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An evaluation of process parameters to improve coating efficiency of an active tablet film-coating process

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ABSTRACT

Effects of material and manufacturing process parameters on the efficiency of an aqueous active tablet film-coating process in a perforated pan coater were evaluated. Twenty-four batches representing various core tablet weights, sizes, and shapes were coated at the 350–500 kg scale. The coating process efficiency, defined as the ratio of the amount of active deposited on tablet cores to the amount of active sprayed, ranged from 86 to 99%. Droplet size and velocity of the coating spray were important for an efficient coating process. Factors governing them such as high ratios of the suspension spray rate to atomization air flow rate, suspension spray rate to pattern air flow rate, or atomization air flow rate to pattern air flow rate improved the coating efficiency. Computational fluid dynamics modeling of the droplets showed that reducing the fraction of the smaller droplets, especially those smaller than 10 μm, resulted in a marked improvement in the coating efficiency. Other material and process variables such as coating suspension solids concentration, pan speed, tablet velocity, exhaust air temperature, and the length of coating time did not affect the coating efficiency profoundly over the ranges examined here.

1. Introduction

An aqueous active tablet film-coating is a process that allows a uniform and thin polymer-based film formation on the surface of the core tablets by spraying the coating liquid containing an active pharmaceutical ingredient (API, dissolved or dispersed in) and coating material. It is becoming a common approach to overcome some formulation stability and/or manufacturing process challenges for fixed dose combinations of oral solid dosage forms in pharmaceutical industry. If a drug molecule is prone to acid or alkali based degradation, one of the commercially viable formulation approaches is to enhance the chemical stability of a drug molecule by incorporating the active pharmaceutical ingredient in the coating layer of the film coated tablets (Desai et al., 2010). The aqueous active film-coating has also been shown to be an effective strategy to minimize chemical interactions between different drug molecules by physically separating one active compound from other core tablet components during the development of a fixed dose combination for tablets. There are three common challenges associated with an aqueous active film-coating process. They are: (1) to accurately determine the active coating end-point to consistently achieve the target potency; (2) to achieve satisfactory and consistent tablet content uniformity; and (3) to maximize the amount of active deposited during the coating process. More precisely, it is described as coating efficiency, the ratio of the amount of active deposited on core tablets to the amount of active sprayed.

There are a number of steps that can be taken to address the difficulty in accurately determining the coating end-point. The end-point of the active coating process may be determined by weighing the tablet samples periodically throughout the coating operation to determine the average tablet weight gain and stopping the coating process when the tablets have reached the target weight. This approach is based on the assumption that the tablet weight gain reflects the proportionate deposition of API and coating material. Greater accuracy can be obtained by carrying out in-process assay to determine the actual amount of API deposited on the core tablets at certain time interval, then spraying additional coating suspension until the coating end-point is reached (Lipper et al., 2006). A linear relationship can be established between the actual amount of the active deposited on the core tablets and coating time if the coating conditions, especially the spray rate, are kept constant during the entire coating process.

The inherent variability in the coating operation presents a second challenge, which is how to ensure that the aqueous film coated tablets have satisfactory content uniformity. Chen et al. (2010) derived an active film coating model based on the physical parameters of the tablets and coating process parameters, enabling an

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à priori prediction of relative standard deviation of the API content uniformity for the film coated tablets. The model shows that the content uniformity, expressed in relative standard deviation, is inversely proportional to the square root of the total number of cycles between the spray zone and drying zone that the tablets undergo in a perforated pan coater. The total number of cycles is a function of the number of tablets in the drying zone, spray zone width, tablet velocity, tablet number density, and total coating time. The validity of the model was experimentally confirmed at both pilot and commercial scale (Chen et al., 2010).

