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Studies on Hard Gelatin Capsules. II.[1] The Capsule Filling on Powders and Effects of Glidant by Ring Filling Method-Machine[2]

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The filling characteristics of capsules were studied on cornstarch and lactose with and without Aerosil as glidant, using industrially semiautomatic-ring filling method-machine with the flat and the screw auger.

On powders without Aerosil, the coefficient of variation of the dose showed that the filling by the screw auger was more accurate than that by the flat one. Deviations of the dose containing Aerosil became smaller and showed maximum effect between 0.1—2% Aerosil contents.

The maximum filled weights were observed at 0.1—0.5% Aerosil contents but on lactose filling by the screw auger the filled weight decreased with Aerosil contents.

The filled weight variation was compared with U.S.P. requirements.

As the approach to reviewing the filling properties, two usual packing equations were applied for the relation between the filled weight and velocity of the ring.

Hard gelatin capsules are precise container and are available in eight sizes of contents from 0.13 to 1.37 ml. Most capsules are industrially filled by an automatic or semi-automatic machine. But large deviations of the weight filled are pointed out sometimes and the uniform filling are more difficult than in the case of tablets.

In recent years capsules are getting popular and the knowledge of capsules has become very important, but very little work has been reported concerning the filling characteristics.[4]

There are several types of filling methods, such as the direct filling into capsules and premeasuring by the auger or the plunger. In this report the semi-automatic machine for the direct filling by the ring method was used on cornstarch and lactose. The relation among the average weight filled, weight variation, the revolution velocity of the capsule ring and the kind of auger in the hopper were studied and the effects of the glidant were discussed. As an approach to reviewing the filling properties, two usual packing equations were applied.

Experimental

Materials——J.P. cornstarch and lactose were used. The diameter distribution of cornstarch was relatively sharp in the range of 6 to 20 μ and that of lactose was broad in the range of 10 to 50 μ. The water contents were 13.3% (110°, 1 hr) and 0.21% (80°, 1 hr), respectively. Aerosil[5] was used as a glidant and its primary particle size was 10 to 40 mμ.

The commercially available capsule,[6] size No. 1, was used throughout this study.

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1) Part I: K. Ito, S. Kaga and Y. Takeya, *Chem. Pharm. Bull.* (Tokyo), **17**, 1134 (1969).
2) Presented at the 88th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1968.
3) Location: *5-6-9, Narihira, Sumida-ku, Tokyo.*
4) T. Furukawa, Y. Iwasaki and S. Nakamura, *Yakuzaigaku*, **20**, 66 (1960); H.C. Lindenwald and R. Tawashi, *Pharm. Ind.*, **27**, 146 (1965); H.C. Lindenwald and A.F. Asker, *ibid.*, **28**, 614 (1966).
5) Light Anhydrous Silicic Acid, Aerosil/uncompressed, Degussa.
6) Park–Davis capsule.

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Apparatus and Procedure——The semi-automatic filling machine[7] for a ring method of direct filling to individual capsules was used with the flat[8] and the screw[9] augers of the powder hopper. Fig. 1 shows the capsule ring, the hopper and the auger.

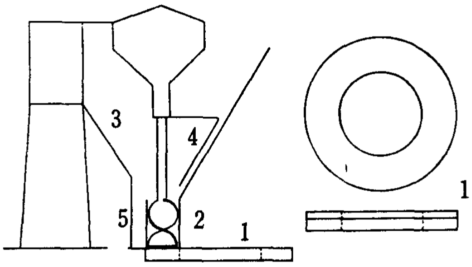

Fig. 1. Sketch of Capsule Filling Machine

1: capsule ring, upper and lower
2: auger, flat and screw
3: powder hopper
4: stirring arm
5: relief hole

Table 1. Time required for One Complete Revolution of the Ring

Sign	Time in sec
A-1	9.5
A-2	11.3
A-3	13.7
A-4	17.1
B-1	20.5
B-2	24.5
B-3	29.8
B-4	37.1

Empty capsules were put into the ring which had 420 capsule holes for size No. 1 capsule, and the cap was separated in the upper and the body in the lower ring automatically. The body ring was then placed on the turn table where the powder hopper was pulled over it for one revolution of the ring. The auger speed was 432 rpm. Weights of the powder in the hopper were adjusted to one kg in this filling experiment. The weight filled could be changed with the rotational velocity of the table. There were eight selections of speed, A-1, -2, -3, -4 and B-1, -2, -3, -4, from faster to slower and the time required for one revolution are shown in Table I. The cap ring was then placed again on the filled body ring and capsules were closed by the peg ring device.

