Mathematical Model in the Kinetics of Agitation Fluidized Bed Granulation. Effects of Moisture Content, Damping Speed and Operation Time on Granule Growth Rate

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A population balance equation, in which moisture content was taken into consideration for the coalescence probability of two colliding granules, was proposed to investigate the kinetics of granule growth in agitation fluidized bed granulation. The effects of operating variables such as moisture content, damping speed and operation time on the granule growth and its rate were numerically examined. It was found that the theoretical results intrinsically revealed these effects on granule size, size distribution and granule growth rate. The theory also showed good agreement with the experimental granulation data for pharmaceutical powders. As a result, the granule growth mechanism in agitation fluidized bed granulation was elucidated in detail.

Key words population balance; kinetics; granulation; granule growth; fluidized bed; moisture content

Industrial granulation has been widely used as a method of size enlargement of powdered materials. It is applied to produce granules of the required size, density and strength from powdered materials by means of some binding liquid.

The first systematic investigations into granulation were carried out by Rumpf[1] and Newitt and Conway-Jones,[2] who considered that granule growth by direct coalescence took place under an appropriate moisture content, and the tumbling action kneaded a pair into a nearly spherical shape. In reference to this coalescence mechanism model, various mathematical models have been reported by Capes and Danckwertz,[3] Kapur *et al.*[4-7] and Ouchiyama and Tanaka.[8-11]

As for the layering mechanism, models have also been proposed by Harada *et al.*,[12,13] Sherrington,[14] Uemaki and Mathur,[15] Mann,[16] Smith and Nienow,[17] and Waldie *et al.*[18,19] All of these models, however, lacked consideration of the fundamentals of pre-wetted powder granulation. In practice, the existence of granule surface water in collision is necessary to form a liquid bridge, which produces an adhesion force between the colliding granules, leading to granule growth. On the other hand, Haung and Kono[20,21] proposed a coalescence probability function and a nondimensional model predicting granule growth rate, in which the liquid bridge formation by colliding granules was taken into consideration. However, change in the granule size distribution with elapsed time was not investigated, and the effects of operating variables on granule growth rate were not sufficiently examined.

In this study, a population balance equation, in which moisture content was taken into consideration for the coalescence probability, was proposed to analyze the kinetics of granule growth in agitation fluidized bed granulation theoretically. The effects of operating variables such as moisture content, damping speed and operation time on the granule properties and the granule growth rate were numerically examined. Comparisons of the simulated results with experimental granulation data for pharmaceutical powders were conducted.

Modeling of Granulation Ouchiyama and Tanaka[8-11] proposed a population balance equation to analyze the mechanism of granule growth and its rate in tumbling granulation. In this study, an agitation fluidized bed granulator, in which granules were fluidized by fluidizing air and tumbled by agitator rotation, was used. The movement and flow pattern of granules have many similar features to those in the tumbling granulator. Therefore, in this study, an improved population balance equation proposed by Ouchiyama and Tanaka[8-11] has been used to analyze the mechanism of granule growth and its rate in agitation fluidized bed granulation.

Total Number of Collisions per Unit Time Figure 1 illustrates a basic random packing model for the theoretical analysis of contact number.

Let us assume that spherical particles are randomly placed on a solid sphere of diameter D. The number of contacts $C(D)$ between the spherical particles on the solid sphere was discussed by Ouchiyama and Tanaka[8] as,

$$C(D)=16(1-\varepsilon_A)\left(\frac{D+\bar{D}}{2\bar{D}}\right)^2 \qquad (1)$$

where ε_A shows surface porosity, which was assumed to be constant during granulation, and $\bar{D}$ indicates the average size of granules defined as

$$\overline{D^m}=\int_0^\infty D^m f(D,t)\mathrm{d}D \quad \text{for } m=1,2 \qquad (2)$$

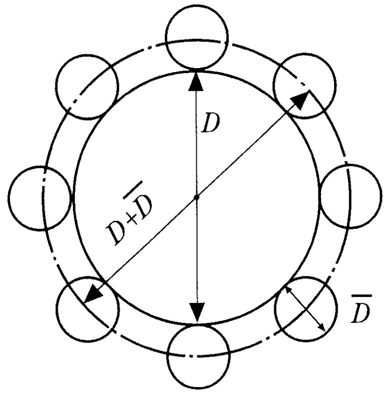

Fig. 1. Basic Random Packing Model

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Here, in this equation, $f(D,t)$ shows number based frequency size distribution at time t.

The number of contacts between the granules of size fraction $D-D+\mathrm{d}D$ and those of size fraction $d-d+\mathrm{d}d$ at time t can be expressed as

$$n(D,d)\mathrm{d}D\mathrm{d}d=C'C(D,d)N(t)f(D,t)f(d,t)\mathrm{d}D\mathrm{d}d \tag{3}$$

where $n(D,d)$ and $N(t)$ show the contact number function in a completely mixed packing, and the total number of granules in a granulator, respectively.

