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Effects of Operational Variables on the Properties of Granules Prepared by Moisture Control Method in Tumbling Fluidized Bed Granulation

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Effects of operational variables such as liquid flow rate, inlet air temperature and inlet air humidity on the properties of granules, prepared by a tumbling fluidized bed granulation while controlling the moisture content with an IR moisture sensor, were investigated experimentally. An increase in the liquid flow rate, *i.e.* the increase of the droplet size resulted in a slight increase of granule size and size distribution, while little influence was found of the inlet air temperature and humidity on granule size, size distribution or the apparent density. Remarkably good reproducibility was obtained in the granules prepared by the moisture control method. It was therefore concluded that by applying this method to the wet granulation by a type of fluidized bed, the effects of external circumstances could be fully eliminated and good reproducibility maintained.

Keywords moisture control; tumbling fluidized bed granulation; liquid flow rate; inlet air temperature; inlet air humidity; process variable

Wet granulation in a type of fluidized bed has been widely used in the pharmaceutical and other industries, because this type of granulation has significant process advantages in reducing handling and contamination by dust. This also saves several unit operations such as mixing, granulation and drying which must otherwise be conducted in separate equipment.

Agglomeration by this type of method is so complicated that the effects of process variables on the properties of granules must be understood. Davis and Gloor,[1] Rankell *et al.*[2] and Shinoda *et al.*[3] have experimentally studied the effects of some variables, while Schæfer and Wørts[4,5] synthetically quantified the effects of process variables given in fluidized bed granulation. In these papers, it was commonly said that the moisture content was one of the most important factors for the binding mechanism, hence its control was necessary. Accordingly, Nishii[6] and Shibata[7] both described a practical method of measurement and control of the moisture content using an IR moisture sensor. We[8,9] also reported on the moisture control in fluidized bed granulation. In these studies, however, most attention was paid to the process control and the process efficiency, and there has been no study which addressed the reproducibility or the effects of process variables on the properties of granules when the moisture control method was applied.

In this paper, effects of the liquid flow rate and of the external conditions such as inlet air temperature and humidity on the properties of granules, prepared by tumbling fluidized bed granulation while controlling moisture content, were investigated experimentally. Reproducibility of the properties of granules prepared by this method is also discussed here.

Experimental

Equipment Figure 1 illustrates the experimental set up. For the wet granulation, a tumbling fluidized bed granulator (New Marumerizer NQ-Labo, Fuji Paudal Co., Ltd.) was used. This granulator consisted of two parts: a lower cylindrical vessel (0.125 m in diameter, 0.10 m in depth), and an upper cone vessel tapered 15 degrees (0.20 m in height), both made of acrylic resin to permit visual observation. On the bottom of the cylindrical vessel, an agitator blade was turning on a center axis to create a tumbling and compacting motion on the granule particles; under the blade, three circular plates of different diameter were superimposed 3 mm apart. Heated air needed for the fluidization of the particles was blown from the slit between each plate creating a circulating flow. Fine powders accompanied by the fluidizing air were entrapped by bag filters and brushed down by a pulsating jet of air.

Moisture content of granules during the operation was continuously measured by an IR moisture sensor (Wet eye, Fuji Paudal Co., Ltd.) The main body of the IR sensor and the granulator were connected with an optical fiber. The extremity of the fiber was located on the side wall of the bottom cylindrical vessel so as to measure the moisture content at the most dense powder concentration.

Inlet air humidity was measured by a ceramic humidity sensor and controlled by an ultrasonic humidifier. Other operational variables such as inlet air temperature, air flow rate and agitator rotational speed were also controlled. The output signal from the sensors were simultaneously digitalized in a 12 bit A/D converter to be monitored in a personal computer and finally memorized on floppy disks.

Powder Samples Starting materials were 0.300 kg, which consisted of lactose and cornstarch (mixing ratio was 7 : 3 by weight). 0.015 kg of hydroxypropylcellulose (HPC EF-P) was adopted as a binder, and was mixed as a form of dry powder into starting materials before granulation. Purified water was used as a binder solution, which was sprayed through a binary nozzle.

Evaluation of the Granules The droplet size of the binder liquid was measured by a light scattering method using He–Ne laser beam (LDSA-1300A, Meiwashoji Co., Ltd.) at room temperature and humidity.

Particle size distribution of the granules was measured by sieve analysis with a row-tap shaker.

