Measurement of Moisture Content by IR Sensor in Fluidized Bed Granulation. Effects of Operating Variables on the Relationship between Granule Moisture Content and Absorbance of IR Spectra

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In this study, the validity of moisture measurement by an IR sensor was investigated in fluidized bed granulation. The effects of operating variables on the relationship between granule moisture content and the absorbance of IR spectra were examined experimentally. It was found that the air flow rate of purge air used for preventing powder adhesion, fluidizing air velocity, agitator rotational speed and spray mist size had no effect on the relationship. However, if the dampening speed was extremely low, the effects of fluidization air temperature and liquid flow rate on the relationship could be recognized. This was because the surface drying due to the extremely low dampening speed caused water to transfer from the inside to the surface. As a result, it can be concluded that the measurement of moisture content by an IR moisture sensor can be conducted with high accuracy, free of operating conditions, unless the granulation is conducted under an extremely low dampening speed.

Key words moisture content; IR moisture sensor; validation; fluidized bed granulation; operating variable

Recently, the words of "process validation" have become an extensive subject especially in the pharmaceutical industry, because GMP (good manufacturing practice) has strongly required proof of the validity of the manufacturing process and the security of product quality. To verify the process validation, the accuracy of sensors, installed to continuously monitor process conditions, must first be guaranteed.

In the manufacturing process of products by wet granulation, the monitoring of moisture content has been conducted extensively using an IR moisture sensor,[1)] because it can measure granule moisture content, a most important factor in determining granule growth, continuously and accurately without contacting the powder bed. However, the effects of operating variables on the accuracy of moisture measurement have not been well studied, although they are of great importance in guaranteeing the product quality.

In this study, the validity of moisture measurement by an IR sensor was investigated under various operating conditions in fluidized bed granulation. Guidelines for measuring moisture content correctly during granulation was also suggested here.

Experimental

Equipment For wet granulation, an agitation fluidized bed[1−3)] (NQ-125, Fuji Paudal Co., Ltd.) was used. Moisture content during granulation was continuously measured by an IR moisture sensor (Wet-eye, Fuji Paudal Co., Ltd.).[1−3)]

Powder Samples For agitation fluidized bed granulation, 0.300 kg of a mixture of lactose and cornstarch, of which the mixing ratio was 7 : 3 by weight, was used. Hydroxypropylcellulose (HPC EF-P) was used as a binder, which was mixed at a level of 5% (0.015 kg) as a dry powder into the mixture before granulation. Purified water was sprayed through a binary nozzle, located 100 mm above the powder bed.

Operating Conditions The basic operating conditions used are listed in Table 1. Most of the operating variables were optimized previously.[2)] In this study, the fluidizing air velocity, agitator rotational speed, temperature of heated air, liquid (water) flow rate, and flow rate of purge air used for preventing powder adhesion at the pointed end of the sensor varied.

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Results and Discussion

Figures 1, 2 and 3 show the effects of fluidization air velocity u, agitator rotational speed N, and velocity of the purge air v on the relationship between granule moisture content W and the absorbance of IR spectra X. Here, granule moisture content was actually measured using a drying method, which was the same as previously reported.[1)] Also, Fig. 4 illustrates the effect of a median size of spray mist (d_{m50}) on the relationship between granule moisture content and the absorbance of IR spectra. Here, the spray air pressure varied from 0.4×10^5 to 1.0×10^5 Pa (spray mist median size thus varied from 51.4 to 33.3 μm) to maintain a constant dampening speed and suitable particle fluidizing condition. The geometric standard deviation of the spray mist was about 1.6, which was almost constant if the air pressure varied. Seen from these figures, it seemed that these operating variables had no effect on the relationship between granule moisture content and the absorbance of IR spectra. Also, extremely high accuracy and good reproducibility of the measurement could be recognized. Therefore, in case of granulation under this variety of operating conditions, there is no need to consider the effects of these operating variables on the measurement of moisture content.

Figures 5 and 6 indicate the effects of binder (water)

Table 1. List of Operating Conditions

Fluidizing air velocity	0.6	m/s
Agitator rotational speed	10.0	s^{-1}
Flow rate of purge air	6.3×10^{-4}	m^3/s
Liquid flow rate	1.5×10^{-4}	kg/s
Fluidizing air temperature	313	K
Spray air pressure	1.5×10^5	Pa
Nozzle insert (i.d.)	1.0	mm

