Evaluation of the effect of granulation processing parameters on the granule properties: Lactose-Cornstarch case study

Elham Heidari, Salman Movahedirad*, Mohammad Amin Sobati

School of Chemical Engineering, Iran University of Science and Technology (IUST), P.O. Box 16765-163, Tehran, Iran

A B S T R A C T

Understanding the relationship between processing parameters of fluidized bed wet granulation and the characteristics of intermediate and final products is crucial in the pharmaceutical processes. This research examined a fluidized bed wet granulation process containing a cornstarch solution as binder and lactose particles as powder. The design of experiment (DoE) was performed according to an L9 Taguchi method with three replications. The variables considered in the experimental design were binder flow rate, drying air temperature, spraying pressure, and initial mass of particle. The physical properties of the granules were evaluated in terms of granule mean size and granule size uniformity. A predictive model for each individual response was proposed. In addition, optimum conditions for each response were also obtained. Finally, the effect of the granule mean size on the flowability of granules was also investigated.
1. Introduction

Granulation is defined as a size enlargement process which is applied in the pharmaceutical industry, mineral processing, the manufacture of agricultural chemicals, food, and etc. [1].

There are two major granulation methods i.e., wet and dry granulation processes [2]. Wet granulation includes the application of a binder liquid, which is introduced onto agitated powder particles in order to bind the particles together through a combination of capillary and viscous forces [1]. During subsequent drying, the solvent is removed by evaporation, and more stable bonds are formed. Dry granulation methods are based on the compaction of the powder mass, before it is broken and fractionated. Hence, this process particularly suitable for – heat-or moisture-sensitive materials. Comparing the dry and wet granulation processes, wet granulation offers a better control of drug content uniformity, product bulk density, and compatibility [3]. However, the process is more complicated to operate and control due to the additional preparation of binder liquid and supplementary drying step. It is also more costly regarding the required labor, equipment, energy, and space [4].

The size range for pharmaceutical granules such as Lactose is usually from 100 μm to 2 mm [5]. Granules are common intermediates in tablet processing. Powders are granulated before tableting to modify the properties such as flowability and compression characteristics. Many pharmaceutical primary powders have small size, irregular shape, and unoptimal surface characteristics, thus flow poorly. On the other hand, the segregation of different components may occur due to their differences in particle size or density in the pharmaceutical powders. All components are mixed in appropriate proportions in an ideal granule, while segregation in the granular level may affect the content uniformity of the final tablet. Granulation may has several advantages such as prevention of the hygroscopic materials caking during storage, low risk of contamination, and dust formation in production [6]. Maybe, the main motivations of research for granulation process are: improvement in production to ensure the high quality of granules, requirement for producing low-dose tablets (drug concentration may be as low as 0.001% w/w), and the content uniformity [7]. Fluidized bed granulation (FBG) is a widely applied wet granulation process in the pharmaceutical industry, which has several advantages in comparison with the multistage wet granulation methods (i.e., high shear granulation, low shear granulation, and etc.). Wetting, drying, particle enlarging, homogenization and separation processes are coupled in a single unit operation in fluidized bed granulation, and consequently there is more saving in time and labor costs and also transfer losses can be reduced using this process intensification [8]. Uniform temperature distribution due to continuous heat and mass transfer between the fluidizing air and particles, relatively short processing times, and producing high density granules are the other advantages of FBG against high/low shear granulation [9].

In spite of its widespread research, economic importance and functionality, granulation has remained more of an art than a science in practice [1]. During wet granulation process, a number of various mechanisms occur. According to the classification presented by Iveson et al. [1], the wet granulation process is considered as a combination of three different mechanisms include the following (Fig.1, [10]):

- wetting and nucleation of particles
- consolidation and growth
- attrition and breakage

It is essential to study the simultaneous effects of different parameters (i.e., drying air temperature (T), spraying air pressure (P), binder flowrate (F), and initial mass of particle (m)). These parameters need to be optimized to achieve the appropriate mean size, size distribution, and flowability of the product. Taguchi method is an effective statistical technique, which organizes systematic experiments to determine the optimum settings of design parameters for performance, quality, and cost. In this method, a large number of variables can be studied with a small number of experiments by the aid of orthogonal arrays [11-14].

