

## Effect of Powder Flowability on Capsule-Filling-Weight-Variation

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The relation between variation of filling-weight and powder-flowability was studied in connection with filling mechanism.

OCF-120 and Höfliger-Karg-GKF-1000 were used as a capsule-filling machine of the pouring type and of the stamping type, respectively.

The angle of repose, the minimum orifice diameter and the discharge rate through orifices were measured. The minimum orifice diameter was closely related to the discharge rate through orifices. No good correlations were found between the angle of repose and the minimum orifice diameter. The angle of repose was used as an index of flowability representing the mobility of the particles on the surface of a powder bed and the minimum orifice diameter was used as one representing the mobility of the particles in a powder bed under dynamic conditions.

In the case of OCF-120, a good correlation between the variation of filling-weight and the minimum orifice diameter was found.

In the case of Höfliger-Karg-GKF-1000, the variation of filling-weight was closely related to the angle of repose but a minimum point appeared in the plots of the angle of repose *vs.* the coefficient of variation of filling-weight. This finding is explained as follows: as the angle of repose increases, the variation of filling-weight is governed by both the increasing factor and the decreasing factor, namely the variation of the powder-bed-height in the filling box and that of the amount of jumping-out of the filled powder, respectively.

**Keywords**—capsule; powder; variation of filling-weight; filling mechanism; angle of repose; minimum orifice diameter; discharge rate through orifices

### Introduction

Content-uniformity of dosage-form-products is a very important quality related to efficiency and safety in treating with drugs. Weight-variation of the products is one of the factors related to content-uniformity. In tableting machines or capsule-filling machines, powdery materials are not divided gravimetrically but filled volumetrically into the die-cavities or the capsule-bodies. Therefore, it is important to know the effect of powder characteristics and filling-mechanism on weight-variation in the case of such volumetrical dividing.

Some relations between powder characteristics and weight-variation in the hard-capsule-filling machines or in the rotary presses have been published.<sup>2)</sup> The relations, however, have been determined empirically and the physical meaning of the relations has not been elucidated in connection with the filling mechanism of the machines. Therefore, the relations are considered to be applied only within the conditions of the experiments and not beyond the range with high reliability.

Automatic high-speed hard-capsule-filling machines on the market are classified into three types from the point of filling mechanism as follows:

Type-A: by pouring powder into capsule-bodies

Type-B: by stamping powder with plungers into die-cavities or capsule-bodies

1) Location: *Hiromachi, Shinagawa-ku, Tokyo.*

2) G.M. Irwin, G.J. Dodson, and L.J. Ravin, *J. Pharm. Sci.*, **59**, 547 (1970); G. Reier, R. Cohn, S. Rock, and F. Wagenblast, *J. Pharm. Sci.*, **57**, 660 (1968); G. Gold, R.H. Duvall, B.T. Palermo, and J.G. Slater, *J. Pharm. Sci.*, **57**, 2153 (1968).

Type-C: by inserting hollow cylindrical dosing funnels equipped with pistons into a powder bed and consolidating the powder in the funnels by the pistons and carrying the molded powder on capsule-bodies and dropping into the bodies.

Type-A machines are almost equipped with powder-fluidifying devices, for example, vibrators or agitators. In the case of Type-C machines, weight-variation is related mainly to moldability and adhesiveness of powder.<sup>3)</sup>

The relations between the weight-variation of capsules filled with Type-A or B machines and the angle of repose or the discharge characteristics from orifices were studied in connection with the filling mechanism. The physical meanings of the discharge characteristics from orifices and the angle of repose are different from each other and have been reported in the previous papers.<sup>4)</sup>

### Experimental

**Apparatus and Method**—The angle of repose and the discharge characteristics from orifices were determined by use of the same apparatus and procedure as in the previous papers.<sup>4)</sup>

OCF-120 was used as a machine of Type-A. The filling mechanism of OCF-120 is shown in Fig. 1 and the shaded portion indicates a powdery sample. The perforated plate set in the powder bed was connected to a vibrator and the powder bed was fluidified by vibration of this plate. The block holding the capsule-bodies is a disk plate and turns continuously in a constant speed. In this experiment OCF-120 was driven at the filling rate of 1500 capsules/min.