Powder samples of Aerosil mixture were made as follows. Powder containing 5% Aerosil was made by mixing in a V-type mixer[10] for 20 minutes using Aerosil passing through 50 Mesh sieve, and diluting this powder by mixing another 20 minutes to give powders with Aerosil contents 0.1, 0.2, 0.3, 0.5, 1.0 and 2.0%.

The average weight filled and the coefficient of variation (CV) were calculated from the weight of 20 or 40 capsules.

Estimation of the pressure applied to capsules was made from the data of pressure and density of powders by Konsisto-meter.[11]

Temperature and humidity of the room were maintained at 26° and 50% RH.

Results and Discussion

Effect of Aerosil on the Weight Filled and the Weight Variation

In the case of a normal operation, powders are pushed into capsule bodies by an auger in the hopper and excess powders are circulated back through a relief hole. But in the case containing no Aerosil, circulating through the hole could not be seen because of their poor flow characteristics.

Fig. 2—7 show average weights filled and coefficient of variations (CV) plotted against velocities of the turntable and Aerosil contents.

From these data, following results were obtained. Average weight filled by the screw auger was more than that by the flat auger, *i.e.*, 30 to 60% more for lactose and 15 to 30% more for cornstarch. CV of weight filled by the flat auger was about two times as large as that by the screw auger and became very large at fast velocities, A-1 and A-2. But for powders

7) Park-Davis Type 8 Capsule Filling Machine.
8) Self made, 53.8 mm × 77.9 mm
9) Type E, 270° twist, 31° pitch.
10) 10 liter V-Type Mixer, 33 rpm.
11) Haake, Berlin.

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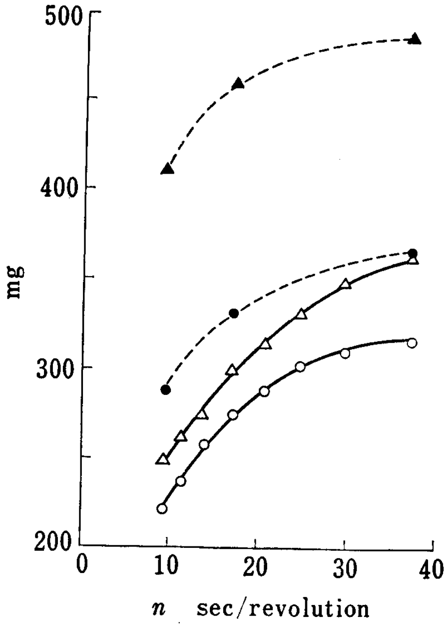

Fig. 2. Changes of Filled Weight in Capsule Size No. 1 with Time for One Revolution of Body Ring (n)

○, ● : cornstarch —— : flat auger
△, ▲ : lactose ---- : screw auger

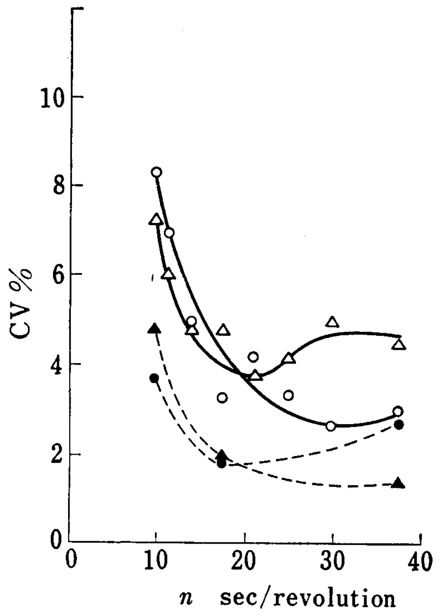

Fig. 3. Changes of Coefficient of Variation of Filled Weight in Capsule Size No. 1 with Time for One Revolution of Body Ring

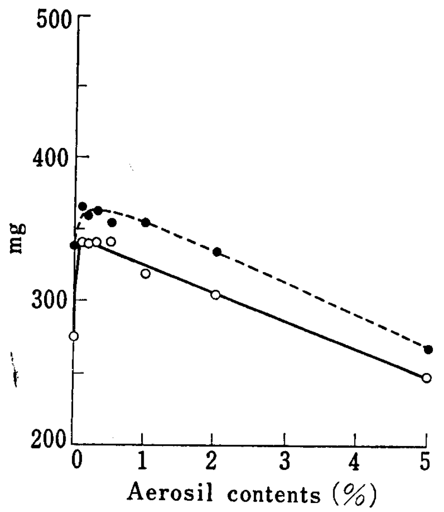

Fig. 4. Effect of Aerosil on Filled Weight of Cornstarch at Constant Ring Velocity 17.1 sec/revolution (A–4)