The third challenge presented by the coating operation relates to how to maximize the coating efficiency of the active film coating process. In practice, the volume of the API-containing coating solution or suspension prepared for the active coating process must contain some excess amount to allow for sufficient material to fill the lines in the spraying system and to cover the material loss caused by the less-than-hundred percent coating efficiency. No coating process can be expected to be 100% efficient as there will always be some loss of coating materials, which often ultimately get exhausted, during the coating process. Production loss of API due to limited and/or inconsistent active coating process efficiency is of great concern due to the typically high cost of API. There is also the added benefit of reducing the cycle time if the efficiency of the coating process can be improved. Given the importance of these factors and their inadequate coverage in the pharmaceutical literature, this article focuses on the issues related to coating efficiency.

Tablet coating often takes place in a controlled atmosphere inside a perforated pan coater. Angled baffles fitted into the pan and air flow inside the pan provide means of mixing the tablet bed when the pan is rotating. As a result, all tablets are exposed to even amount of sprayed coating over time. The liquid sprayed onto the tablet surface is then dried by heated air which enters the coater from an inlet vent. Schick and Knasiak (2009) proposed an approach of maintaining optimized spray flux density and spray overlap, as well as an understanding of the effects of spraying conditions to achieve uniform droplet size and distribution onto the tablets in a perforated pan coater. They found that lower coating efficiency was often due to excess spray drying of the coating spray prior to reaching the tablet surface. Small mean droplet size, high atomization air velocity/pressure, and high inlet air temperature facilitated spray drying. Excessive spray drying of the coating spray should therefore be minimized in order to maintain good coating efficiency (Yang and Kim, 2000; Mosén et al., 2009). Rege et al. reported that lower pattern air pressure and lower inlet air temperature were statistically important for good efficiency in the film coating process (Rege et al., 2002). Tobiska and Kleinebudde, on the other hand, did not find significant correlations between the efficiency of the coating process and process variables such as tablet size, batch size, pan load, and inclination of the rotation axis in a perforated pan coater (Tobiska and Kleinebudde, 2003). According to Aliseda et al., the application of coating material to the tablets is carried out in four major steps: spray atomization, droplet transport, droplet impact/spreading/drying, and tablet mixing (Aliseda et al., 2010). They described a mathematical model of the atomization process that enabled the droplet size to be predicted. In a separate investigation, Chen et al. found that the mean droplet size was most affected by the ratio of the atomization air flow rate to the pattern air flow rate (Chen et al., 2008). An increase in this ratio led to smaller droplet size although there was a limit beyond which the droplet size can no longer be decreased. Overall, it is generally considered that the efficiency of an aqueous film coating process is dependent on the spray droplet size. The size of the spray droplet is itself a function of the rheological properties of the coating liquid, spray nozzle and atomizing and pattern air flow rates.

Table 1
Physical appearance of the core tablets used for film coating.

Designation of tablets	Tablet shape	Tablet dimension	Core tablet weight
A	Round	8.0 mm in diameter	200 mg
B	Biconvex capsule-shaped	19.0 mm × 9.2 mm	1024 mg
C	Biconvex capsule-shaped	23.2 mm × 10.9 mm	1450 mg
D	Biconvex round	11.0 mm in diameter	529 mg
E	Biconvex round	12.7 mm in diameter	899 mg
F	Biconvex oval-shaped	19.0 mm × 10.5 mm	1058 mg

In this article, we present the results of an investigation carried out with a perforated pan coater at commercial scale and designed to determine the effects of core tablet and manufacturing process variables on the efficiency of an aqueous active film coating process for tablets. To author's knowledge, it has been the first time that the subject matter was comprehensively studied with a variety of core tablets in different weights, sizes, and shapes at a scale up to 500 kg. The desired benefit of this study was to gain fundamental knowledge of the aqueous active film coating process for tablets and the subsequent leverage of that process knowledge for guiding and maximizing the coating efficiency at large-scale production.

2. Materials and methods

2.1. Tablet active film coating equipment

A perforated pan coater (L.B. Bohle, model BFC-400, Ennigerloh, Germany) was used for all active coating experiments described in this article. The liquid delivery system was a two-fluid coaxial type with two auxiliary gas jets and consisted of six identical spray nozzles (Dusen-Schlick GmbH, model 930/7-1 S35, Untersiemau, Germany) each with an insert diameter of 1.2 mm. The atomization and pattern air were each delivered *via* a volumetric flow controller to assure a more accurate and consistent air delivery.