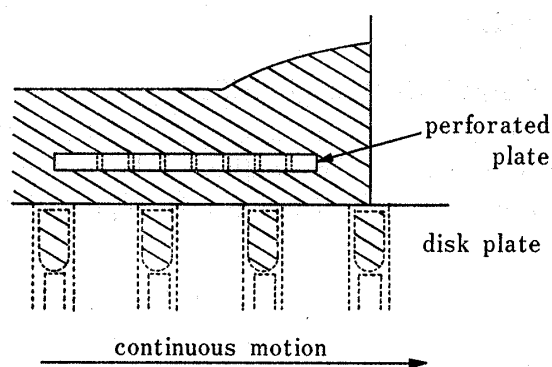


Fig. 1. Schematic Representation of Filling Mechanism of OCF120

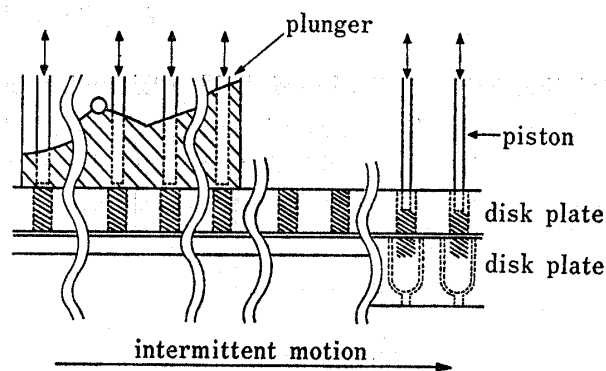


Fig. 2. Schematic Representation of Filling Mechanism of HöfligerGKF1000

Höfliger-Karg-GKF-1000 was used as a machine of Type-B and its filling mechanism is shown in Fig. 2, the shaded portion indicating a powdery sample. In the case of Höfliger-Karg-GKF-1000, a powdery sample is filled into the die-cavities and molded by stamping with the plungers and successively the powder mass in the cavities is dropped down into the capsule-bodies with the pistons. The plungers stamp each cavity 6 times. When the plungers reached at the lowest position, the bottom-faces of the plungers were in the same level as of the upper surface of the disk plate holding the cavities. The diameter of each plunger was 4.3 mm and the inner diameter of each cavity was 4.5 mm. The motion of the disk plate holding the cavities or the capsule-bodies is intermittent because the disk plates must be stopped while the plungers are stamping. In this experiment Höfliger-Karg-GKF-1000 was driven at the filling rate of 1000 capsules/min.

There are 8 kinds of hard capsule sizes, that is No. 000, No. 00, No. 0, No. 1, No. 2, No. 3, No. 4, and No. 5. No. 000 is the largest and No. 5 the smallest capsule of the 8 kinds. Most of the capsules used in Japan are of sizes ranging between No. 1 and No. 5. No. 3 capsule was used in this experiment. The inner diameter and the capacity of No. 3 capsule-body were about 5.4 mm and 0.300 cm<sup>3</sup>, respectively.

**Materials**—Table I shows the characteristics of the samples used in the capsule-filling experiment. In the previous papers,<sup>4)</sup> the samples classified with the sieves have been used for the fundamental researches

3) Y. Miyake, A. Shinoda, T. Nasu, M. Furukawa, K. Uesugi, and K. Hoshi, *Yakuzaigaku*, **34**, 32 (1974); K. Takagi, M. Sugihara, and S. Kimura, *Yakuzaigaku*, **29**, 245 (1969).

4) a) K. Kurihara and I. Ichikawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 394 (1973); b) K. Kurihara and I. Ichikawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 2278 (1973).

