Quantitative Analysis of Water Dispersion Conditions and Pressure Transmission Characteristics of a Wet Kneaded Mass

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In our previous paper [Watano S. *et al.*, *J. Powder Technology Japan*, 37, 362–370 (2000)], a novel compaction tester was developed to quantitatively evaluate the water dispersion condition of a wet kneaded mass prepared by a paddle type kneader. It has been demonstrated that the physical properties of pellets prepared by extrusion granulation after the kneading can be well predicted by the pressure transmission obtained through the compaction tester.

This paper describes a more detailed investigation of the water dispersion, its mechanism and pressure transmission characteristics of wet kneaded masses prepared under various operating conditions. First, kneading by a paddle type kneader was conducted to prepare wet masses under various binder contents using different additional methods and different starting materials. Secondly, water dispersion and pressure transmission characteristics of wet masses were investigated. After the wet kneading, the wet kneaded masses were extruded through a dome type extruder and were dried by a fluidized bed to prepare dry pellets.

The relationship between water dispersion and pressure transmission can be expressed by a single line, regardless of binder content or methods of addition. This implies that these parameters have no effect on the water dispersion condition of the wet kneaded mass prepared by a high shear paddle type kneader. Different water dispersion characteristics and the mechanism obtained by different starting materials can also be evaluated by the pressure transmission data. Properties of dry pellets can also be predicted by the pressure transmission. It can be concluded that the developed compaction tester can quantitatively evaluate the water dispersion condition of a wet kneaded mass and also predict properties of the final extruded products.

Key words water dispersion; kneading; pressure transmission; extrusion granulation

Kneading of powdered materials[1—3] has been widely used in the pharmaceutical, agriculture, food, chemical, forage and fertilizer industries. Most of the cases, kneading is conducted before the granulation and molding processes, and the performance of kneading seriously affects the quality of the final product or process efficiency. Therefore, it is very important to quantitatively monitor kneading conditions during the kneading operation. With the present technical levels, however, most operations in the manufacturing process are controlled by an expert's decisions, relying on empirical knowledge based on past experience involving "a sense of feeling determined by the hand".

In the previous study, we developed a compression tester to measure pressure transmission among a wet kneaded mass.[4] It has been demonstrated that the pressure transmission can predict the water dispersion condition among the mass, the degree of kneading attained, and properties of dry pellets prepared by extrusion granulation after the kneading. In the kneading operation, a binder should be used and its additional weight varies depending on the applications. The binder additional methods (solution or powder) and properties of starting materials (soluble or sparingly soluble to water) seriously affect the water dispersion as well as the kneading condition during the kneading. Therefore, it is very important to investigate the effects of these parameters on the water dispersion, kneading condition and on the properties of final dry pellets. However, there has been no research that has studied the effect of binder on the water dispersion, much less on the final products' qualities.

The present study investigates the effects of binder content, its methods of addition and properties of starting materials on the water dispersion, pressure transmission characteristics of wet kneaded masses and on the properties of the dry pellets obtained through extrusion granulation after kneading. The mechanism of water dispersion during the paddle kneading is also discussed.

Experimental

Powder Samples Table 1 lists powder samples used.[4] The excipient consisted of lactose, cornstarch and crystallinecellulose, and main ingredients (acetaminophen) were used as powder samples.[5] The total weight of the powder samples was 300.0 g. Three levels of hydroxypropylcellulose (HPC-L) were adopted as a binder, which was added by two methods; one was mixed as a dry powder into the starting materials before kneading (referred to as the "solid method"), and the other was dissolved into water and added to the binder solution (named the "liquid method"). In both cases, purified water was used as a binder liquid.