2.2. Core tablets and film coating suspension

Tablets of six different weights, sizes and shapes were used as substrates for the active film coating experiments. The tablets were designated as A, B, C, D, E, and F. The information of the tablet physical appearance is summarized in Table 1. Only one type of tablets was used for each film coating run.

The aqueous film coating suspension was prepared by dissolving the API in water, followed by mixing the powder of the polyvinyl alcohol-based film coating material (Opadry II®, Colorcon Inc., Pennsylvania, USA) into the solution. With the weight ratio of API to coating material at 1:4 or 1:8, the aqueous film coating suspension contained 3.6–15.0% (w/w) of solid material which consisted of the API and the coating materials.

2.3. Manufacture of the tablet active film-coating batches

A total of 24 experimental batches were coated using the core tablets described in Table 1. Each type of core tablets was film coated in the perforated pan coater to produce tablets containing 2.5–10.0 mg of API in the coat layer. The film-coated tablets were manufactured in the batch size range of 350–500 kg. The tablet fill volume in the pan stayed approximately the same for various core tablets. The film coating process parameters were recorded using the pan coater's control system and they are summarized in Table 2. Four of the 24 batches made in this study had identical process parameters while each of the remaining 20 batches had unique combinations of the material and process variables. The tablet velocity and spray zone width was measured off-line using

Table 2
Ranges of main input variables and resulting parameters for the 24 tablet active film coating runs.

Variable		Range used
Main input material and process variables	Tablet weight	200–1450 mg
	Batch size, in total tablet weight	350–500 kg
	Batch size, in number of tablets	300,000–2,000,000 tablets
	Coating suspension concentration	3.6–15.0%
	Total suspension spray rate (SR)	300–555 g/min
	Total spray atomization air flow rate (AA)[a]	420–720 standard L/min
	Total pattern air flow rate (PA)[a]	480–840 standard L/min
	Pan speed	8–10 rpm
	Inlet air temperature	50–55 °C
	Inlet air dew point	10 °C
	Inlet air flow rate	2500–2900 standard ft^3/min
	Exhaust air temperature	38–44 °C
	Gun-to-bed distance	15–25 cm
	Angle of inclination of the pan	0°
Resulting parameter	Spray droplet particle size D_{10} [b]	13.2–19.1 μm
	Spray droplet particle size D_{50} [b]	34.9–44.4 μm
	Spray droplet particle size D_{90} [b]	71.2–87.0 μm
	Spray droplet particle size D_{32} [b]	27.2–35.8 μm
	Spray droplet particle size D_{43} [b]	40.9–49.5 μm
	Spray droplet velocity	8.7–10.5 m/s
	Total droplet concentration	502–2082 droplets/mL
	Spray volume flux	0.0026–0.0081 mL/s
	Actual coating time	460–1210 min
	Environment equivalency factor	2.2–3.7
	Coating efficiency	86–99%

[a] Total air flow rate used atomize the coating suspension (AA) or form the spray plume of the coating suspension (PA).
[b] Spray droplet particle size may be expressed in the forms of D_{10} where 10 wt% of the droplets have a larger equivalent diameter, D_{50} where 50 wt% of the droplets have a larger equivalent diameter, D_{90} where 90 wt% of the droplets have a larger equivalent diameter, D_{32} which is the surface area moment mean diameter, or D_{43} which is the volume moment mean diameter.

an imaging system (SprayWatch® Limited, Tampere, Finland) by employing previously reported methods (Chen et al., 2008).

2.4. Determination of the environmental equivalency factor

As an indicator of the relative rate of water evaporation from the tablet surface, the Environmental Equivalency Factor (EEF) is derived from a first-principle model built upon the coupling of heat and mass transfer in evaporative mass transfer for an aqueous film coating process (Ebey, 1987). In a perforated pan coater, the environment of an aqueous film coating operation may be characterized by an EEF which incorporates many process variables such as inlet air temperature, humidity and flow rate, solid concentration of the coating liquid, coating liquid spray rate, atomization air flow rate as well as temperature of the exhaust air and its humidity. Generally speaking, the range of the EEF values fall between 1.0 (very wet) and 5.2 (very dry), with 2.5–3.5 being the typical values (Novit, 2008). The EEF value was calculated using the Thermodynamic Analysis of Aqueous Coating program (Thomas Engineering Inc., Illinois, USA) for each batch in this study.