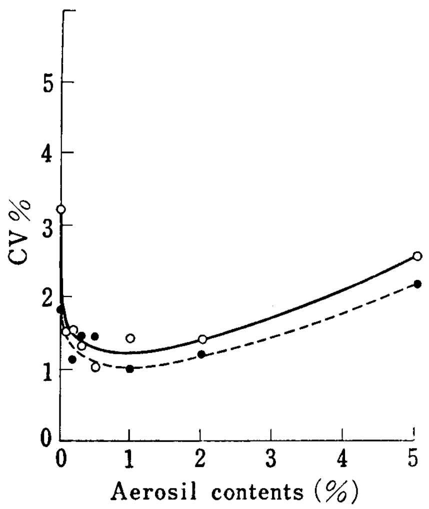

Fig. 5. Effect of Aerosil on Coefficient of Variation of Filled Weight of Cornstarch at Ring Velocity 17.1 sec/revolution

containing Aerosil, deviations of the dose became smaller and showed maximum effect between 0.1 and 2% Aerosil contents for cornstarch and lactose by both augers. The maximum weight filled were observed at 0.1—0.5% Aerosil contents, but on filling lactose by the screw auger the weight became smaller with Aerosil contents.

Comparison with U.S.P. Test

To compare the weight variations with U.S.P. requirements, 20 capsules were examined and numbers of capsules, whose weight deviated more than 10% from the average gross and net weight, are shown in Table II.

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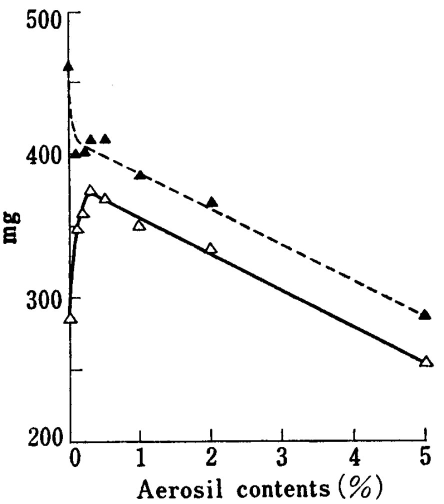

Fig. 6. Effect of Aerosil on Filled Weight of Lactose at Ring Velocity 17.1 sec/revolution

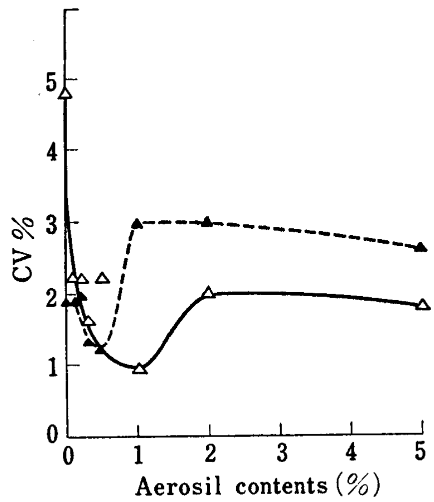

Fig. 7. Effect of Aerosil on Coefficient of Variation of Filled Weight of Lactose at Ring Velocity 17.1 sec/revolution

Table II. Numbers of Capsules deviated from the Average Gross and Net Weight between 10 and 20% $n=20$

Auger	Powder		Ring velocity A–1	A–2	A–3	A–4	B–1	B–2	B–3	B–4
Flat	cornst.	gross	3	1	0	0	1	1	0	0
		net	6	3	0	0	1	1	0	0
	lactose	gross	3	2	0	1	0	0	1	2
		net	3	3	0	1	0	0	1	2
Screw	cornst.	gross	1			0				0
		net	1			0				0
	lactose	gross	2			0				0
		net	2			0				0

According to U.S.P., capsules must meet the requirements of the following test. (A) Weigh 20 capsules. Each capsule weighs between 90 and 110% of the average gross weight. (B) If not all capsules fall within A test, weigh 20 capsules to calculate the net weight and the average weight and if (1) not more than two of the differences are greater than 10% of the average and (2) in no case is the difference greater than 25%. (C) If more than 2 but less than 7 capsules deviate from the average between 10 and 25%, determine the net weight of additional 40 capsules. In not more than 6 of the entire 60 capsules does the difference exceed 10% of the average and in no case does the difference exceed 25%.