Also, C' and $C(D,d)$ are defined as[8)]

$$C'=16(1-\varepsilon_A) \tag{4}$$

$$C(D,d)=\left(\frac{D+\bar{D}}{2D}\right)^2\left(\frac{d+\bar{D}}{2D}\right)^2\Bigg/\frac{3+\bar{D}^2/(\bar{D})^2}{4} \tag{5}$$

Coalescence Rate During granulation, granule growth takes place by effective coalescence between the granules. Here, the following assumptions were used to express granule growth by a population balance equation.

(i) Granules in the granulator were completely mixed and coalescence occurred by the combination of two spherical granules.

(ii) Coalescence occurred whenever adhesion force was experienced.

(iii) Difficulty of coalescence was determined by a coalescence probability.

(iv) Attrition or crushing of granules was disregarded.

Assuming that the coalescence probability between granules of diameters D and d can be described as $P(D,d)$, and the loading frequency, which expresses the frequency of adhesion force (load) experienced to a pair, can be given as q, the number of pairs combined by the adhesion force per unit time is written as

$$\begin{aligned} &n(D,d)\mathrm{d}D\mathrm{d}d\times q\times P(D,d)\\ &=C'qN(t)C(D,d)P(D,d)f(D,t)f(d,t)\mathrm{d}D\mathrm{d}d\\ &=R(D,d)\mathrm{d}D\mathrm{d}d \end{aligned} \tag{6}$$

where, $R(D,d)$ shows a coalescence rate function. Finally, Eq. 6 expresses the loading-coalescence rate between the granules of size D and d.

Population Balance Equation According to the paper by Ouchiyama and Tanaka,[11)] the number of granules going out of a specified size fraction $D-D+\mathrm{d}D$ in a unit time can be given as

$$N_{\mathrm{out}}=\int_{d=0}^{\infty}R(D,d)\mathrm{d}d\times\mathrm{d}D\mathrm{d}t \tag{7}$$

and the number of granules coming into the size fraction in a unit time as

$$N_{\mathrm{in}}=\frac{1}{2}\int_{d=0}^{D}R(\sqrt[3]{D^3-d^3},d)\left(\frac{D}{\sqrt[3]{D^3-d^3}}\right)^2\mathrm{d}d\times\mathrm{d}D\mathrm{d}t \tag{8}$$

Disregarding granule crushing and attrition, $N_{\mathrm{in}}-N_{\mathrm{out}}$ should be equivalent to the amount of accumulation between the size fraction of $D-D+\mathrm{d}D$. This relationship can be written as

$$\frac{\partial}{\partial t}[N(t)f(D,t)\mathrm{d}D]\times\mathrm{d}t=N_{\mathrm{in}}-N_{\mathrm{out}} \tag{9}$$

Substituting Eqs. 7 and 8 into Eq. 9, and rearranging both sides of the above equation, the following expression is obtained.

$$\begin{aligned} \frac{\partial}{\partial t}[N(t)f(D,t)]=&-C'qN(t)\int_0^{\infty}C(D,d)P(D,d)f(D,t)f(d,t)\mathrm{d}d\\ &+\frac{1}{2}C'qN(t)\int_0^{D}C(\sqrt[3]{D^3-d^3},d)P(\sqrt[3]{D^3-d^3},d)\\ &\times\left(\frac{D}{\sqrt[3]{D^3-d^3}}\right)^2f(\sqrt[3]{D^3-d^3},t)f(d,t)\mathrm{d}d \end{aligned} \tag{10}$$

This equation expresses the basic population balance in a batch granulation system.

To make Eq. 10 dimensionless, the following equations are introduced

$$u=D/\delta \tag{11}$$

$$v=d/\delta \tag{12}$$

where δ is a characteristic limiting size,[11)] which is defined as

$$P(D,d)=0 \quad \text{for} \quad D\geqq\delta;\ d\geqq\delta \tag{13}$$

Using Eqs. 11 and 12, Eq. 5 can easily be rewritten as

$$C(D,d)=C(u,v)=\left(\frac{u+\delta\bar{u}}{2\delta\bar{u}}\right)^2\left(\frac{v+\delta\bar{u}}{2\delta\bar{u}}\right)^2\Bigg/\frac{3+\bar{u}^2/\delta(\bar{u})^2}{4} \tag{14}$$

If we use dimensionless time, τ, which expresses the frequency of adhesion force (load) per time t

$$\tau=C'qt \tag{15}$$

Equation 10 can be rewritten as

$$\begin{aligned} \frac{\partial}{\partial\tau}[N(\tau)f(u,\tau)]=&-\delta N(\tau)\int_0^{\infty}C(u,v)P(u,v)f(u,\tau)f(v,\tau)\mathrm{d}v\\ &+\frac{1}{2}\delta N(\tau)\int_0^{u}C(\sqrt[3]{u^3-v^3},v)P(\sqrt[3]{u^3-v^3},v)\\ &\times\left(\frac{u}{\sqrt[3]{u^3-v^3}}\right)^2f(\sqrt[3]{u^3-v^3},\tau)f(v,\tau)\mathrm{d}v \end{aligned} \tag{16}$$