Fig. 1. Key mechanisms of granulation [10].
In the present work, L9 Taguchi approach has been applied to understand the relationship between processing parameters of a fluidized bed top-spray granulator and the characteristics of intermediate and final products and also to find the optimum effective parameters. In this regard, the experiments were carried out in a small scale batch fluidized bed granulator (Glatt Co., Model: Uniglatt) with cornstarch solution as binder and lactose particles as powder.

2. Experimental

2.1 Materials

The α-lactose anhydrate granules supplied by Lactochem Co., (The Netherlands) as initial particles and solution of cornstarch powder (supplied by Ebne masoooye Co., (Saveh, Iran)) in distilled water as binder were used. The packed density of primary lactose was 897.2 kg/m\(^3\) and its size was less than 0.2 mm in higher than 95 % (w/w) while average mass percent size of primary particles were 0.136 mm. In all of the experimental tests, the concentration of aqueous cornstarch solution was fixed at 3 wt.% Physical properties of the binder solution at different temperatures are shown in Table 1.

Table 1. Physicochemical properties of binder solution at different temperature and mass percent of cornstarch.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>40.0</th>
<th>55.0</th>
<th>70.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interfacial tension (mN/m)</td>
<td>47.0</td>
<td>42.5</td>
<td>42.0</td>
</tr>
<tr>
<td>Viscosity (mPa.S)</td>
<td>4.3</td>
<td>4.2</td>
<td>4.1</td>
</tr>
</tbody>
</table>

2.2 Particle size analysis

The granules size distribution was measured using a series of standard sieves provided by Damavand Co., (Iran) according to the American standards. The size range of sieve mesh is 0.053 to 0.841mm.

2.3 Flowability test

Powder flowability is the capability of a powder to flow. In this work, the test of funnel discharge time is used for measurement of granules flowability. Discharge time of a determined mass of granules vertically out of a funnel was measured and reported in unit of time per mass. The funnel as described in the European Pharmacopoeia’s flowability test [15, 16] was constant in vertical position. The bottom opening was blocked impermeably. 100 g of samples were weighed and introduced carefully into the dry funnel. The funnel was unblocked and the time required for the entire powder to flow out of the funnel was measured. The values obtained in this work indicate the flowability measurements reproducibility.

2.4 Experimental setup

In the present work, a top spray fluidized bed granulator was used ( supplied by Glatt Co., model: Uniglatt, Switzerland) with about 1 kg powder capacity. The schematic of the experimental setup is shown in Fig. 2. In each experiment, the temperature of fluidizing air from blower (1) was regulated using an electrical heater (2) before entering the granulator through a distribution plate. The binder solution was pumped to the spray nozzle which was placed 25.5 cm above the distribution plate by a peristaltic pump with variable rate. The temperature of binder solution was set equal to the air temperature in each experiment. The bag filters mounted on the air outlet stream were shaken in a predetermined time interval, automatically. Shaking and rest time intervals were variable in different experiments depending on the binder spraying rate.

2.5 Experimental design

In tableting, thoughtful experimental plan is needed in the early development phase due to the complex interaction between materials and processes [17]. The main purpose of an experimental design is to plan the required experiments in such a way to obtain the optimum with the small number of runs. Design of Experiments (DoE) begins with the selection of factors, i.e. parameters that can be applied to affect responses. Then, the target is to detect the combination of factors that generate the most optimal set of responses. The results are usually presented as mathematical models [18]. In the present work, Taguchi method, one of the most relevant methods of DoE, has been applied for the evaluation of the granule and tablet production. The Taguchi method is applied through the following steps:
1. Identification of the independent variables with the greatest effect on the response.