Equipment and Procedures For wet kneading, a developed paddle type

Table 1. Powder Samples

	Mean particle diameter	Charge ratio (Charge weight)	
		Sample I	Sample II
Lactose[a]	60 μm	67.2% (201.6 g)	47.2% (141.6 g)
Cornstarch[b]	15 μm	28.8% (86.4 g)	20.2% (60.6 g)
Crystalline cellulose[c]	40 μm	4.0% (12.0 g)	4.0% (12.0 g)
Acetaminophen[d]	44 μm	—	28.8% (86.4 g)
(Total)		100.0% (300.0 g)	100.0% (300.0 g)
Hydroxypropyl cellulose[e]	21 μm	0% (0 g), 1.5% (4.5 g), 3.0% (9.0 g)	
Purified water		25.0% (75.0 g)	

a) DMV (Pharmatose 200 M). *b*) Nihon Shokuhin Kako Co., Ltd. (Cornstarch W). *c*) Asahi Chemical Industry Co., Ltd. (Avicel PH-101). *d*) Yamamoto Chemical Industrial Co., Ltd. *e*) Nippon Soda Co., Ltd. (HPC-L).

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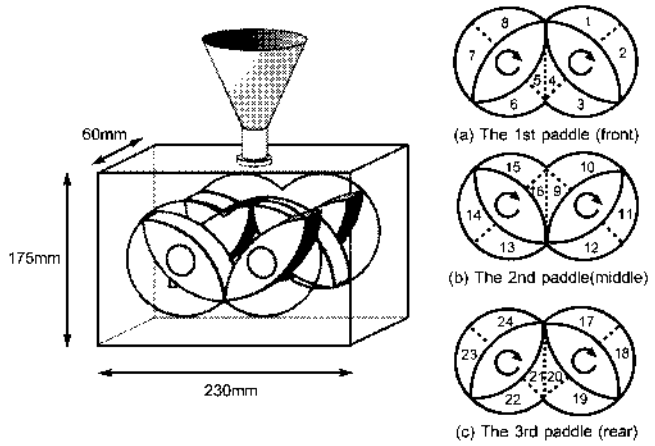

Fig. 1. Schematic Diagram of Paddle Type Kneader and Sampling Locations

kneader[4] was used (Fig.1). The kneading chamber has two parallel shafts, each of which has three sets of convex-lens shaped paddles. The paddles in the front and in rear make an angle of 90 degrees, so that the major axis of one paddle is always touching the minor axis of the opposite one. Therefore, the shear stress is incredibly large compared to the other kneader, such as a high shear mixer and vertical paddle kneader, which results in a very short kneading time and precise kneading without generating any damp clumps. The major axis of the paddle is 44.2 mm and the minor 19.6 mm. The effective charge volume is approximately 300 cm^3.

A kneading experiment was conducted as follows: powder samples and binder liquid were fed into the kneading chamber and kneaded at a constant paddle rotational speed of 30 rpm.

The water dispersion among the kneaded mass was measured using a water-soluble pigment (Food blue No. 1, Toushiki Pigment Co., Ltd.) as a tracer; 0.1 wt% of the pigment (maximum solubility to water is 4.0 wt% at 300 K) was dissolved into water or binder solution before kneading, and the kneaded mass (3.0) was periodically sampled out during the kneading operation (total number of the sampling location was 24 points). The sample was dissolved into purified water (900 cm^3, 27 °C), then absorbance of the pigment (wave length of 629 nm) was measured by a UV-visible recording spectrophotometer (UV-160A, Shimadzu Co., Ltd.). By substituting the obtained absorbance to the Eq. 1, water dispersion, σ^2, is calculated (it is assumed that behavior of the pigment is the same as water, since the pigment is extremely soluble in water).

$$\sigma^2=\frac{1}{24}\sum_{i=1}^{24}(A_i-A_0)^2 \quad (1)$$

where A_i is the absorbance of the pigment among each sample and A_0 is the one among the 3.0 g of mixture, which accurately contains powder samples, binder, water and the pigment.

A compression test of the kneaded mass was conducted using a developed compression tester.[4] As shown in Fig. 2, the tester consists of a hydraulic cylinder, displacement sensor, upper and lower punches, cylinder, and computer. A cylinder having an outside diameter of 40 mm, an inside diameter of 11.3 mm (cross sectional area is just 1.0 cm^2) and height of 110 mm was placed between the upper and lower punches, and 3.0 g of wet kneaded mass was fed into the cylinder. The upper punch pressed the mass at the moving speed of 1.0 cm/min, then the pressure transmission, G, was calculated using the following Eq. 2.

$$G=P_L/P_U\times 100 \quad (2)$$

where P_L and P_U indicate the pressure of the upper and lower punches, respectively. In this experiment, the pressure transmission was calculated when the upper punch pressure reached 4.9 MPa (exactly 50 kgf per cm^2).