Multiplying $\delta\mathrm{d}u$ on both sides of the above equation, and integrating it between $u=0$—∞, the left side of Eq. 16 can be expressed as

$$\begin{aligned} (\text{left side})&=\delta\int_0^{\infty}\frac{\partial}{\partial\tau}[N(\tau)f(u,\tau)]\mathrm{d}u\\ &=\delta\int_0^{\infty}\left[\frac{\partial N(\tau)}{\partial\tau}\cdot f(u,\tau)+\frac{\partial f(u,\tau)}{\partial\tau}\cdot N(\tau)\right]\mathrm{d}u\\ &=\frac{\partial N(\tau)}{\partial\tau}\delta\int_0^{\infty}f(u,\tau)\mathrm{d}u+N(\tau)\delta\int_0^{\infty}\frac{\partial f(u,\tau)}{\partial\tau}\mathrm{d}u \end{aligned} \tag{17}$$

Substituting

$$\delta\int_0^{\infty}f(u,\tau)\mathrm{d}u=1 \tag{18}$$

and,

$$\int_0^{\infty}\frac{\partial f(u,\tau)}{\partial\tau}\mathrm{d}u=0 \tag{19}$$

which express that the sum of the frequency distribution per unit time is zero, the left side of Eq. 16 can be described as

$$\delta\int_0^\infty \frac{\partial}{\partial\tau}[N(\tau)f(u,\tau)]\mathrm{d}u=\frac{\partial}{\partial\tau}N(\tau) \tag{20}$$

Similarly, the right side of Eq. 16 is given as

$$(\text{right side})=-\delta^2N(\tau)\int_0^\infty\int_0^\infty C(u,v)P(u,v)f(u,\tau)f(v,\tau)\mathrm{d}v\mathrm{d}u$$
$$+\frac{1}{2}\delta^2N(\tau)\int_0^\infty\int_0^u\left[C(\sqrt[3]{u^3-v^3},v)P(\sqrt[3]{u^3-v^3},v)\right.$$
$$\left.\times\left(\frac{u}{\sqrt[3]{u^3-v^3}}\right)^2 f(\sqrt[3]{u^3-v^3},\tau)f(v,\tau)\right]\mathrm{d}v\mathrm{d}u \tag{21}$$

Therefore, the dimensionless rate of change in the number of granules can be given by the combination of Eqs. 20 and 21.

$$\frac{\partial}{\partial\tau}N(\tau)=-\delta^2N(\tau)\int_0^\infty\int_0^\infty C(u,v)P(u,v)f(v,\tau)f(u,\tau)\mathrm{d}v\mathrm{d}u$$
$$+\frac{1}{2}\delta^2N(\tau)\int_0^\infty\int_0^u\left[C(\sqrt[3]{u^3-v^3},v)P(\sqrt[3]{u^3-v^3},v)\right.$$
$$\left.\times\left(\frac{u}{\sqrt[3]{u^3-v^3}}\right)^2 f(\sqrt[3]{u^3-v^3},\tau)f(v,\tau)\right]\mathrm{d}v\mathrm{d}u \tag{22}$$

Furthermore, substituting Eq. 22 into Eq. 16 and dividing it by $N(\tau)$, the following expression is obtained.

$$\frac{\partial}{\partial\tau}f(u,\tau)=-\delta\int_0^\infty C(u,v)P(u,v)f(u,\tau)f(v,\tau)\mathrm{d}v$$
$$+\frac{1}{2}\delta\int_0^u\left[C(\sqrt[3]{u^3-v^3},v)P(\sqrt[3]{u^3-v^3},v)\right.$$
$$\left.\times\left(\frac{u}{\sqrt[3]{u^3-v^3}}\right)^2 f(\sqrt[3]{u^3-v^3},\tau)f(v,\tau)\right]\mathrm{d}v$$
$$+\delta^2\int_0^\infty\int_0^\infty C(u,v)P(u,v)f(u,\tau)f(v,\tau)\mathrm{d}v\mathrm{d}u$$
$$-\frac{1}{2}\delta^2\int_0^\infty\int_0^u\left[C(\sqrt[3]{u^3-v^3},v)P(\sqrt[3]{u^3-v^3},v)\right.$$
$$\left.\times\left(\frac{u}{\sqrt[3]{u^3-v^3}}\right)^2 f(\sqrt[3]{u^3-v^3},\tau)f(v,\tau)\right]\mathrm{d}v\mathrm{d}u \tag{23}$$

Since frequency distribution after infinitely small time can be expressed as

$$f(u,\tau+\Delta\tau)=f(u,\tau)+\frac{\partial f(u,\tau)}{\partial\tau}\Delta\tau \tag{24}$$

the frequency distribution of granules after $\Delta\tau$ can be calculated by means of Eq. 24.