From Table II capsules filled at the velocities between A–3 and B–3 are allowable but others exceed the limits of A and B test of U.S.P. If A and B (1) test, for examples, are considered to see the required CV of the gross weight and the net weight of capsules, following equations of probability for a lot to pass the test are used to calculate CV of a lot.

$$L_{PA}=(1-P)^{20} \qquad (1)$$

$$L_{PB}=\sum_{r=0}^{2} {}_{20}C_r P^r (1-P)^{20-r} \qquad (2)$$

where L_P is a probability to pass the test and P is a rate of the capsule whose weight deviated more than 10% from the average. Assuming a normal distribution, CV of a lot is obtained

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and listed in Table III. The required CV may be estimated in relation to L_P and P. It is understood that the values of CV obtained in this experiments on cornstarch and lactose were relatively large. But as shown in Fig. 5 and 7, CV of the powders containing Aerosil become very small especially between 0.1 and 2% Aerosil contents and these capsules passed the U.S.P. requirements.

Table III. Relation between the Probability for a Lot to pass the A and B (1) Test and CV of the Filled Weight

Test	L_P	α (%)	P	CV (%)
A	0.99	1.0	0.0005	2.9
	0.90	10.0	0.0053	3.6
	0.80	20.0	0.0111	3.9
B (1)	0.999	0.1	0.00975	3.88
	0.995	0.5	0.01725	4.20
	0.990	1.0	0.02200	4.37

Filling Equations

The capsule filling equations have examined as an approach to know the filling characteristics of the powders.

The weight filled changes with velocities of the body ring, namely with the lapse of time for each capsule to contact with the powder hopper. The lapse of time may correspond to the number of tapping or the pressure of the usual packing equations such as (3) and (4),

$$\rho_f-\rho_n=(\rho_f-\rho_0)e^{-kn} \tag{3}$$

$$\frac{n}{C}=\frac{1}{ab}+\frac{n}{a}, \quad C=(V_0-V_n)/V_0 \text{ or } (v_0-v_n)/v_0 \tag{4}$$

where n: number of tapping or pressure; ρ_o, ρ_n, ρ_f: densities of packing powder at initial, n and final; V, v: volume and specific volume; k, a, b: constants.

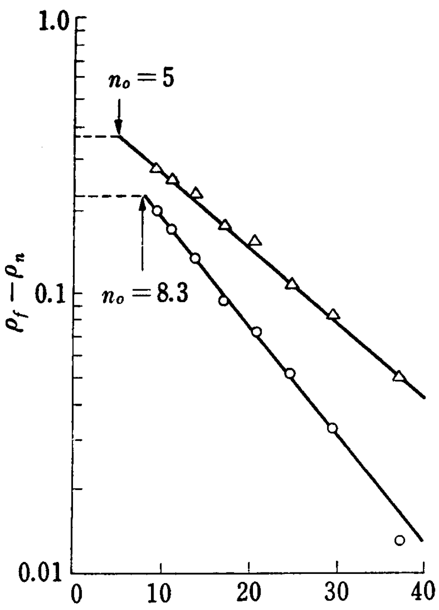

Fig. 8. Density Difference and n by Eq. (3) on Filling by Flat Auger

ρ_f : tapping dencity ρ_{300} was used

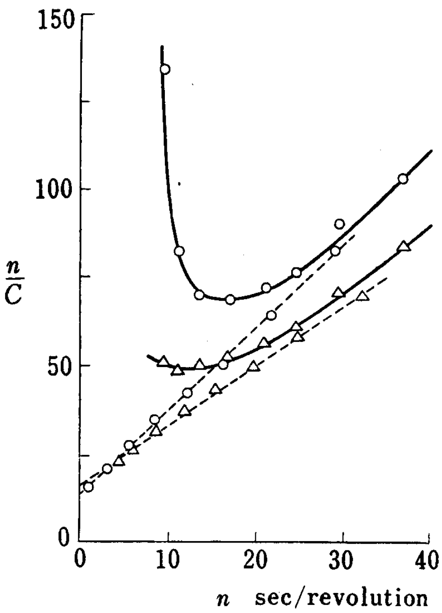

Fig. 9. n/C and n by Eq. (4) on Filling by Flat Auger

---- : corrected, $n \rightarrow n-n_0$

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Fig. 8, 9, 10 and 11 for the capsule filling on cornstarch and lactose alone were obtained by replacing n with the time for one complete revolution of the body ring which was proportional to the time for each capsule filling. On usual packing, powders are loosely pre-packed in some container and then pressure or tapping is applied to them. But in this study of capsule filling, initial state of the body cap was not loosely packed but empty. If capsules were filled at higher velocity than A-1 there might be taken place the case that the filled weight