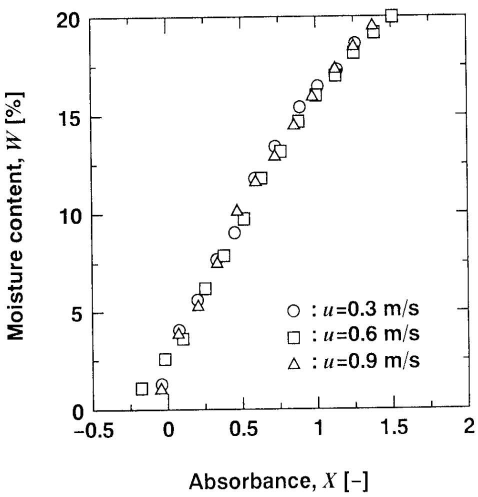

Fig. 1. Plots of Moisture Content as a Function of IR Absorbance at Varying Fluidizing Air Velocity

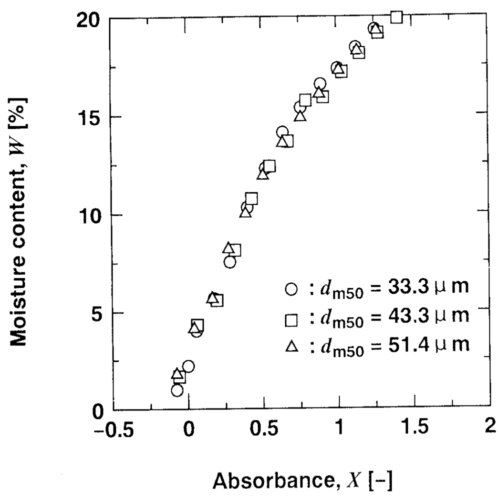

Fig. 4. Effect of Spray Mist Size on the Relationship between Moisture Content and the Absorbance of IR Spectra

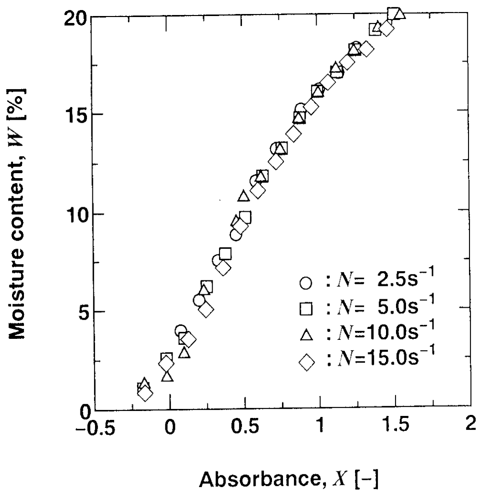

Fig. 2. Plots of Moisture Content as a Function of IR Absorbance at Varying Agitator Rotational Speed

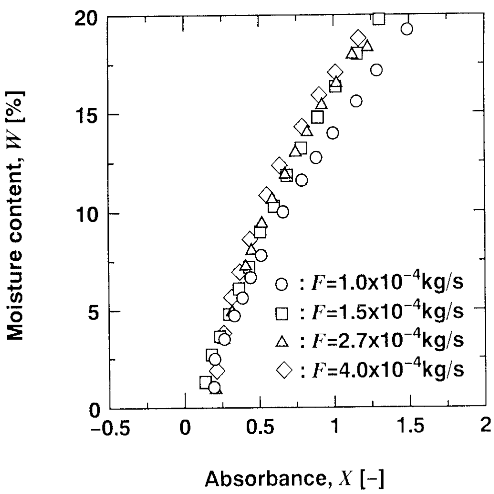

Fig. 5. Effect of Liquid Flow Rate on the Relationship between Moisture Content and the Absorbance of IR Spectra

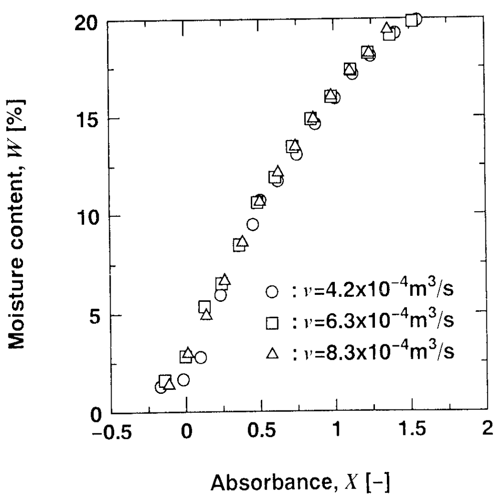

Fig. 3. Plots of Moisture Content as a Function of IR Absorbance at Varying Purge Air Velocity

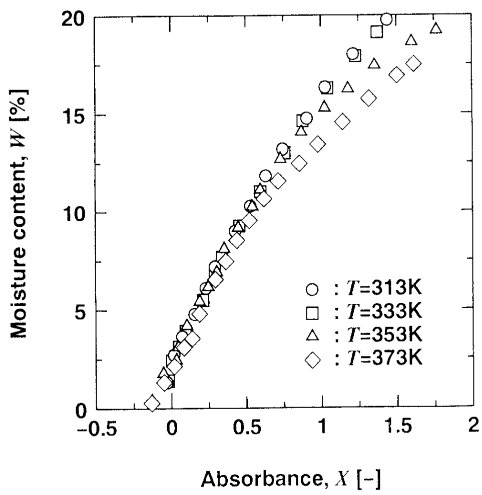

Fig. 6. Effect of Fluidizing Air Temperature on the Relationship between Moisture Content and the Absorbance of IR Spectra