Coalescence Probability The difficulty of coalescence between granules was determined by a coalescence probability. In this study, the dimensionless coalescence probability introduced by Ouchiyama and Tanaka[11] is basically used:

$$P(D,d)=P(u,v)=\lambda^n\left[1-\left\{\frac{(uv)^{\gamma-3\eta/2}}{\left(\frac{u+v}{2}\right)^{2\gamma-4-3\eta/2}}\right\}^{2/(3\zeta)}\right]^n \tag{25}$$

where γ, ζ, η, λ and n are physical constants dependent on the physical properties of powder; according to Herts,[22] $\zeta=1$ and $\eta=0$ was equivalent to plastic, and $\zeta=\eta=2/3$ was the same as elastic. In addition, Kapur and Fuerstenau[5] have reported that the granule growth rate of batch granulation increases with the increasing moisture content of the granules. These facts imply that the coalescence probability between the two contacting granules increases with increasing moisture content.[11] Thus, the parameters of coalescence probability (Eq. 25) must be determined in relation to the moisture content dependence.

Experimental

Equipment A schematic diagram of the experimental apparatus is illustrated in Fig. 2. For wet granulation, an agitation fluidized bed[23–26]

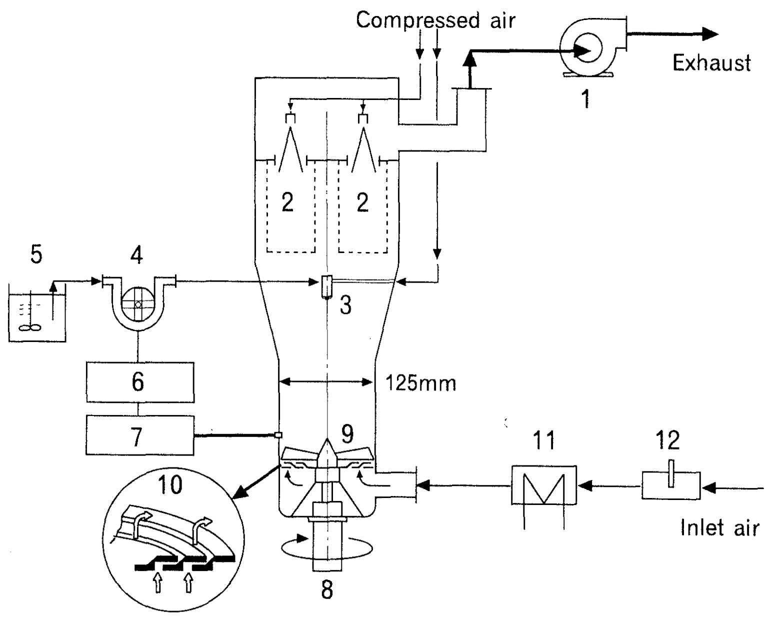

Fig. 2. Schematic Diagram of Experimental Apparatus Employed

1, blower; 2, bag filter; 3, spray nozzle; 4, pump; 5, binder liquid; 6, controller; 7, IR moisture sensor; 8, motor; 9, agitator blade; 10, slit plate; 11, heater; 12, hot-wire anemometer.

Table 1. List of Powder Samples Used

Sample	Number median diameter (μm)	Geometric standard deviation (—)	Mixing weight (kg)
Lactose[a]	60	1.52	0.21
Cornstarch[b]	15	1.54	0.09
Hydroxypropylcellulose[c]	21	1.55	0.015
(Total)			0.315

a) Pharmatose 200M, DMV. b) Cornstarch W, Nippon Shokuhin Kakou Co., Ltd. c) HPC EF-P, Shin-Etsu Chemical Co., Ltd.

Table 2. Operating Conditions

Inlet air velocity	0.6 m/s
Inlet air temperature	333 K
Agitator rotational speed	5.0 rps
Spray mist size	40 μm

(NQ-125, Fuji Paudal Co., Ltd.), with a vessel diameter of 125 mm was used. In this fluidized bed, an agitator blade was included to provide tumbling and compacting effects on granules, which make the granules spherical and well-compacted. Under the blade, three circular plates of different diameters were superimposed 3mm apart to function as air distributors. Heated air for particle fluidization was blown from the slit between each circular plate to create a circulating flow. Fine powders lifted up by the fluidization air were entrapped by bag filters and brushed down by a pulsating jet of air.

The moisture content of granules during granulation was measured by an infrared (IR) moisture sensor (Wet-eye, Fuji Paudal Co., Ltd.).[23-25] Based on the preliminary correlation between IR absorbance and moisture content measured by a drying method, moisture content by a wet basis was measured automatically.

Powder Samples Table 1 gives the properties of the powder samples used. Starting materials for granulation were pharmaceutical formulations, which consisted of lactose and cornstarch (mixed at 7 : 3 by weight). Hydroxypropylcellulose was added to the above mixture at a level of 5 wt% before granulation. Purified water was sprayed by a binary nozzle located at the top of the vessel (top spray method).