Granulation after the kneading was carried out using a dome type extruder[4,6] (DG-L1, Fuji Paudal Co., Ltd.). The kneader consisted of a hemispherical dorm type punching screen (diameter of the dome was 58mm, diameter of each hole and width of the screen were both 0.8 mm, and the opening area ratio was 22.5%), a single shaft, screws and an extrusion blade at the extremity of the shaft. The kneaded mass moved forward by the screws then being extruded through the screen. The combined compression force and tensile stress when the mass passed through the screen caused a plastic deformation of the mass. Here, the feeding speed of the kneaded mass was kept constant at 5 kg/min.

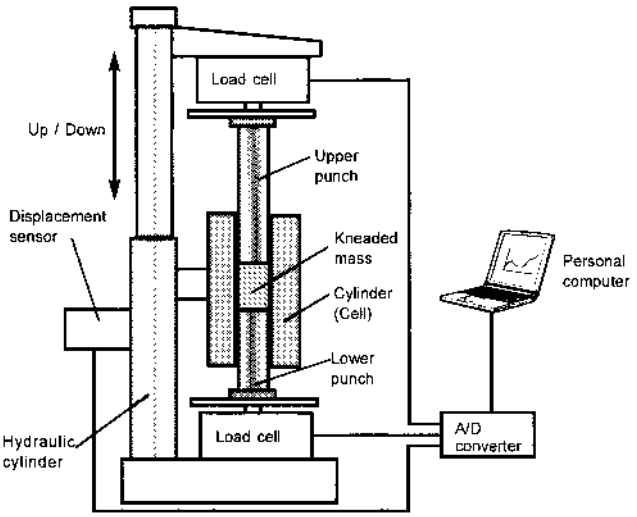

Fig. 2. A Newly Developed Compression Tester

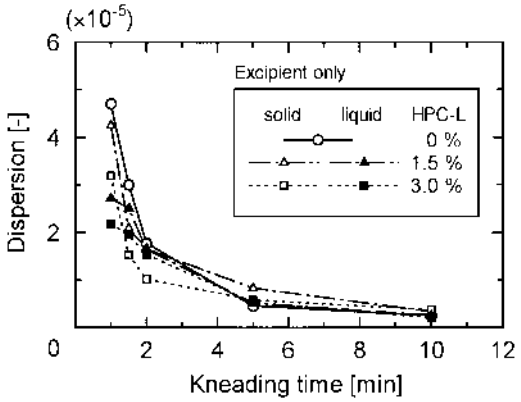

Fig. 3. Temporal Change in Water Dispersion under Various Binder Contents and Different Methods of Binder Addition

Excipient only.

After the granulation, the pellets (granules) were dried by a fluidized bed drier (NQ-160, Fuji Paudal Co., Ltd.)[7] at 353 K until the moisture content measured by an IR moisture sensor[7] was less than 0. Their specific surface area and friability were then measured. The specific surface area was measured by a BET automatic surface area analyzer (Model 4200, Nikkiso). The friability of dry pellets was measured based on the following Eq. 3,

$$F=\frac{M_f}{M_0}\times 100 \quad (3)$$

where M_0 is a mass of dry pellets (100 g) and M_f is the mass of pellets which are smaller than 32 mesh (600 μm), obtained after sieved pellets (12 mesh/32 Mesh, between 600 and 1400 μm) were ground with an alumina ball (ϕ30 mm, 58 g×5) using a rotating ball mill pot (ϕ100 mm×H134 mm, effective volume 950 cm^3) at 75 rpm for 10 minutes. These evaluation methods were the same as previously reported.[4]

Results and Discussion

Figure 3 shows the relationship between water dispersion and kneading time under various binder contents and different binder additional methods when the excipient shown in Table 1 was used as the powdered material (sample I). Here, HPC-L 0% means that no hydroxypropylcellulose was added,