TABLE I. Materials Tested

Sample No.	Substance	Angle of repose (°)	Minimum orifice diameter (cm)
20	Cryst. cellulose	44	0.55
21	Potato starch	31	0.40
22	$\alpha$ -Lactose monohydrate, powdery	46	0.60
23	$\alpha$ -Lactose monohydrate, cryst.	37	0.20
24	Equi-ratio mixture of No. 20 and 23	38	0.35
25	Equi-ratio mixture of No. 20 and 21	38	0.45
26	Equi-ratio mixture of No. 22 and 23	44	0.35
27	$\alpha$ -Lactose monohydrate, granulated <sup>a)</sup>	35	0.25

a) Granulated with hydroxypropyl cellulose as a binder.

but in the present paper the samples were prepared without such treatment as classification because of practical purposes. Magnesium stearate was added to all the samples in concentration of 0.5%.

In addition to the samples shown in Table I, many samples were used in order to examine the relations between the minimum orifice diameter and the discharge rate from orifices or the angles of repose. The main constituents of each of them were powdery or crystalline  $\alpha$ -lactose monohydrate, crystalline cellulose, corn starch, potato starch, benzoyl thiamine monophosphate, glass beads, ball-milled glass and spray-dried wax and in some samples magnesium stearate and/or fumed silicon dioxide were added to the main constituents.

## Results and Discussion

### Relation between Minimum Orifice Diameter and Discharge Rate through Orifices

As shown in the previous paper,<sup>4a)</sup> both the minimum orifice diameter ( $\phi_0$ ) and the discharge rate through orifices ( $Q$ ) are the characteristics representing the mobility of the particles in a powder bed under dynamic conditions. The relation between them has been represented by Eq. 1 and Eq. 2.

$$Q = a((\phi/d_p)^2 - (\phi_0/d_p)^2) \quad \text{Eq. 1}$$

$\phi$ : diameter of discharge-orifice  
 $d_p$ : particle diameter

$$a = \beta(\phi_0/d_p)^{-m} \quad \text{Eq. 2}$$

Here,  $m$  and  $\beta$  are constants, and  $m$  is nearly equal to 2. Eq. 3 is derived by substituting Eq. 2 into Eq. 1.

$$Q = \beta d_p^{m-2} (\phi^2/\phi_0^m - \phi_0^{2-m}) \quad \text{Eq. 3}$$

Assuming that  $d_p^{m-2}$  is a constant nearly equal to 1 because  $m$  is nearly equal to 2, Eq. 4 is obtained.

$$Q = \beta(\phi^2/\phi_0^m - \phi_0^{2-m}) \quad \text{Eq. 4}$$

Eq. 4 indicates that when the discharge rate ( $Q$ ) of some samples is determined by use of a fixed orifice and the discharge rate is plotted against the minimum orifice diameter, the discharge rate is closely related to the minimum orifice diameter.

In the previous paper which reported the results obtained by use of the monodispersed samples, each of them consisting of one main component, the relation between  $Q$  and  $\phi^2$  was linear.<sup>4a)</sup> Nonlinear relations were observed, however, in some samples of mixtures, as shown in Fig. 3. Fig. 4 shows the plots of the discharge rate through the orifice with a diameter of 7 mm against the minimum orifice diameter of all the samples, some of which showed nonlinear relations between  $Q$  and  $\phi^2$ . Similar relations between  $Q$  and  $\phi_0$  to that shown in Fig. 4 were obtained when they were determined on the discharge rate through different discharge orifices than the orifice with a diameter of 7 mm. From Fig. 4, it can be seen that the discharge

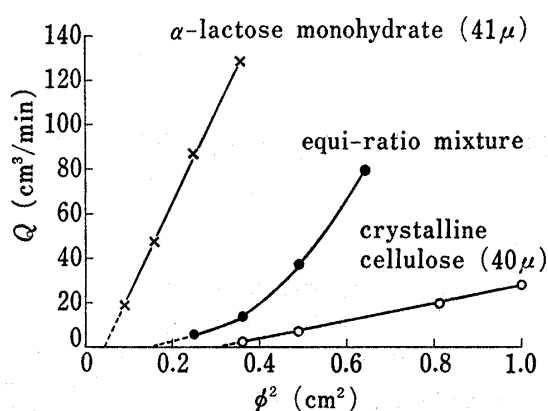


Fig. 3. Discharge Behavior of Mixture  
(All samples contained 0.5% magnesium stearate.)