2. Determination of the level of differences for each independent variable

3. The choice of the appropriate orthogonal array,

4. Assignment of design parameters to the orthogonal array

5. Carrying out the experiments according to the arrangement of orthogonal array, and finding the responses.

6. Analysis of the experimental results using the S/N ratio for determination of the optimal design parameters and ranking of parameters. S/N ratio used to identify control factors (i.e., design and process parameters) that reduce variability in a process by minimizing the effects of uncontrollable factors (noise factors). Higher values of the signal-to-noise ratio (S/N) identify control factor settings that minimize the consequences of the noise factors. The S/N ratios are different according to the type of desirability. For mean size of granule the “larger the better” S/N (i.e., maximum of the response) is considered which can be calculated by the following formula [19]:

\[
S/N = -10\log\left(\frac{\sum \frac{1}{y^2}}{n}\right)
\]  

But, for particle uniformity index (D80-D20) the “smaller the better” S/N (i.e., minimum of the response) is considered according to following formula [19]

\[
S/N = -10\log\left(\frac{\sum y^2}{n}\right)
\]

Where, Yi is the characteristic property and n is the replication number of the experiment. Ranking is based on the difference between the maximum and minimum mean response across levels of a factor (delta). The optimal level of parameters is the level with the greatest or smallest S/N values according to the type of desirability.

7. Analysis of Variance (ANOVA) in order to determine the contribution of each parameter in the response. The percentage contribution (P.C.) is defined as the significance rate of the process parameters on each response prior pooling process and can be calculated as:

\[
P.C. = \frac{\text{sum of the squared deviations}}{\text{total sum of squared deviations}} \times 100
\]

Fig. 2. Experimental setup of fluidized bed granulator: (1) air blower; (2) air heater; (3) binder vessel; (4) binder pump; (5) binder nozzle; (6) air outlet connection; (7) air filters [8].
ANOVA is a decision making tool to detect any differences in the mean performance of groups of tested parameters. ANOVA helps in formally testing the significance of all main factors and their interactions by comparing the mean square versus an approximate of the experimental errors at specific confidence levels [20]. When the degree of freedom for the error term achieves zero (calculated as the difference among the total degree of freedom and the accumulative degree of freedom (DoE) of all parameters), the variance of the error and ultimately the p-value could not be calculated [21]. Therefore, pooling process is unavoidable for ANOVA the mentioned problem was also occurred in this study which pooling process was applied with the elimination of the variable with the lowest amount of sum of square error (SSE).

8. Regression analysis to fit the regression model for each response. The Taguchi model includes linear and quadratic variables:

\[ Y = A_0 + \sum_{i=1}^{k} A_i Z_i + \sum_{i=1}^{k} A_{ii} Z_i^2 \] (4)

Where, \(A_0\), \(k\), \(A_i\), and \(A_{ii}\) represent a constant, the number of variables, the coefficients of the linear terms, and the coefficients of the quadratic parameters, respectively.

The obtained experimental data were used to calculate the coefficients of the second-order polynomial equation by the LSM technique. It is should be noted that pooling process was applied for the determination these coefficients and also, non-significant parameters were eliminated by F-value and P-value tests. The F-value is a ratio of the mean square error to the residual error [20] which if \(F<4\) and \(P>0.3\) then the variation of the design parameter has no significant impact on the response and the contribution of this parameter on the response could be neglected [22].

9. Verification of the optimal design parameters through the additional confirmation tests [20, 22, 23].

2.6 Implementation of Taguchi method

The independent variables are drying air temperature (T), spraying nozzle air pressure (P), binder flow-rate (F), and initial mass of particle (m) in the range of 40–70 °C, 1.5-2.5 bar, 5-20 mL/min, and 500-900 g, respectively. For granule property evaluation, mean size, size distribution, and granules flowability were considered. Input variables and their levels are shown in Table 2. The granulation experiments were conducted according to the L9 Taguchi design presented in Table 3.

Table 2.
Factors and their levels for fluidized bed granulation study of Lactose Particles using Taguchi method.

<table>
<thead>
<tr>
<th>Levels</th>
<th>T (°C)</th>
<th>P (bar)</th>
<th>F (mL/min)</th>
<th>m (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>40</td>
<td>1.5</td>
<td>12.5</td>
<td>500</td>
</tr>
<tr>
<td>Level 2</td>
<td>55</td>
<td>2</td>
<td>20</td>
<td>700</td>
</tr>
<tr>
<td>Level 3</td>
<td>70</td>
<td>2.5</td>
<td>5</td>
<td>900</td>
</tr>
</tbody>
</table>
Table 3. 
Experimental runs in the Taguchi’s L9(3^4) orthogonal array.