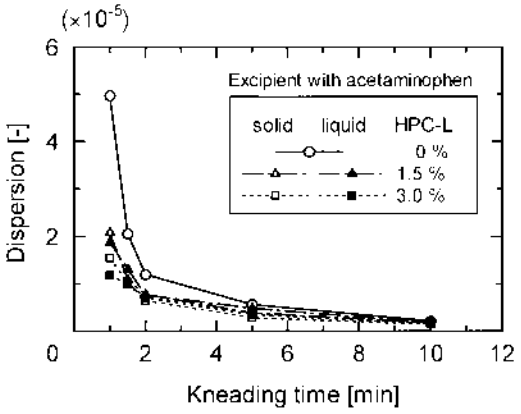

Fig. 4. Temporal Change in Water Dispersion under Various Binder Contents and Different Methods of Binder Addition
Excipient and acetaminophen.

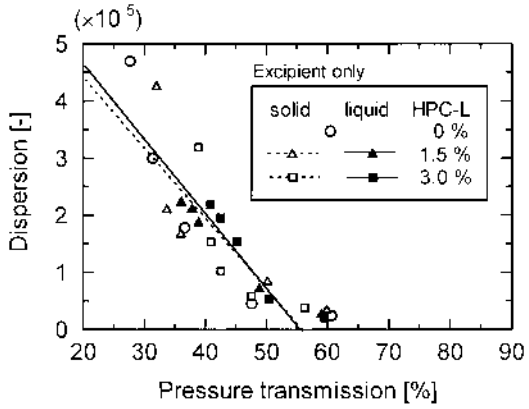

Fig. 5. Relationship between Water Dispersion and Pressure Transmission
Excipient only, R_S^2: 0.779, R_L^2: 0.871.

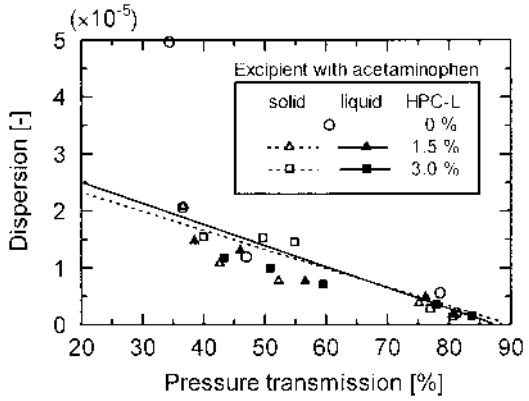

Fig. 6. Relationship between Water Dispersion and Pressure Transmission
Excipient and acetaminophen, R_S^2: 0.858, R_L^2: 0.892.

so that the solid and liquid methods should be done in the same manner (using only purified water). With elapsed time, water dispersion decreases; especially, at the beginning of the kneading, a decrease in the dispersion is significant, followed by a slow decrease. It is because the macro-scale water dispersion took place between coagulated powder masses at the initial stage, followed by the micro-scale water dispersion between each primary powder.

Figure 4 illustrates water dispersion in the case of using acetaminophen as a main ingredient (sample II). The water dispersion shows a decrease with kneading time, which is almost the same behavior as shown in Fig. 3. However, the water dispersion at each time obtained here is smaller than the one in Fig. 3. This means that a powder sample containing sparingly soluble acetaminophen has a better water dispersion property. Without the acetaminophen, the excipient can absorb water very quickly, so that the wetted coagulated masses are formed soon after the addition of water, then the water transforms between the masses. By contrast, since the powder with acetaminophen does not readily absorb water, water exists on the surface of the powder. The water is supposed to distribute easily between powders due to its surface transformation.

Figures 5 and 6 show a relationship between water dispersion and pressure transmission without and with the presence of acetaminophen, respectively (R_S^2 and R_L^2 in the figure caption mean correlation coefficients of each linear line for a solid and liquid system, respectively). The both cases, water dispersion with various binder contents and different methods of addition can be well expressed by a single linear line, although the inclination of each line differs depending on the properties of starting materials, such as solubility to water, water absorption potential, *etc.*[8] Also, the plots at the beginning of the kneading tend to show larger dispersion and lower pressure transmission, because the binder liquid needs at least 1 min to be roughly distributed among the powder samples; before that period, some samples are completely dry and others are wet among the 24 samples used to measuring water dispersion.