Particles used for the simulation have the same particle size distribution as the powder sample mixture for granulation experiments. They obeyed log-normal distribution and have a number median diameter of 33 μm and a 1.55 geometric standard deviation.

The particle size distributions of granulated products and powder samples were measured by an image processing system[26] (Image Eye, Fuji Paudal Co., Ltd.).

Operating Conditions Basic operating conditions for the granulation experiments are summarized in Table 2.

The spray mist size of a binder liquid (water) was measured by a laser scattering method using a He-Ne laser beam (LDSA-1300A, Meiwashoji Co., Ltd.) at room temperature and humidity.

Results and Discussion

Determination of Coalescence Probability Determination of coalescence probability is most important when the population balance equation is applied to the analysis of the granule growth process.

First, parameters ζ and η were determined. According to Ouchiyama and Tanaka,[10] ζ and η were physical constants dependent on the physical properties of powder. They stated that $\zeta=1$ and $\eta=0$ was equivalent to plastic, and $\zeta=\eta=2/3$ was the same as elastic. They also examined the moisture content dependence of coalescence probability; however, there was no concrete data for these parameters and the moisture content dependence.

In this study, these parameters were determined as follows: Granulation using the pharmaceutical powder listed in Table 1 can be conducted when the moisture content W is between 0 and 20%. If the moisture content is greater than 20%, the granule-water packing condition is nearly slurry, leading to blocking or defluidization simultaneously. Thus, it was assumed that the granules at $W=0\%$ were equivalent to elastic ($\zeta=\eta=2/3$), and granules at $W=20\%$ were the same as plastic ($\zeta=1$, $\eta=0$); in addition, the parameters of ζ and η varied in proportion to the moisture content. Thus, the parameters could be given as

$$\eta=-\frac{1}{30}W+\frac{2}{3} \tag{26}$$

$$\zeta=\frac{1}{60}W+\frac{2}{3} \tag{27}$$

Secondly, we determined parameters n and γ. It has been reported that the granule growth rate of batch granulation increases rapidly with increasing moisture content of the granules.[5] This fact implies that the coalescence probability between the two contacting granules also increases drastically with an increase in moisture content.[10] As a result of preliminary investigations, the actual granule growth was well expressed when an exponential function was used for the coalescence probability. Thus, the parameters n and γ were determined to be expressed as a form of $\exp(a+bW)$, where a and b were constants. Preliminary investigations elucidated that $(a, b)=(0.211, 3.742)$ for n and $(a, b)=(-3.022, 0.201)$ for γ were the optimum values.

As to a model parameter of λ, λ was defined by Ouchiyama and Tanaka[11] as

$$\lambda=\frac{Q_M}{Q_M-Q_m} \tag{28}$$

where, Q_M and Q_m showed the maximum and minimum compressive forces between two granules. Assuming that the minimum compressive force is zero, the parameter of λ is determined to be 1. In this study, we have used $\lambda=1$ to express the coalescence probability.

Figures 3 and 4 illustrate the shape of the coalescence probability function at various moisture contents and colliding granule sizes. Seen from Figs. 3 and 4, coalescence probability indicated that it was possible to create adherence between larger granules if the moisture content was large; in addition, it was easy to achieve coalescence if the colliding granule size was small under the same moisture content.

Kinetics of Granule Growth In fluidized bed granulation, granule growth is advanced under an equilibrium of damping by the addition of a binder liquid and drying by heated fluidization air. Therefore, moisture content and the damping speed are very important for granule growth. Here, the effects of moisture content on granule growth at various damping speeds were examined theoretically.

Figures 5 and 6 show the effects of moisture content on the granule number median diameter and the geometric standard deviation, respectively. Here, the moisture content was expressed as a function of the damping speed and the operation time:

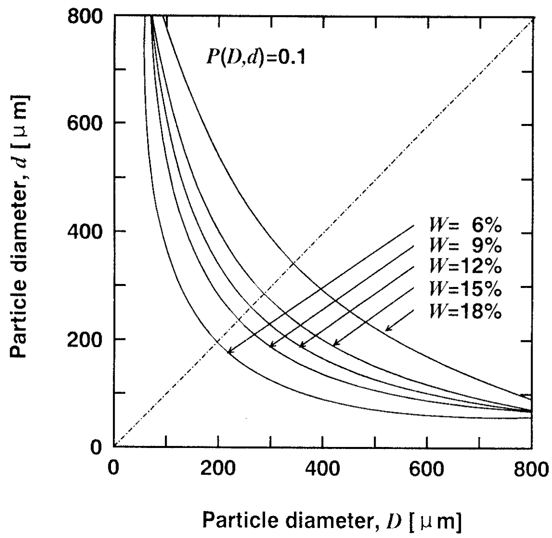

Fig. 3. Shape of Coalescence Probability at Various Moisture Content and Particle Sizes ($P(D, d)=0.1$)