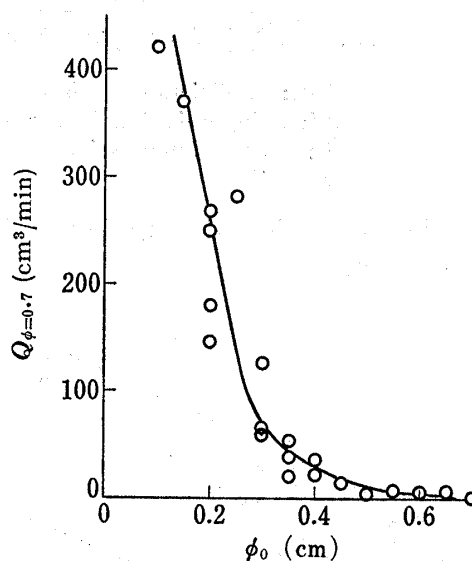


Fig. 4. Relation between Discharge Rate and Minimum Orifice Diameter

rate is closely related to the minimum orifice diameter, although the deviation of the data from the curve drawn in Fig. 4 is comparatively large. Both the discharge rate and the minimum orifice diameter are the characteristics indicating the mobility of the particles in a powder bed, but the minimum orifice diameter is expressed with one single numerical value for one sample, while the discharge rate varies with the diameter of the discharge orifices. It is somewhat difficult to select predetermined orifice diameter for the measurement of discharge rate which is used as the index of flowability. For example, in a study on the relation between this index and filling weight variation, if this index is determined by use of the orifice with the same diameter as that of the cavity or the capsule body used in the filling experiment, all the samples which do not discharge through this orifice have an identical value, 0, as the indexes, while among them there may be actually considerable differences in such flowability. Such situation does not seem preferable because the means and the degrees of powder-fluidisation in filling machines are usually different from those in the flow test apparatus. On the other hand, the minimum orifice diameter is expressed with one single numerical value for one sample and by use of this index the flowability is expressed in order over a wide range. On the basis of the above considerations, in the present study it was determined to use the minimum orifice diameter as an index of flowability representing the mobility of the particles in a powder bed under dynamic conditions.

#### Relation between Minimum Orifice Diameter and Angle of Repose

Fig. 5 shows the plots of the minimum orifice diameter against the angle of repose of many samples. It can be seen from Fig. 5 that there are no good correlations between the minimum orifice diameter and the angle of repose. These results are explained in terms of the following findings shown in the previous papers<sup>4</sup>): the angle of repose indicates the mobility of the particles on the surface of a powder bed and is affected by the particle shape, while the minimum orifice diameter indicates the mobility of the particles in a powder bed and is greatly affected by the co-ordination number and hardly by the particle shape.

#### Relation between Filling-Weight-Variation and Minimum Orifice Diameter or Angle of Repose

Table II shows the coefficients of filling-weight-variation of the capsules filled with OCF-120 or with Höffiger-Karg-GKF-1000. The coefficient of variation was calculated by use of Eq. 5 from 140 capsule-filling-weight-data on each sample.

$$C.V. = \left[ \sqrt{\frac{\sum_{i=1}^n (W_i - \bar{W})^2}{(n-1)\bar{W}}} \right] \times 100$$

Eq. 5

C.V.: coefficient of variation  
 $W_i$ : filling weight of  $i$ -th capsule  
 $\bar{W}$ : average filling weight  
 $n$ : =140

The capsules were collected by taking out 20 capsules at intervals of 10 min under a continuous filling operation.