<table>
<thead>
<tr>
<th>No. of Experiments</th>
<th>T (ºC)</th>
<th>P (bar)</th>
<th>F (mL/min)</th>
<th>m (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>1.5</td>
<td>12.5</td>
<td>500</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>2</td>
<td>20</td>
<td>700</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>2.5</td>
<td>5</td>
<td>900</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>1.5</td>
<td>20</td>
<td>900</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>2</td>
<td>5</td>
<td>500</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>2.5</td>
<td>12.5</td>
<td>700</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>1.5</td>
<td>5</td>
<td>700</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>2</td>
<td>12.5</td>
<td>900</td>
</tr>
<tr>
<td>9</td>
<td>70</td>
<td>2.5</td>
<td>20</td>
<td>500</td>
</tr>
</tbody>
</table>

3. Results and discussion

3.1 Granule mean size

The results of the experimental runs according to Taguchi design are shown in Table 4. It is desired to analyze the mean response for each run in the inner array and to analyze the variation using an appropriate signal-to-noise (S/N) ratio. The S/N ratios for various outputs on different levels are shown in Table 5. The rank of variables for the different parameters as for proper S/N ratio is also specified in the same table. The relevance of variables is determined by variables ranking. The binder flowrate is the most effective variable and spraying nozzle air pressure, drying air temperature, and initial mass of particles are followed, respectively. Effects of process parameters on the granule mean size are shown in Fig. 3.

As can be observed, an increase in the air temperature from 40 to 55 ºC leads to a decrease in the granule mean size, but further increase in temperature up to 70ºC leads to an increase in the mean granule size. Rising the air temperature leads to further evaporation and drying of droplets before a successful contact with particles. Moreover, the wetted area of the particles has more potential to dry at higher temperatures. On the other hand, as illustrated in table 3 the surface tension of the binder is decreased from 47.0 to 42.5 mN/m by changing the temperature from 40 to 55ºC, but further increase in temperature up to 70ºC does not change the surface tension, considerably. Binder droplets tend to spread more effectively at lower values of surface tension which results in more effective collisions and subsequent particle agglomeration. So, the observed trend can be attributed to these two opposing phenomena.

Table 4.
Column assignment for the various outputs in the Taguchi’s L9(3^4) orthogonal array.

<table>
<thead>
<tr>
<th>Outputs/Experimental runs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>The mean size of granule (mm)</td>
<td>0.354</td>
<td>0.372</td>
<td>0.123</td>
<td>0.263</td>
<td>0.171</td>
<td>0.192</td>
<td>0.166</td>
<td>0.347</td>
<td>0.221</td>
</tr>
<tr>
<td>Granule Size Distribution: (D_{80}-D_{20})</td>
<td>0.337</td>
<td>0.334</td>
<td>0.099</td>
<td>0.225</td>
<td>0.136</td>
<td>0.239</td>
<td>0.118</td>
<td>0.280</td>
<td>0.205</td>
</tr>
</tbody>
</table>
Table 5.
Column assignment for the S/N ratios of various outputs onto different levels.

<table>
<thead>
<tr>
<th>Outputs</th>
<th>Factor</th>
<th>L1</th>
<th>L2</th>
<th>L3</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>The mean size of granule (mm)</td>
<td>T</td>
<td>-11.94</td>
<td>-13.76</td>
<td>-12.63</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>-12.07</td>
<td>-11.04</td>
<td>-15.22</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>-10.85</td>
<td>-11.10</td>
<td>-16.38</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>-12.49</td>
<td>-12.84</td>
<td>-13.00</td>
<td>4</td>
</tr>
<tr>
<td>Granule Size Distribution: (D80-D20)</td>
<td>T</td>
<td>13.02</td>
<td>14.24</td>
<td>14.46</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>13.66</td>
<td>12.64</td>
<td>15.43</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>10.98</td>
<td>12.08</td>
<td>18.66</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>13.51</td>
<td>13.51</td>
<td>14.70</td>
<td>4</td>
</tr>
</tbody>
</table>