Each figure implies that there is no apparent effect of the binder addition ratio on water dispersion. It is considered that the powder properties such as water absorbing potential and dissolution property mainly determine the water dispersion characteristics, so that the effect of the binder addition ratio is negligibly small compared with these effects. Also, the paddle type kneader used in this study was able to knead the wet materials with high shear stress; the high shear kneading mechanism may contribute to the water dispersion. Detailed discussion on the kneading mechanism will be addressed in the next paper.

Comparison of the line of inclination in both cases reveals that the powder samples with acetaminophen (sample II) show a high pressure transmission, up to 90%, though the pressure transmission of excipient only (sample I) is less than 60%. This implies that the water dispersion in the case of acetaminophen is pretty good (uniformly distributed), so that the pressure can easily be transported between powders. Also, since powder samples containing acetaminophen do not easily dissolve in water, the viscosity of the power surface is relatively small, thus the friction between the powder bed and the inside wall of the cylinder became small compared to that of the soluble material.

Figures 7 and 8 describe the specific surface area of dry pellets prepared by wet kneading, extrusion granulation and drying as a function of the pressure transmission in the case of excipient only (sample I), or of excipient with acetaminophen (sample II), respectively (R^2_0, $R^2_{1.5}$ and $R^2_{3.0}$ in figure's caption represent correlation coefficients of each linear line for binder contents of 0, 1.5 and 3.0%, respectively).

In both cases, the specific surface area can be linearly ex-

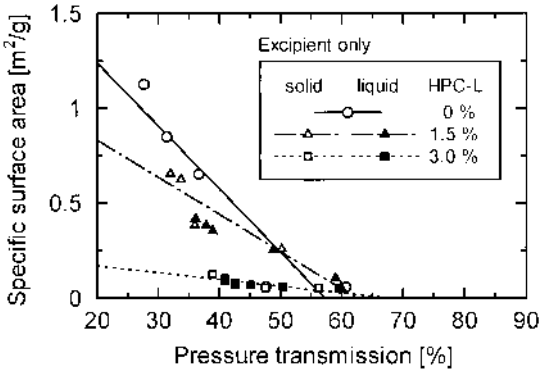

Fig. 7. Relationship between Specific Surface Area of Pellets and Pressure Transmission

Excipient only, R_0^2: 0.933, $R_{1.5}^2$: 0.947, $R_{3.0}^2$: 0.805.

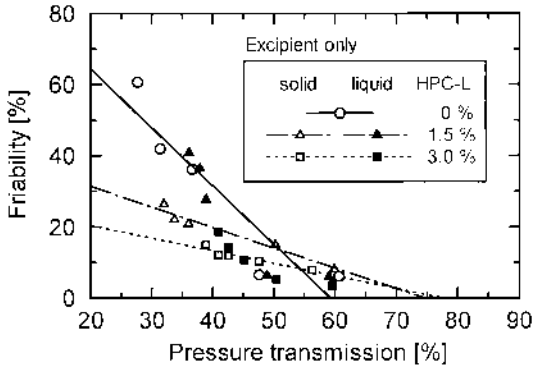

Fig. 9. Relationship between Friability of Pellets and Pressure Transmission

Excipient only, R_0^2: 0.925, $R_{1.5}^2$: 0.979, $R_{3.0}^2$: 0.947.

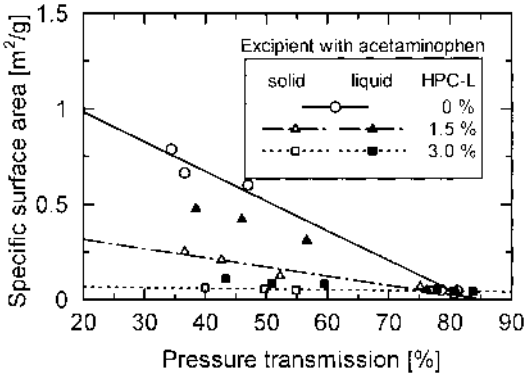

Fig. 8. Relationship between Specific Surface Area of Pellets and Pressure Transmission

Excipient and acetaminophen, R_0^2: 0.994, $R_{1.5}^2$: 0.975, $R_{3.0}^2$: 0.931.