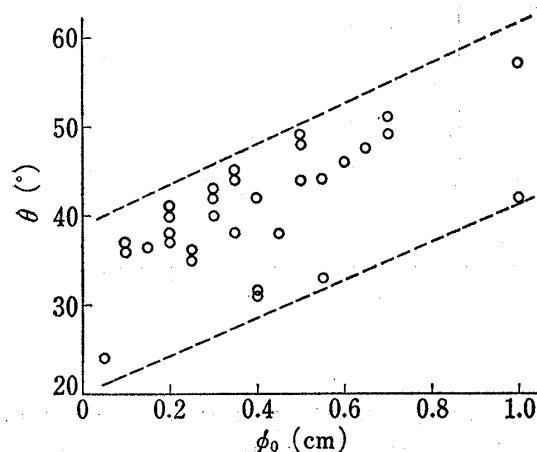


Fig. 5. Relation between Angle of Repose and Minimum Orifice Diameter

TABLE II. Coefficient of Variation of Filling-Weight (%)

Sample No.	OCF120	Höfliger GKF1000
20	3.41	1.47
21	—	11.8
22	4.40	6.08
23	1.92	—
24	2.26	2.04
25	2.68	0.93
26	2.34	1.07
27	2.25	3.57

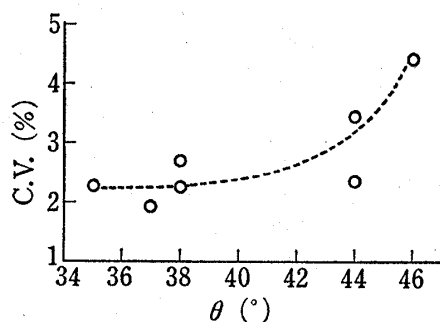


Fig. 6. Relation between Angle of Repose and Filling-Weight-Variation in Case of OCF120

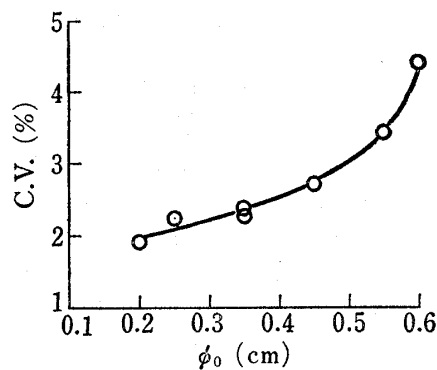


Fig. 7. Relation between Minimum Orifice Diameter and Filling-Weight-Variation in Case of OCF120

In the case of OCF-120, the coefficient of variation of filling-weight was more closely related to the minimum orifice diameter than to the angle of repose (see Fig. 6 and 7). The good correlation between the coefficient of variation and the minimum orifice diameter seems to be natural when it is considered that in OCF-120 powder is filled by flowing into the capsule-bodies and the minimum orifice diameter expresses the mobility of the particles in a powder bed under dynamic conditions.

On the other hand, in the case of Höfliger-Karg-GKF-1000 the variation of filling-weight was not correlated with the minimum orifice diameter as shown in Fig. 8. It is considered from this finding that the effect of the particle mobility in a powder bed on the variation of filling-weight is small because powder is filled forcibly into the die-cavities by stamping with the plungers. Fig. 9 shows the relation between the angle of repose and the variation of filling-weight. It can be seen from Fig. 9 that the filling weight variation of the samples having large and small angle of repose is larger than that of the samples having intermediate

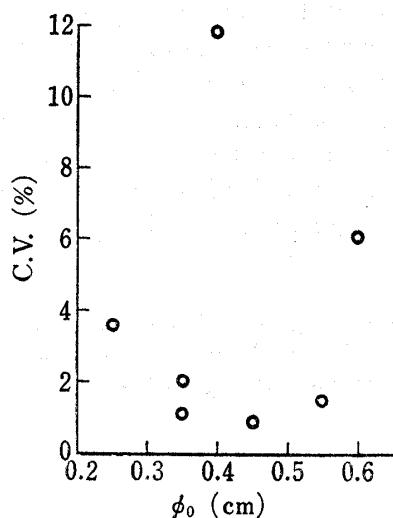


Fig. 8. Relation between Minimum Orifice Diameter and Filling-Weight-Variation in Case of Höfliger GKF1000