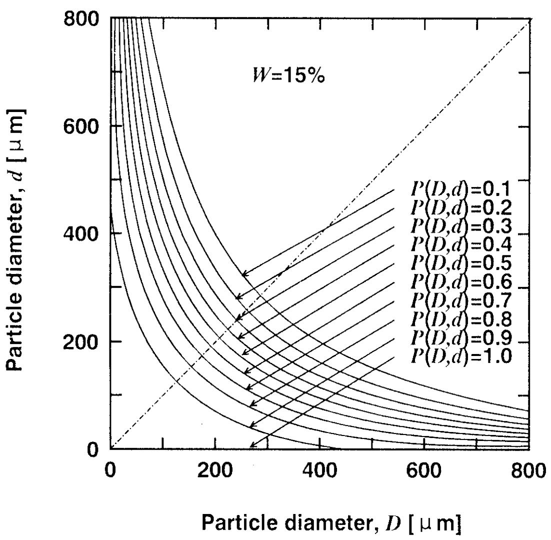

Fig. 4. Graphic Representation of Coalescence Probability Function at $W=15\%$

$$W=\mathrm{d}W/\mathrm{d}t\times t \tag{29}$$

where $\mathrm{d}W/\mathrm{d}t$ (%/min) indicated the rate of moisture content increase per minute (damping speed). For example, $\mathrm{d}W/\mathrm{d}t=1$ expressed that the moisture content increased by 1% per minute. In the actual granulation, damping speed was controlled by regulating the binder addition speed.

As seen in Fig. 5, the granule number median diameter increased with moisture content, while under the same moisture content, granule growth was advanced by a decrease in damping speed (small $\mathrm{d}W/\mathrm{d}t$). The former phenomenon occurred because the adhesion force increased with an increase in moisture content, and the latter originated from the fact that the operation time increased with decreased damping speed. In the actual granulation, granule growth was encouraged with the operation time because the frequency of granule collision increased. Similarly, in the simulation, the frequency with which the granules received adhesion force (load) increased with the operation time because the frequency of granule collision was defined by $\tau=C'qt$. Thus, it could be said that the granule growth was promoted not only by a moisture content increase but also by an increase in operation time. The present model simulated the granule growth process correctly.

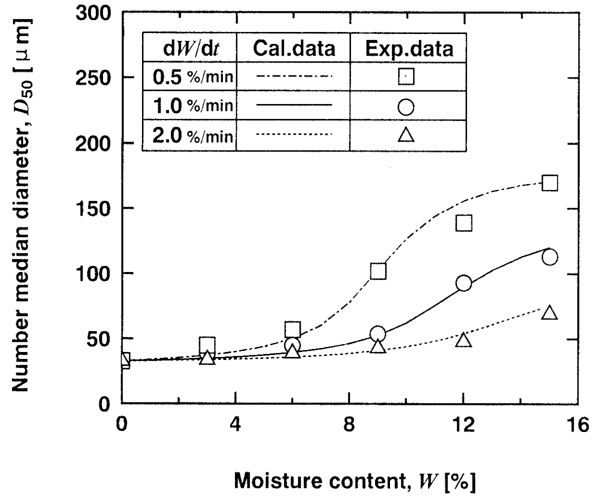

Fig. 5. Effect of Damping Speed on Number Median Diameter of Granules

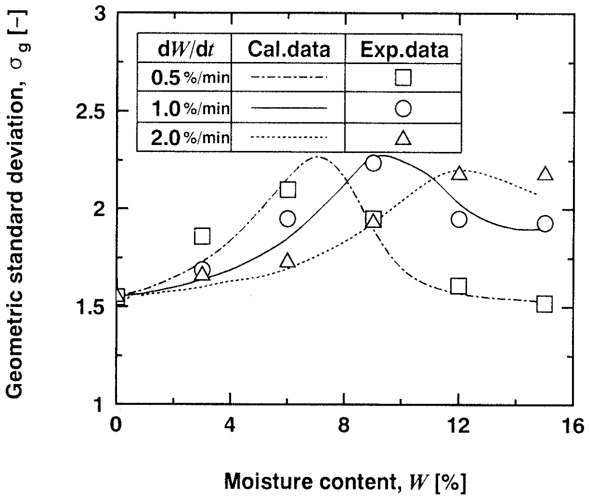

Fig. 6. Effect of Damping Speed on Geometric Standard Deviation of Granules

As seen in Fig. 6, the geometric standard deviation (particle size distribution) of granules showed a tendency to increase (wide particle size distribution) in a low moisture content range, while it decreased (sharp distribution) in a high moisture content range. Also, the deviation reached a maximum value at a smaller moisture content level, when the damping speed was small. This implied that granules of each size fraction were randomly adhered during the initial stage, but gradually they were arranged by differences in the granule growth rate of each size fraction; the large granules had difficulty coalescing, but the small granules easily coalesced with each other or adhered to larger granules. In addition, granule growth was found to be sufficiently promoted even at a low moisture content if the operation time increased (slow damping speed).