Experimental Procedure Table I lists the experimental conditions. To vary the droplet size, only the liquid flow rate was varied from 10 to 40 g/min. The evaporaion speed at the drying phase was fixed to a constant value in order to avoid the effect of drying time on granule attrition.

Results and Discussion

Effects of Liquid Flow Rate on the Properties of Granules

Figure 2 explains the experimental procedure of the moisture control method. Here, W, t and dW/dt denote moisture content, processing time and moisture rising gradient, respectively. In this experiment, the damping speed (moisture rising gradient, $dW/dt = 1\%/\text{min}$), set point value of the moisture content ($W = 15\,\text{wt}\%$), the time required for the fixed command control of the moisture content ($t = 15\,\text{min}$) and the drying condition

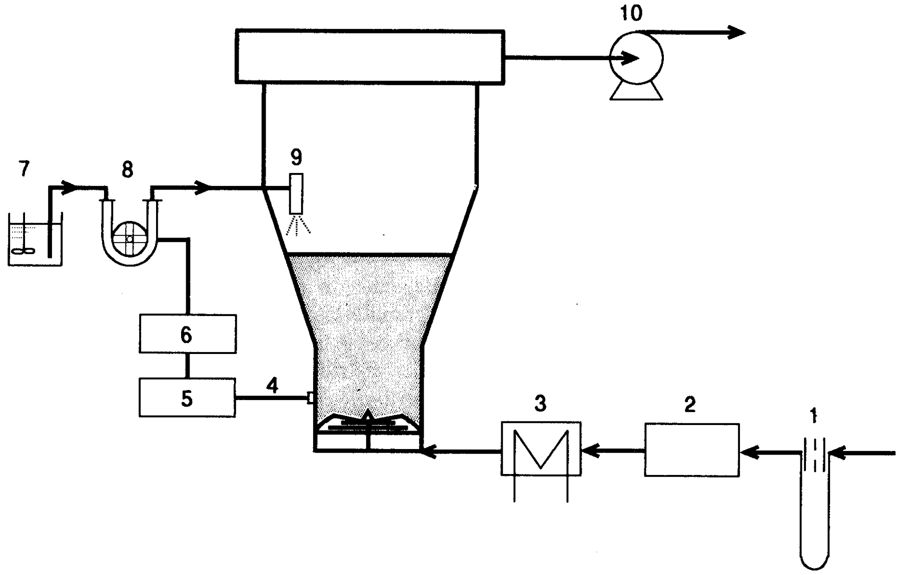

Fig. 1. Experimental Set Up

1, orifice flow meter; 2, ultrasonic humidifier; 3, heater; 4, optical fiber; 5, IR moisture sensor; 6, controller; 7, binder liquid; 8, pump; 9, binary nozzle; 10, blower.

Table I. Experimental Conditions

Air flow rate	0.4 m/s
Agitator rotational speed	300 rpm
Spray air pressure	1.5×10^5 Pa
Nozzle insert	i.d. 1.0 mm
Moisture content	15 wt%

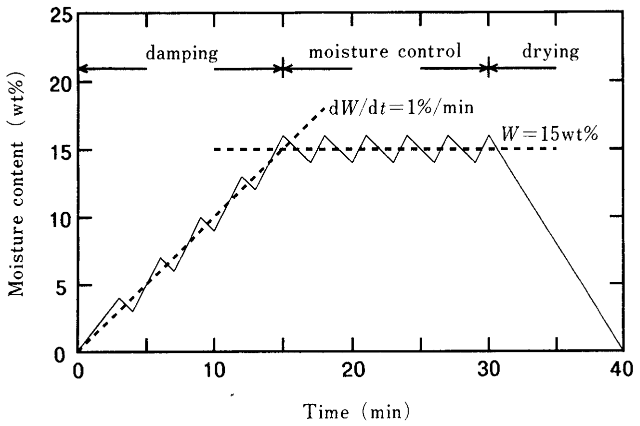

Fig. 2. Example of Moisture Control with On–Off Controller

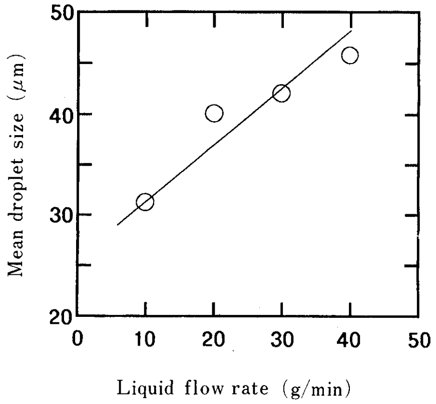

Fig. 3. Plots of Mean Droplet Size as a Function of Liquid Flow Rate

Nozzle insert i.d. = 1.0 mm, spray air flow rate = 40 l/min, spray air pressure = 1.5×10^5 Pa.

were fixed every experiment to avoid disturbance. Here, the amount of water sprayed, however, was not constant because the drying efficiency should change if the inlet air condition of temperature and humidity varied.