Fig. 3. Effects of process parameters on granule mean size.
Moreover, variations of the spraying nozzle air pressure versus granule mean size is shown in the Fig. 3. As can be observed, changing the pressure from 1.5 to 2.0 bars increases granule mean size but further increase in the pressure leads to a decrease in the granule mean size. This can be attributed to two different phenomena: the increase in the number of binder droplet per granulator active volume and consequent rise in the probability of droplet-particle collision and subsequent better particle wetting. On the other hand, the reduction in droplet size of binder solution has two major effects: (1) More probable droplet drying before collision with particles, (2) reduction of the ratio of the binder thickness on the particle surface, which leads to an increase in the probability of bouncing for collided particles.

The influence of the binder flow rate on the mean granule size is also shown in Fig. 3. The observed trend illustrates an increase in the binder flow rate from 5.0 to 12.5 mL/min leads to increase in the granule mean size but further increasing of the binder flow rate from 12.5 to 20.0 mL/min does not affect granule mean size, significantly. The observed trend can be attributed to the increase in the mean size because of increasing the number of droplets per unit volume of granulation bed and, as a consequence, the probability of particle-droplet collision increases which leads to more efficient particle agglomeration. The observed trend beyond F=12.5 mL/min can be explained by a decrease in the rate of drying of binder due to fixed heat input into the bed which in turn increase the probability of liquid bridge rapture.

As can be observed in Fig. 3, initial mass of particle has no considerable influence on the granule mean size. By increasing the mass of initial particles, the number of particles per unit volume of granulation bed increases and consequently a dual effect is observed. In one hand, the probability of particle-droplet collision is increased and on the other hand, the probability of breakage and attrition of granules is increased. Almost, the two effects cancel out each other.

The optimal performance of the granule mean size is obtained at 40°C, 2 bar, 12.5 mL/min and 500 g A similar trend was also obtained in the investigation of effect of process variables on growth kinetics of lactose particles in a wet spray fluidized bed granulator [8].

The result of the ANOVA test for granule mean size is shown in Table 6 and P.C. depicts the contribution of each parameter in this table. As can be observed, the P.C. of binder flowrate is 55.89% and the initial mass of particle (F<4 and P> 0.3) has negligible effect on the granule mean size. A second-order polynomial correlation was also obtained for the granule mean size.

\[
\text{mean size} = 0.2388 - 0.2398T + 0.2662P + 0.1672F + 0.05517 F^2 - 0.07683 P^2 - 0.05983 T^2,
\]

\[
R^2 = 98.58\%
\]

3.2 Granule Size Distribution

The S/N ratio analysis is shown in Table 5. The effectiveness of variables on granule size distribution is ranked as follows: binder flowrate, spraying nozzle air pressure, drying air temperature, and initial mass of particle, respectively. Fig. 4 depicts the effects of process parameters on the granule size distribution. It should be noted that (D_{80}-D_{20}) is considered as a criterion of the size distribution narrowness. In this regard, lower values of (D_{80}-D_{20}) is preferred due to more uniform size distribution. D_{80} and D_{20} are the sizes in which 80 and 20 percent of particles lay below them, respectively. As can be observed, (D_{80}-D_{20}) is decreased by an increase in the air temperature from 40°C to 55°C but further increase in the air temperature beyond this limit has practically no effect on (D_{80}-D_{20}). The observed trend can be attributed to the two different effects: In the one hand, rising the air temperature increases the probability of the drying of liquid bridges between wetted particles and caused to prevent from breakage of the adjoining particles which in turn leads to the production of more uniform granules. On the other hand, the probability of the droplet drying is increased at higher temperature, which in turn leads to reduction of the droplet size and subsequent inefficient particle wetting. It seems that the former effect is dominant up to 55°C and the latter diminishes the former beyond this limit.