Figures 7, 8 and 9 show the change in particle size

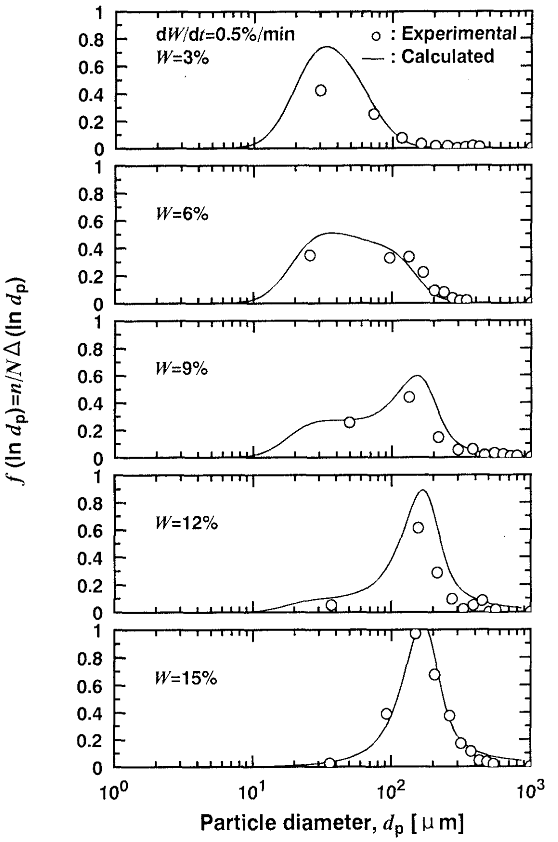

Fig. 7. Change in Particle Size Distribution ($dW/dt = 0.5\%/min$)

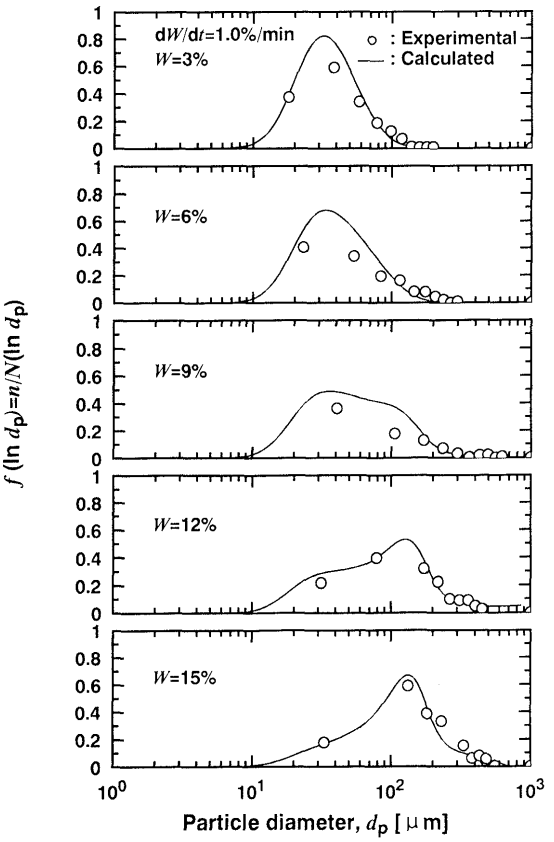

Fig. 8. Change in Particle Size Distribution ($dW/dt = 1.0\%/min$)

distribution of granules at various damping speeds. These figures clearly revealed that the granule growth of a large sized fraction was slow but the growth of a small sized fraction was promoted actively. This phenomena answered why granules with the same moisture content should show a narrower particle size distribution when the damping speed was low; in the case of a slow damping speed, since there was sufficient time (= chance for granules to contact each other), granules of a large size fraction could grow sufficiently even when the growth rate was slow. By contrast, in the case of fast damping speed, granule growth, especially the growth of large sized fractions, was insufficient, although granules were dampened to the same moisture content. In such cases, granule size distribution should be wide.

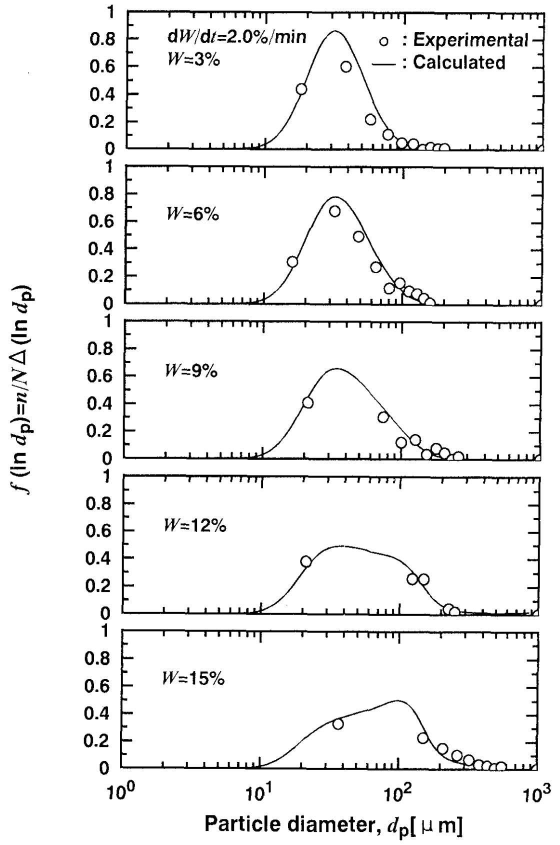

Fig. 9. Change in Particle Size Distribution ($dW/dt = 2.0\%/min$)