The control of the moisture content was done by an on–off controller, which functioned to move (on) the pump if the moisture content was lower than the predetermined set point value and to stop it (off) if the moisture content was higher than the set point value. Since this method has the advantages of regulating the moisture content by controlling the on and off time without changing the liquid flow rate, the droplet size in spraying can be maintained at a constant value throughout the operation. Accordingly, only the effects of the droplet size on the properties of granules can be estimated.

Figure 3 shows the plots of the mean droplet size as a function of the liquid flow rate. Figure 4 illustrates the droplet size distribution with variation in the liquid flow rate, *F*. As seen in Fig. 4, droplets ranged from 10 to 90 μm with a sharp size distribution were obtained. Coarse droplets which would result in coarse granules were rarely found, but a slight increase in size distribution was observed as liquid flow rate increased. The curves of accumulation at each flow rate were almost the same, suggesting that there was a favorable contact of liquid to air within this range. In addition, since the mean droplet size was linearly increased with increase in liquid flow rate, the estimation of effects of droplet size on granule growth could be conducted correctly.

Figure 5 shows the relation between the mean particle diameter, geometric standard deviation and the liquid flow rate. With increase in liquid flow rate, only slight granule growth was found whereas Schæfer and Wørts,[4,5]

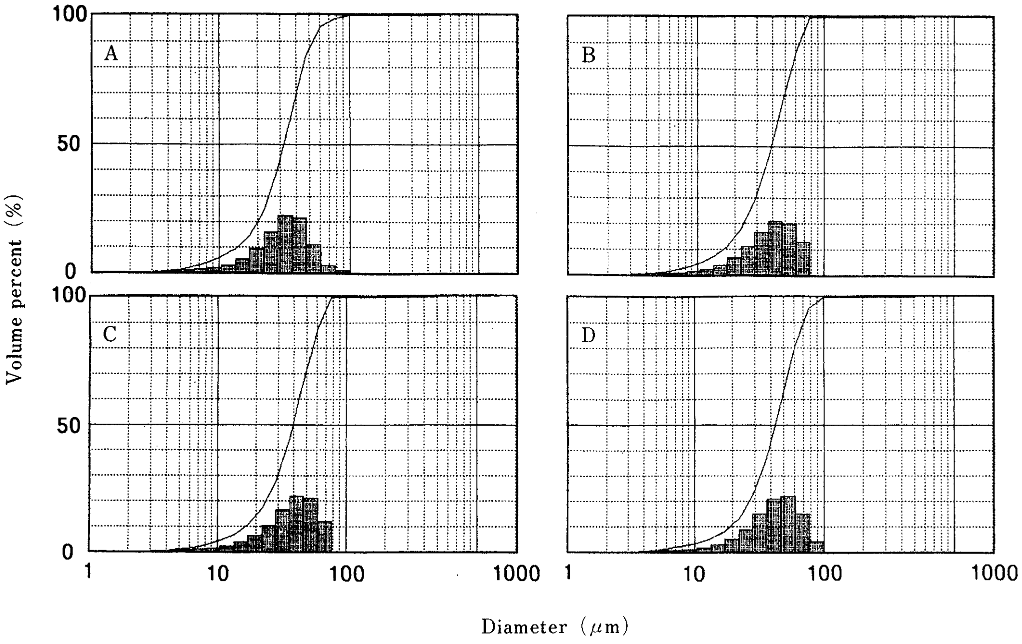

Fig. 4. Droplet Size Distribution

A, $F=10$ g/min; B, $F=20$ g/min; C, $F=30$ g/min; D, $F=40$ g/min. Nozzle insert i.d. = 1.0 mm, spray air flow rate = 40 l/min, spray air pressure = 1.5×10^5 Pa.