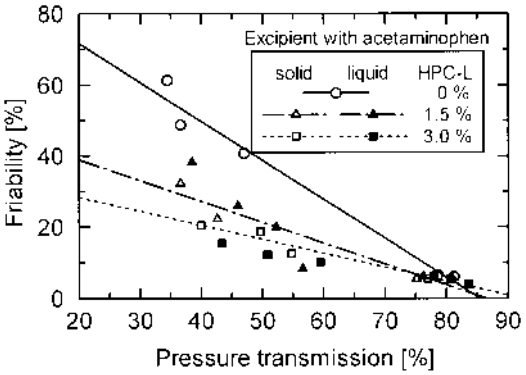

Fig. 10. Relationship between Friability of Pellets and Pressure Transmission

Excipient and acetaminophen, R_0^2: 0.989, $R_{1.5}^2$: 0.977, $R_{3.0}^2$: 0.977.

pressed by the pressure transmission. Since binder content seriously affects the binding force between particles, the inclination of each line is different, depending on the binder content. Generally, a large amount of binder can generate a large adhesion (binding) force, thus the void and pore size should be small, resulting in a small surface area. The plots of 3.0 wt% of HPC-L content with and without the acetaminophen showed a very small specific surface area, while they were almost the same during the kneading process. Deformation during kneading is a very important factor in reducing surface roughness, and the deformation is caused by moisture content. Therefore, the deformation effect may be worse if a binder content increases, because the solubility of the powder to a binder liquid decreases. Therefore, in the high binder content range, deformation during kneading cannot be expected, leading to have almost the same surface area.

Figures 9 and 10 indicate the friability of dry pellets as a function of the pressure transmission in the case of excipient only (sample I) and with acetaminophen (sample II), respectively. As shown in the previous figures, the friability of pellets can also be well expressed by a linear line, though the powder sample containing a larger binder amount shows larger friability. The large binding force generated by the large amount of binder also increases a pellet's physical strength.

From the findings obtained, it can be concluded that both the binder contents and its methods of addition have very little effect on the water dispersion condition during the wet kneading. The water dispersion is linearly expressed by the pressure transmission through the wet mass. All the data regarding the water dispersion under various binder contents and the two different methods (solid and liquid) can be well expressed by a single line. Also, the physical properties of dry pellets prepared by extrusion granulation after the kneading can be linearly expressed by the pressure transmission, although the inclination of the line differs according to binder content, not by the methods of addition.

In the case of using different starting materials, the degree of dispersion, pressure transmission and inclination of the line between water dispersion and pressure transmission differ considerably, although their behaviors are the same. From our findings, in the case of using sparingly soluble acetaminophen as a main ingredient, water dispersion and pressure transmission are better than with starting materials using excipient only. Physical properties such as solubility and water absorbing potential supposedly affect the water dispersion conditions during the kneading. Even in the cases, the effects of binder and its methods of addition have no effect on the water dispersion and pressure transmission.

Conclusion

The water dispersion conditions and pressure transmission characteristics among wet kneaded masses have been investi-

gated under varying conditions, including binder contents, different methods of addition (solid/dry) and different properties of starting materials using a newly developed compaction tester. The binder content and its methods of addition showed no effect on the water dispersion conditions; a single line was able to express the relationship between water dispersion and pressure transmission. This proves that the compression tester can evaluate the water dispersion conditions among the wet kneaded masses prepared under various operating conditions of the binder. However, the properties of starting materials affected the water distribution significantly. Sparingly soluble materials showed better water dispersion than the soluble materials. In all cases, the properties of dry pellets prepared by extrusion granulation after kneading could be expressed linearly by the pressure transmission, although each inclination differed from the operating conditions of various binder contents and properties of starting materials. It can be concluded that the developed compaction tester can be a very useful and practical tool to generally predict water dispersion and properties of the final products.

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