The influence of spraying nozzle air pressure on the particle size distribution is shown in Fig. 4. This trend illustrates that rising the pressure from 1.5 to 2.0 bar leads to an increase in (D_{80}-D_{20}) but further increase in atomizing air pressure to 2.5 bar leads to a decrease in (D_{80}-D_{20}). It should be noted again that the lower values of (D_{80}-D_{20}) is preferred due to more uniform size distribution. The observed trend can be explained by two contrary effects: Increasing the nozzle air pressure leads to reduction in droplet size. At a constant binder flow rate this leads to subsequent increase in number of droplets available per active volume of the fluidized bed which in turn increases the probability of droplet-particle collision. On the other hand, solidifying
of the smaller binder droplets in comparison with larger ones took place more probably before effective collision with particles. Obviously, when more wetted particles are available in the fluidized bed the probability of uniform growth of particles increases and \( (D_{80} - D_{20}) \) will be smaller when the volume number density of droplet increases.

From Fig. 4, increasing the binder flowrate from 5 to 12.5 mL/min has a negative effect on the particle size distribution but further increase in the binder flowrate to 20 mL/min, leads to more uniform particle size distribution. It should be noted that the number of droplets per volume and mean droplet size are increased by an increase in the binder flow rate which in turn increase the probability of uniform wetting of particles and subsequent uniform size distribution. The observed trend of \( (D_{80} - D_{20}) \) in the range of \( Q = 12.5 \) to 20 mL/min can be explained accordingly.

**Fig. 4.** Effects of process parameters on granule size distribution.

**Fig. 5.** Effect of granule mean size on flowability.
However, in the case of low binder flow rate (i.e., Q=5 mL/min) the more uniformity is observed in term of \((D_{80} - D_{20})\) but it should be noted that no considerable growth is carried out in this binder flow rate. In other words, as can be seen in Fig3, the lowest value of mean particle size is observed using Q=5 mL/min and the particle size distribution is similar to the starting powder. In the other words, at lower binder flow rates the droplet size is smaller and the number of droplet per volume is reduced which in turn leads to more probable droplet drying before collision to particles. In comparison with other parameters, initial mass of particle has no significant effect on the granule particle size distribution considering variable ranking (Table 5) and Fig. 4. It should be noted that the set of granulation parameters which produce the most uniform sized granules (the lowest \(D_{80} - D_{20}\)) are at \(T=55°C\), (level 2), \(P=2.5\) bar (level 3), \(F=5\) mL/min (level 3) and \(m=900\) g (level 3).

The accuracy of the granule size distribution was confirmed with triplicate experiments giving the average the granule size distribution uniformity index of \((D_{80} - D_{20}) = 0.079\pm 0.02\) mm.

Table 7 illustrates the ANOVA results and P.C. of each parameter in related to particle size distribution of granules. The contribution of binder flowrate is 75.92 % from total of regression and the parameters \(m\) and \(T^2\) (F<4 and P>0.3) have negligible contribution on the regression model. Thus, the second-order polynomial model of particle size distribution of granule obtains as a function of effective variables shows in Eq. 6. \(R^2=95.03\) % for this model states that the model satisfactorily represented the experimental data and all variations could be covered by the recommended model approximately.

\[
size \text{ distribution} = 0.157 - 0.027T + 0.1618P + 0.1288F - 0.0462F^2 - 0.0532T^2,
\]

\(R^2 = 95.03\) %
3.3 Flowability analysis

The powder flowability is the main property which affects the handling and processing operations, such as storage in hoppers and silos, transportation, mixing, compression and packaging [24]. On the other hand, particle size is one of the most important physical properties which affects the powders flowability. So, powders with larger particle sizes are free flowing, while fine powders are subject to cohesion and their flowability is more difficult [25]. This fact is proved with investigation of the flowability trend versus granule mean size in Fig. 5. As can be observed in Fig. 5, the larger particle sizes have lower discharge time, and consequently, the better flowability.

Conclusions

In this research, Taguchi method was employed to investigate the effects of process parameters on the granule mean size and granule size distribution in a fluidized bed granulation process. A L9 Taguchi array was selected with four independent variables including binder flow rate, drying air temperature, spraying air pressure, and initial mass of particles at three levels to obtain the variables ranking and fitting second-order polynomial model for each response. Finally, optimization of each response was carried out considering the greatest mean size and more uniform size distribution (the lowest D80-D20). The predictive data of Taguchi method are very compatible in comparison with experimental results. Moreover, the effect of granule mean size on the granules flowability was investigated which shows the larger granules size leads to the better flowability behavior.

References