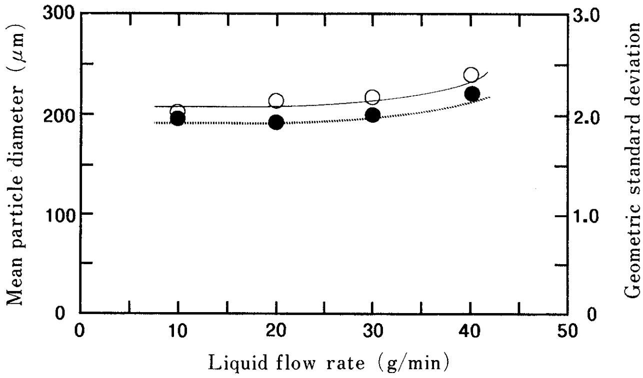

Fig. 5. Relation between Mean Particle Diameter, Geometric Standard Deviation and Liquid Flow Rate

Inlet air temperature, 60 °C; humidity, 50%. ○, mean particle size; ●, geometric standard deviation.

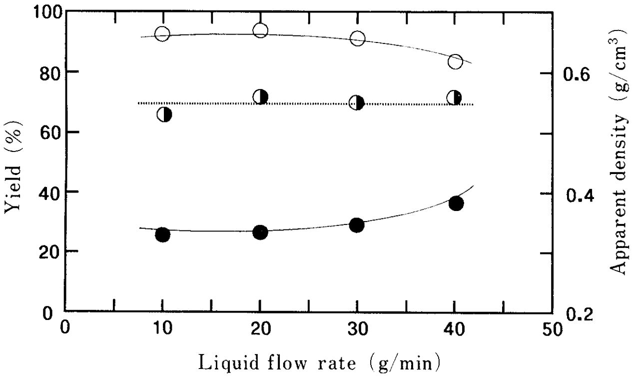

Fig. 6. Relation between Yield of Granules, Apparent Density and Liquid Flow Rate

Inlet air temperature, 60 °C; humidity, 50%. ○, yield of fine granules ($74\leq d<500\,\mu$m); ●, yield of coarse granules ($355\leq d<1400\,\mu$m); ◑, apparent density.

who also investigated the effects when drying rate was controlled by measuring the difference in temperature between drying air and product surface, stated that the increased rate of flow resulted in large granule growth. Although it was possible to control the drying rate by the indirect method, this was valid only if the particle surface was completely covered with water. In addition, since not all the spray mist always reached the particles, this technique did not always give a correct estimate of the effects of surface moisture content. On the contrary, as the method using the IR moisture sensor can control the surface moisture content which directly affects the number of liquid bridges, it is able to estimate the effects of droplet size correctly. As a result of the exact control of the surface moisture content and the damping speed using purified water of low viscosity, the effects of droplet size on granule growth were believe to be quite small. Seen in Fig. 6 which denotes the effects of liquid flow rate on the yield of coarse ($355\leq d<1400\,\mu$m) and fine fractions ($74\leq d<500\,\mu$m), the coarse fraction increased slightly and the fine fraction decreased with the increase in liquid flow rate. (Here, d indicates the particle size.) Increased droplet size resulted in formation of a coarse fraction, which led to an increase in granule size and size distribution. Droplet size seemed to have no influence on the apparent density.

Effects of Inlet Air Temperature on the Properties of Granules Schæfer and Wørts[4,5] varied the inlet air temperature in order to change the drying rate, but made no further comments as to the effects of temperature on granule growth. If we vary the temperature while keeping moisture content constant, the amount of water sprayed must be greatly changed. Therefore, the effects of temperature on the properties of granules are thought to be important, although there has been no study reported

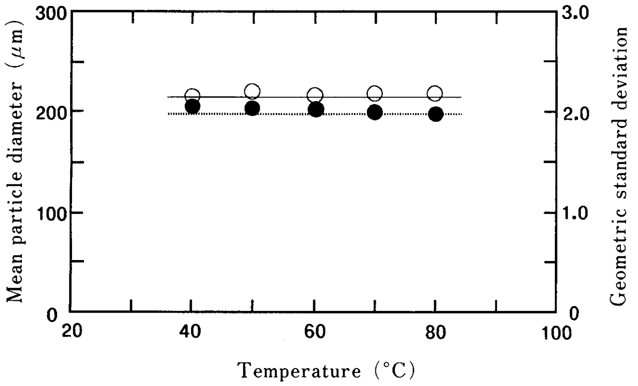

Fig. 7. Relation between Mean Particle Diameter, Geometric Standard Deviation and Inlet Air Temperature

Liquid flow rate, 20 g/min; humidity, 50%. ○, mean particle size; ●, geometric standard deviation.