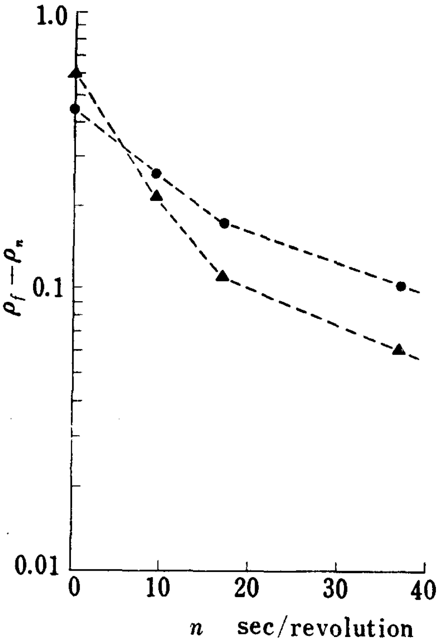

Fig. 10. Density Difference and n by Eq. (3) on Filling by Screw Auger

ρ_f : calculated value from eq. (4) was used

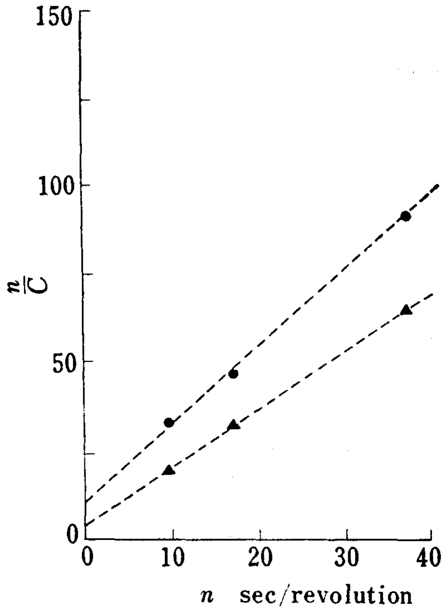

Fig. 11. n/C and n by Eq. (4) on Filling by Screw Auger

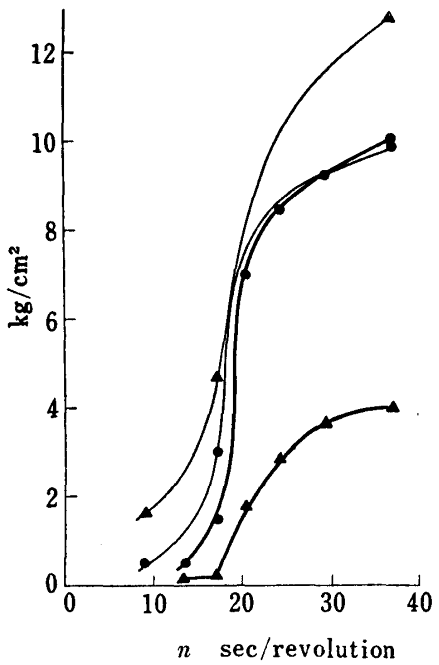

Fig. 12. Pressure Applied to Capsule by Screw Auger-Estimated by Konsisto Meter

—— : without Aerosil
▬▬ : with Aerosil 0.1 %

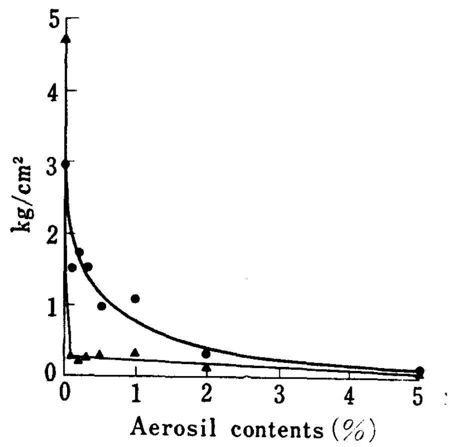

Fig. 13. Effect of Aerosil on Pressure Applied to Capsule by Screw Auger at Ring Velocity 17.1 sec/revolution

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was smaller than the loosely filled capsule. Therefore to treat the capsule filling as the usual packing system, the time required for the loosely filling (n_o) in this filling process had to be considered.

