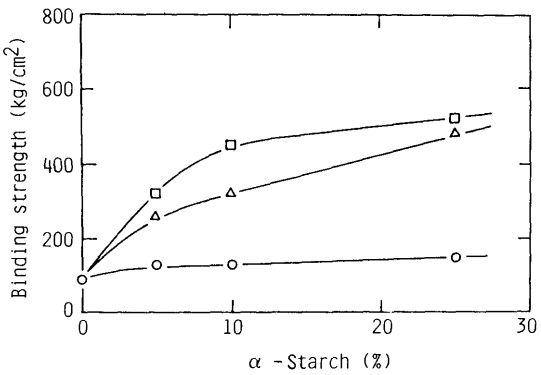

Fig. 8. Binding Strength of Compacts Composed of Ascorbic Acid and α-Starch

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

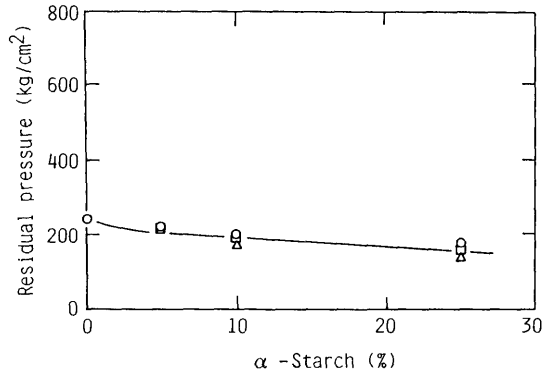

Fig. 9. Residual Die Wall Pressure of Tablets Composed of Ascorbic Acid and α-Starch

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

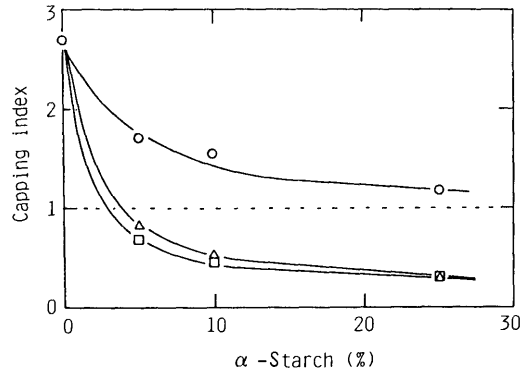

Fig. 10. Capping Index of Flat-Faced Tablets Composed of Ascorbic Acid and α-Starch

○, dry mixing; △, dry mixing (micronized); □, wet granulation.

depend on the rheological properties of powders.

Figure 7 shows the calculated capping indices of flat-faced tablets. The addition of HPC-L by the wet granulation method greatly decreased the capping index, and was considered to be effective in uniformly compacting tablets. This is due to the fact that it decreased the residual die wall pressure and greatly increased the binding strength.

The Role of α-Starch as a Wet Binder in Preventing Capping Another typical binder used in pharmaceutical wet granulation is α-starch. It is often used to granulate water-soluble drugs. In this case, ascorbic acid, as a water-soluble drug powder, was granulated with an aqueous solution of α-starch. For comparison, ascorbic acid was also mixed with unmicronized and micronized α-starch, both in a dry state.

The binding strengths of the compacts are shown in Fig. 8. The wet granulation method remarkably increased the binding strength, and the micronized α-starch mixed by the dry mixing method also increased the binding strength.

The results for the residual die wall pressure are illustrated in Fig. 9. The residual die wall pressure was reduced by the addition of α-starch. No difference was observed in relation to the particle size of the binder or the type of the binder.

The calculated capping indices of the flat-faced tablets are shown in Fig. 10. The results were quite similar to those for the bucetin and HPC-L mixture. However the capping index for the wet granulation method was not much lower than that for the dry mixing with micronized α-starch. It was considered that this was because ascorbic acid partially dissolved in the binder solution and the binding effect of α-starch was reduced.

Criteria for Selecting Binders to Achieve Uniform Compaction In order to obtain uniform tablets, it is necessary that the powders have adequate binding strength and a sufficiently low capping index, *i. e.*, low residual die wall pressure.

Drugs with a high binding strength and low residual pressure can be easily compacted into tablets. Drugs with a high binding strength and high residual pressure will be satisfactorily compacted if a powder, such as L-HPC, is added which decreases the residual pressure without decreasing the binding strength. For drugs with a low binding strength and low residual pressure, a binder which increases the binding strength, such as colloidal silica or fine dry binders, should be added.

Drugs with a low binding strength and high residual pressure are the most difficult to compact uniformly. For such drugs, the binding strength should be increased and the residual pressure should be decreased. The results obtained in this study suggest that a binder with a low residual die wall pressure should be added in a fine state. It was also found that the wet granulation method was useful for the micronization of binder particles and thus was effective to prevent capping.

References

1) D. Train, *J. Pharm. Pharmacol.*, **8**, 745 (1956).
2) E. Shotton and D. Ganderton, *J. Pharm. Pharmacol.*, **13**, 144T (1961).
3) W. M. Long, *Powder Metallurgy*, **6**, 73 (1960).
4) S. Leigh, J. E. Carless and R. W. Burt, *J. Pharm. Sci.*, **56**, 888 (1967).
5) E. Shotton and B. A. Obiorah, *J. Pharm. Sci.*, **64**, 1213 (1975).
6) E. Doelker and E. Shotton, *J. Pharm. Pharmacol.*, **29**, 193 (1977).
7) E. N. Hiestand, J. E. Wells, C. B. Peot and J. F. Ochs, *J. Pharm. Sci.*, **66**, 510 (1977).
8) H. E. N. Hiestand and D. P. Smith, *Powder Technology*, **38**, 145 (1984).
9) P. J. Jarosz and E. L. Parrott, *J. Pharm. Sci.*, **71**, 607 (1982).
10) A. B. Bangudu and N. Pilpel, *J. Pharm. Pharmacol.*, **37**, 289 (1985).
11) O. Ejiofor, S. Esezobo and N. Pilpel, *J. Pharm. Pharmacol.*, **38**, 1 (1986).
12) W. E. Jetzer, *J. Pharm. Pharmacol.*, **38**, 254 (1986).
13) K. Sugimori, S. Mori and Y. Kawashima, *Chem. Pharm. Bull.*, accepted.
14) Y. Funakoshi, T. Kajiura and T. Asogawa, *Zairyo*, **18**, 547 (1969).
15) Y. Funakoshi, *Zairyo*, **24**, 673 (1975).