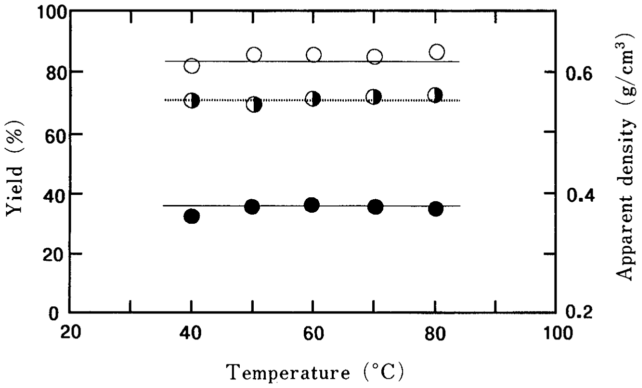

Fig. 8. Relation between Yield of Granules, Apparent Density and Inlet Air Temperature

Liquid flow rate, 20 g/min; humidity, 50%. ○, yield of fine granules ($74 \leqq d < 500\,\mu m$); ●, yield of coarse granules ($355 \leqq d < 1400\,\mu m$); ◑, apparent density.

in the literature.

Figure 7 illustrates the effects of inlet air temperature on mean particle size and size distribution. Effects of the temperature on the yield of coarse and fine fractions and on the apparent density are also indicated in Fig. 8.

No remarkable effects on the properties of granules were found from Figs. 7 and 8. With the increase of inlet air temperature, the spraying on-time was increased and the off-time decreased to maintain a constant moisture content. In spite of the increase in drying rate, since the surface moisture content was maintained with the same droplet size and size distribution (= the same liquid flow rate) by using the on–off moisture control method, no effects were found on the properties of the granules.

Effects of Inlet Air Humidity on the Properties of Granules The air humidity is one of the most important of the external disturbances affecting the properties of the final products. Control of the air humidity is necessary to maintain reproducibility of product quality; not all of the production facilities, however, have been provided with air conditioning equipment capable of this.

In this paper, the effects of inlet air humidity on the properties of granules of which the moisture content was controlled were investigated experimentally.

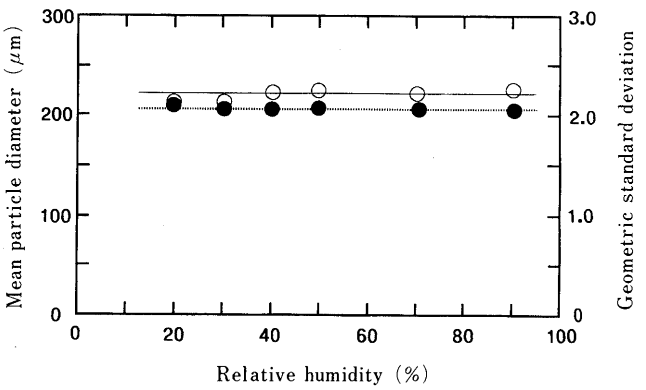

Fig. 9. Relation between Mean Particle Diameter, Geometric Standard Deviation and Inlet Air Humidity

Liquid flow rate, 20 g/min; inlet air temperature, 60 °C. ○, mean particle size; ●, geometric standard deviation.

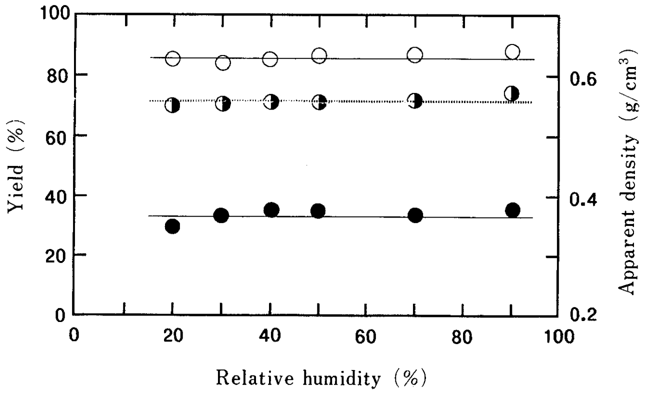

Fig. 10. Relation between Yield of Granules, Apparent Density and Inlet Air Humidity

Liquid flow rate, 20 g/min; inlet air temperature, 60 °C. ○, yield of fine granules ($74 \leqq d < 500\,\mu m$); ●, yield of coarse granules ($355 \leqq d < 1400\,\mu m$); ◑, apparent density.