In Fig. 8, n_o was obtained from an intersection with the straight line and $\rho_f-\rho_o$ where ρ_o is an initial density corresponding to loosely filling. The correction time n_o was 8.3 seconds per one revolution on cornstarch and 5 seconds on lactose. Equation (4) was also recalculated using $n-n_o$ instead of n, and then a good straight line relationship was obtained as in Fig. 9.

For the filling with the screw auger Fig. 10 and 11 were obtained without any correction. This means the loosely packing was made very fast and n_o could not be seen.

The same treatments were also applied to obtaining the relationship to the Aerosil mixtures.

The constants obtained are summarized in Table IV.

Table IV. Constants of the Filling Equations

The Filling by the Flat Auger

Aerosil contents %	Cornstarch n_o	Cornstarch b	Cornstarch k	Cornstarch ρ_f a)	Cornstarch ρ_{300} b)	Lactose n_o	Lactose b	Lactose k	Lactose ρ_f a)	Lactose ρ_{300} b)
0	8.3	0.17	0.041	0.710	0.648	5.0	0.10	0.027	1.000	0.791
0.1	8.0	0.25	0.049	0.755	0.747	8.4	0.098	0.019	0.998	0.986
0.2	6.8	0.18	0.032	0.765	0.749	7.7	0.082	0.016	0.992	0.916
0.3	6.8	0.19	0.033	0.762	0.754	6.1	0.070	0.014	1.035	0.961
0.5	6.8	0.18	0.032	0.779	0.751	7.1	0.055	0.012	1.054	0.973
1.0	6.2	0.16	0.028	0.724	0.737	7.0	0.052	0.011	1.020	0.935
2.0	7.8	0.16	0.028	0.666	0.710	6.8	0.059	0.013	0.945	0.884
5.0	8.9	0.15	0.028	0.610	0.601	7.2	0.054	0.012	0.725	0.689
The filling by the screw auger										
0	0	0.15	0.024	0.733	0.648	0	0.42	0.048	1.013	0.791
0.1	9.1	0.63	0.046	0.777	0.747	8.2	0.23	0.033	1.034	0.896
0.2	7.0	0.21	0.034	0.821	0.749	7.8	0.17	0.029	1.025	0.916
0.3	7.8	0.20	0.034	0.755	0.754	6.1	0.15	0.025	1.026	0.961
0.5	7.2	0.21	0.029	0.838	0.751	7.0	0.15	0.026	1.017	0.973
1.0	6.9	0.28	0.037	0.805	0.737	5.7	0.07	0.012	1.172	0.935
2.0	6.6	0.15	0.025	0.839	0.710	6.4	0.08	0.014	1.099	0.884
5.0	6.0	0.05	0.015	0.829	0.601	6.4	0.06	0.007	1.113	0.689

a) Calcd. from the slope of eq. (4). b) tapping density at number 300

The value of n_o by the flat auger did not change much with Aerosil contents, but that by the screw auger did greatly with and without Aerosil. Flow properties of cornstarch and lactose alone are very bad but pushing powder into capsules by the screw auger may be carried out from early stage of filling process, and the applied pressure become very large within a short period. But powders whose flow properties are improved with Aerosil may be slipped at the auger position and the pressure applied to capsules must be smaller.

The pressure applied by the auger could not be measured directly but could be estimated roughly from the relation between powder density and pressure by Konsisto-meter, direct packing by a piston in a die. These data are plotted in Fig. 12 and 13. The capsule filling and the packing by Konsisto-meter were quite different each other in its process, but a tendency of the data might explain the pressure change.

The result showed that the pressure was smaller at fast velocity of the ring and that its drop was large when Aerosil was mixed. The relation between the pressure and the velocity of the body ring was not simple as in Fig. 12. When equation (3) and (4) were used, n was

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assumed at first to be corresponding to the pressure applied to capsules or to the number of tapping, and this assumption seemed to be correct for the filling by the flat auger and this was confirmed by the density of filled powder in capsules and that of tapping powder, as was contrary to the filling by the screw auger.

But these equations are useful to express the relation among filled weights and velocity of the body ring and mechanism of filling can be estimated to some extent.

The constants k and b of equations of usual packing are said to be related to adhesive property of powders and these values obtained on the filling by the flat auger can be compared each other, but those by the screw auger must have a little different meaning.

To study the flow property under pressure is especially important for the capsule filling. Further experiments with capsules of different sizes and powders with improved flow properties by other glidants will give more precise mechanism of the capsule filling.

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