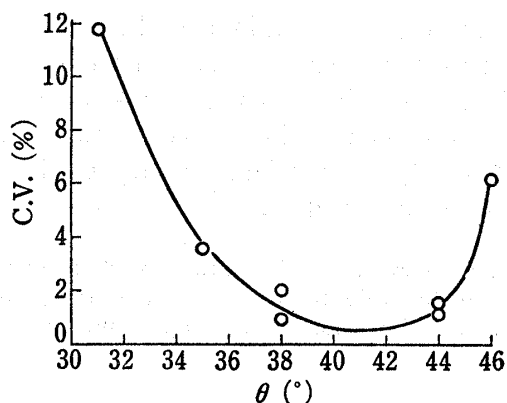


Fig. 9. Relation between Angle of Repose and Filling-Weight-Variation in Case of Höfliger GKF1000

angle of repose, namely the filling weight variation of the samples having intermediate angle of repose is smallest. The behavior of powder in Höfliger-Karg-GKF-1000 was observed in detail during the filling operation. It was found in the case of the samples having large angle of repose that the powder levels at the stamping positions were very different from each other and the levels varied with the lapse of time. The filling-weight of the samples having large angle of repose is considered to vary greatly owing to such variation of the powder level. It was found in the case of the samples having small angle of repose that a portion of the surface-layer of the powder filled in the cavities or the capsule-bodies jumped out when the disk plate holding the cavities or the bodies moved intermittently. When the disk plate turns intermittently, an acceleration acts upon the powder moving with the disk plate. It is considered that a portion of the surface-layer compelled to jump out by the force arising from the acceleration. Whether the particles on the surface jump out by or remain in their conditions against the force proportional to the particle-mass is a similar situation to that in the measurements of the angle of repose. (The angle of repose is determined by the mobility of the particles on a surface under a gravitational acceleration.) Therefore, it is considered that in the case of the samples having small angle of repose the upper portion of the filled powder was apt to leave from the powder bed and to jump out owing to the intermittent motion of the disk plate and the amount of jumping-out varied considerably due to a slight difference of the surface conditions of the filled powder. It was found in the case of the samples having intermediate and large angle of repose that the filled powder scarcely jumped out regardless of the surface conditions. The relation between the angle of repose and the variation of filling-weight is considered to vary with the magnitude of the acceleration taking place due to the intermittent motion of the disk plate, namely with the size and the rotational speed of the disk plate. On the other hand, the angle of repose must be smaller than a certain degree in order to keep the powder level in the filling box constant. Therefore, in the case of the capsule filling machine of this type there is a certain maximum limit to the increase of productive capacity through speeding-up of machine.

From the results obtained in the present study, the following conclusions are derived.

In the case of the capsule-filling machine of the pouring type, the variation of filling-weight is closely related to the minimum orifice diameter and powder having small minimum orifice diameter must be prepared in order to obtain a product of small weight-variation.

On the other hand, in the case of the capsule-filling machine of the stamping type, the variation of filling-weight is closely related to the angle of repose and there is a suitable angle

of repose for a minimum variation of filling-weight. This suitable angle of repose is determined by the size and the rotational speed of a disk plate holding the cavities or the capsule-bodies. Therefore, in order to obtain a product of small weight variation by use of a settled machine, powder must be prepared to have the suitable angle of repose determined by the size and the speed of the disk plate, or if the repose-angle of a sample is smaller than the suitable angle of repose and if the rotational speed of the disk plate (that is, the driving speed of the machine) can be changed, the rotational speed must be decreased to the point that jumping-out of filled powder is not observed at.

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