Figure 9 shows the effects of this on mean particle size and size distribution. The effects on the yield of granules and on the apparent density are also illustrated in Fig. 10. It was obvious that the air humidity had little influence on the particle size, size distribution or the apparent density when the moisture control method was used. As discussed earlier with regard to the effects of inlet air temperature on granule properties, the air humidity also influenced only the drying rate, not the granule properties. Thus, the effects of external disturbances such as inlet air temperature and air humidity on the properties of granules can be fully blocked by the moisture control method.

Reproducibility of the Granules To investigate the robustness of the process control, the reproducibility of granules prepared by several methods was compared.

Figure 11 illustrates the frequency of the number as a function of mean particle diameter of the granules prepared by the following four method:

A: Moisture control. As stated, moisture content was also controlled to maintain 15 wt% and processing time was also programmed to control. B: Control of exhaust air humidity. The exhaust air humidity was measured by

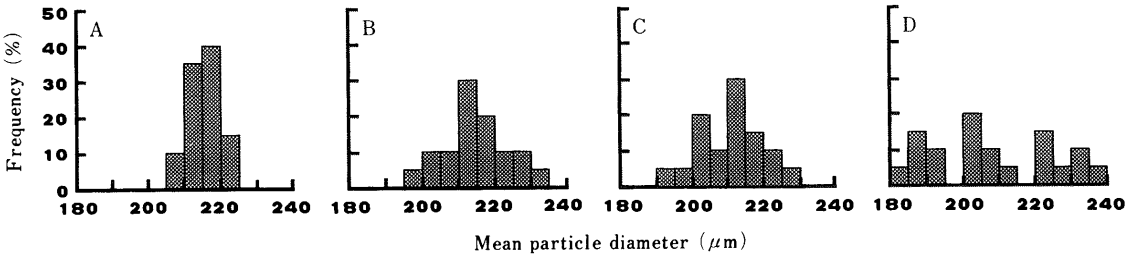

Fig. 11. Reproducibility of the Granules Prepared by Several Methods

A, moisture control; B, control of exhaust air humidity; C, control of drying rate; D, constant spraying.

a ceramic humidity sensor, and spraying on–off time was controlled to maintain a constant relative humidity (=50%). C: Control of drying rate. The spraying on–off time was regulated to maintain a constant drying rate which was calculated by the drying efficiency of the inlet and exhaust air. D: Constant spraying. Spraying of the water was done at a constant speed (=20 g/min).

In every experiment, the spraying rate (=20 g/min) was kept constant to avoid the effects of droplet size, and the processing time was also fixed. In order to vary the influence of the environment, five temperatures (40, 50, 60, 70 and 80 °C) and four variables of inlet air humidity (20, 40, 60 and 80%) were adapted, so that the total number of experiments was 20.

As seen in Fig. 11, the moisture control method exhibited excellent reproducibility of mean particle size, which was the result of the exact control of adhesive power using the control of surface moisture content.

The methods involving control of exhaust air humidity and control of drying rate indicated fairly good reproducibility. Although these methods have been more commonly used, the moisture control technique gave superior results. This was due to the evaporation of water not only from the particle surface but also from the droplets which were not captured by the particles. Surface moisture content was thus not always constant in every experiment.

The constant spraying method lacked reproducibility. As environmental conditions varied, the moisture content of granules changed greatly because the drying efficiency was remarkably influenced by the inlet air temperature and humidity.

The moisture content should therefore be kept constant in the course of the fluidized bed granulation for the best reproducibility.

Conclusions

Wet granulation was conducted in a tumbling fluidized bed, and the moisture content was measured by IR moisture sensor and controlled by the on–off control method. The damping speed, set point value of the moisture content, time required for the moisture fixed command control and the drying rate were exactly fixed to avoid disturbance. The effects of liquid flow rate, inlet air temperature and air humidity on the properties of granules were then investigated experimentally and were found to be as follows:

1) With increase in liquid flow rate, a slight increase in granule size and size distribution were found due to the increase in droplet size. No remarkable effect was observed on the apparent density of the granules. 2) Little effects of inlet air temperature and air humidity on the properties of the granules was found when the moisture content and the processing time of each operation was controlled at a constant value. 3) It was shown that the moisture content should be controlled during the course of fluidized bed granulation for better reproducibility. It was also concluded that problems due to the seasonal effects were fully eliminated by controlling moisture content with the IR moisture sensor.

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