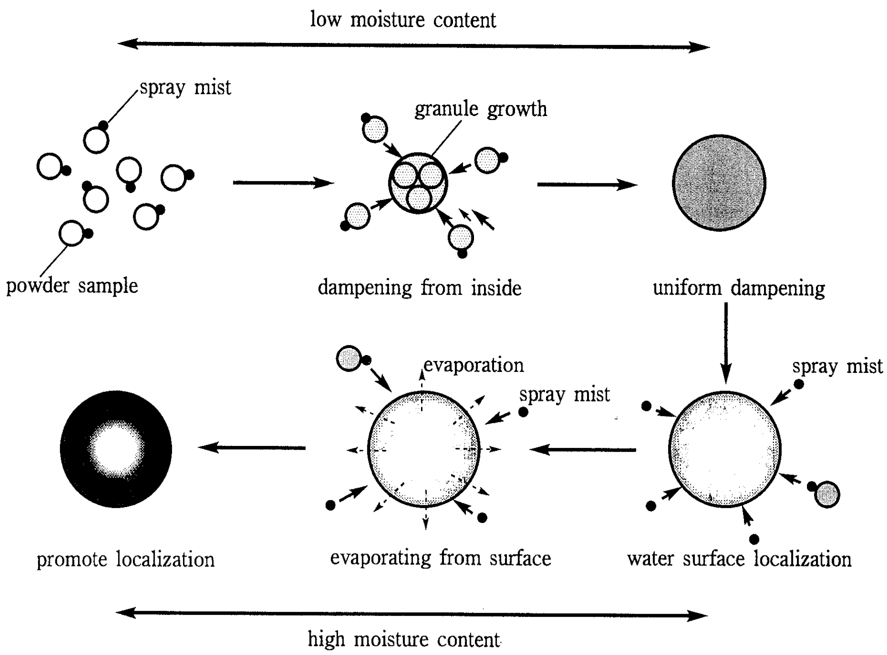

Fig. 7. Model Describing Water Transfer and Distribution

feed rate F and fluidizing air temperature T on the relationship between granule moisture content and the absorbance of IR spectra. As is evident in these figures, there was a significant difference in the case of a very low liquid flow rate ($F=1.0\times10^{-4}$ kg/s) and an extremely high temperature ($T=353$ and 373 K). Although spray mist size had no effect on the relationship (Fig. 4), nor was air temperature considered to influence the absorption characteristics, the dampening speed was supposed to exert a primary influence the relationship.

To express the above phenomena, the following model was proposed (Fig.7). At the initial stage of granulation, fine particles were first dampened by spray mists and an agglomerate was formulated. Secondly, the agglomerate was layered by the damped fine particles to increase its size. In this case, the dampened surface of the agglomerate was moved inside by the layering. By repetition of this process, growth of the agglomerate advanced, and simultaneously, the agglomerate was dampened uniformly from inside. At the final stage of granulation, the agglomerate was filled with water, and after that, the water content near at the surface increased rapidly, leading to a remarkable increase in the absorbance of IR spectra because the energy of the spectra was mainly absorbed by water located near the surface.

On the other hand, if the dampening speed was extremely slow, the surface of the agglomerate was rather dry, leading to the promotion of water localization due to water transfer from the inside to the surface at a high moisture content range. In this case, the amount of surface water increased remarkably by the water transfer, and water distribution with a high surface moisture content arose. Thus, the relationship shifted to the right side, showing substantial IR absorption under the same moisture content; it also indicated a convex pattern.

Based on the above model, if the granulation is conducted with continuous dampening, the effect of dampening speed on the relationship between granule moisture content and the absorbance of IR spectra can be ignored, and extremely high accuracy and good reproducibility of the measurement is expected.

Conclusions

An IR moisture sensor was applied to fluidized bed granulation and the validity of the measurement was investigated. The effects of operating variables on the relationship between granule moisture content and the absorbance of IR spectra was examined experimentally, and it was found that agitator rotational speed, fluidizing air velocity, air flow rate of the purge air and spray mist size had no effect on the relationship. However, if the dampening speed was extremely slow, the effects of fluidization air temperature and liquid flow rate on the relationship could be recognized. This was because the surface drying due to the extremely low dampening speed caused water to transfer from the inside to the surface. It could also be concluded that an IR moisture sensor could measure moisture content continuously with high accuracy, free of operating conditions, unless the granulation was conducted under an extremely low dampening speed.

References

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