The obtained data suggested that granule damping speed should be small in order to produce granules of a narrow size distribution in the fluidized bed granulation process.

As a result, the granule growth mechanism was elucidated and the effects of operating variables on granule growth were analyzed theoretically by means of the simulation model proposed here. In addition, extremely good correlation was obtained between the simulated and experimental data of granulation, which showed that the coalescence probability in the present population balance equation expressed the granulation phenomena correctly.

Conclusions

A population balance equation, in which moisture content was taken into consideration for the coalescence probability of two colliding granules, was proposed to investigate the kinetics of granule growth in agitation fluidized bed granulation. The effects of operating variables such as moisture content, damping speed and operation time on the granule number median diameter and on geometric standard deviation were numerically examined. It was found that granule growth was promoted and the particle size distribution was made narrower when the damping speed decreased (operation time increased). This was because the frequency with which the granules received adhesion force (load) increased with the operation time. It was also found that the simulated results were in good agreement with the experimental granulation data for pharmaceutical powders.

References

1) Rumpf H., *Chemie. Ingr. Tech.*, **30**, 144—158 (1958).
2) Newitt D. M., Conway-Jones J. M., *Trans. Instn. Chem. Eng.*, **22**, 422—441 (1958).
3) Capes C. E., Danckwertz P. V., *Trans. Inst. Chem. Eng.*, **43**, 125—130 (1965).
4) Kapur P. C., Fuerstenau D. W., *Trans. Am. Inst. Min., Metal., Pet. Engrs.*, **229**, 348—357 (1964).
5) Kapur P. C., Fuerstenau D. W., *Ind. Eng. Chem. Process Des. Develop.*, **5**, 5—14 (1966).
6) Kapur P. C., Fuerstenau D. W., *Ind. Eng. Chem. Process Des. Develop.*, **8**, 56—62 (1969).
7) Kapur P. C., *Chem. Eng. Sci.*, **27**, 1863—1869 (1972).
8) Ouchiyama N., Tanaka T., *Ind. Eng. Chem. Fundam.*, **19**, 338—340 (1980).
9) Ouchiyama N., Tanaka T., *Ind. Eng. Chem. Process Des. Develop.*, **13**, 383—389 (1974)
10) Ouchiyama N., Tanaka T., *Ind. Eng. Chem. Process Des. Develop.*, **14**, 286—289 (1975).
11) Ouchiyama N., Tanaka T., *Ind. Eng. Chem. Process Des. Develop.*, **20**, 340—348 (1981).
12) Harada K., Fujita J., *Kagaku Kogaku*, **33**, 793—799 (1969).
13) Harada K., Fujita J., Yoshimura S., *Kagaku Kogaku*, **34**, 102—104 (1970).
14) Sherrington P. J., *Chem. Engr.*, **201**, 201—214 (1968).
15) Uemaki O., Mathur K. B., *Ind. Eng. Chem. Process Des. Develop.*, **15**, 504—508 (1976).
16) Mann U., *Ind. Eng. Chem. Process Des. Develop.*, **17**, 103—106 (1978).
17) Smith P. G., Niemow A. W., *Chem. Eng. Sci.*, **38**, 1233—1240 (1983).
18) Waldie B., Wilkinson D., Zachra L., *Chem. Eng. Sci.*, **42**, 653—665 (1987).
19) Waldie B., *Chem. Eng. Sci.*, **46**, 2781—2785 (1991).
20) Hang C. C., Kono H., *Powder Technol.*, **55**, 19—34 (1988).
21) Hang C. C., Kono H., *Powder Technol.*, **55**, 35—49 (1988).
22) Timoshenko S., Goodier J. N., "Theory of Elasticity," 3rd ed., Mcgraw Hill, New York, 1970, pp. 409—414.
23) Watano S., Fukushima T., Miyanami K., *Powder Technol.*, **81**, 161—168 (1994).
24) Watano S., Yamamoto A., Miyanami K., *Chem. Pharm. Bull.*, **42**, 133—137 (1994).
25) Watano S., Sato Y., Miyanami K., *J. Chem. Eng. Jpn.*, **28**, 282—287 (1994).
26) Watano S., Miyanami K., *Powder Technol.*, **83**, 55—60 (1995).