2.5. Determination of the coating efficiency for each batch

In-process tablet samples were taken for potency testing after 70–90% of the theoretical amount of the coating suspension (*i.e.*, 70–90% point) was sprayed in order to determine the actual amount of API deposited on the core tablets and the amount of additional coating suspension needed to reach the target potency. The film coated product was assayed again to determine the final potency of the tablets after the additional calculated amount of the coating suspension had been sprayed (*i.e.*, coating end point). The efficiency for each coating run was calculated by the product of the theoretical amount of active suspension to be sprayed to achieve target potency and the finished product potency (% label claim) divided by the total amount of coating suspension actually sprayed to reach the coating end point as described in Eq. (1):

$$\text{Coating efficiency}\,(\%) = \frac{a \times b}{a + c} \times 100 \qquad (1)$$

where a is the theoretical weight of suspension to be sprayed to obtain 100% of the active label claim, b is the actual potency in the form of percentage of the label claim (*e.g.*, 99.8% of the label claim) obtained at the coating end point, and c is the additional suspension weight actually sprayed to reach the coating end point.

2.6. Characterization of the spray droplets

The characterization of the spray droplets was conducted offline with a spray nozzle identical to those used in the coating process. A custom-built measurement apparatus consisting of a Niro Mobile Minor™ spray dryer with the nozzle positioned at the top of the dryer was used. The spray dryer was operated with atomization and pattern air to generate a spray plume thus mimicking the spray conditions used during the manufacture of the active coating batches. Spray droplet measurements were collected using a phase doppler particle analyzer with the FLOWSIZER™ software (Version 2.0.4.0) (TSI, Inc., Minnesota, USA). It allows the spray droplet size and velocity at the interface of the droplets and tablet bed, as well as the total number of droplets per unit volume of liquid, to be measured. The principle of the measurement is based on the shift in constructive and destructive inference patterns due to differences in droplet diameter (TSI, 2011). The measurements were made in refractive mode at a receiver angle of 36° relative to the vertical center line and using an argon-ion laser set at a wavelength of 514.5 nm. The spray volume flux was calculated by multiplying the volume of the droplets per unit surface area by the droplet velocity.

2.7. Multivariate analysis of the impact of material and process variables on coating efficiency

The effects of material and process variables on the coating efficiencies of the 24 manufactured batches were statistically evaluated with a partial least square regression method using the Unscrambler® software (CAMO Smart Software Inc., New Jersey, USA).

2.8. Modeling of the spray droplet drying process

The modeling of the spray droplet drying process after leaving the spray nozzle was carried out with a computational fluid dynamics method available commercially as the Fluent® simulation software (ANSYS Inc., Pennsylvania, USA).

3. Results and discussion

The prerequisite for maximizing the aqueous active film-coating efficiency is to develop a robust and reproducible general tablet film-coating process itself. Efficiency gains are often incremental, especially as the maximum efficiency is approached and real changes become difficult to distinguish from process noise and analytical variability. It is critical to maintain a well-controlled, consistent processing environment throughout the entire coating process to obtain consistent coating efficiency. It was found that the EEF model used to describe the water evaporation process during aqueous film coating was a suitable guide to the control of the film coating environment in a perforated pan coater. The EEF value of each coating batch being kept constant for the entire course of operation, the values for the 24 batches used in this study ranged from 2.2 to 3.7, indicating well-balanced thermodynamic conditions of the coating operations for all batches. As a result, the film coated tablets from all 24 batches demonstrated satisfactory physical appearance with few undesirable tablet coating defects such as tablet surface erosion or poor inter-tablet color uniformity.

3.1. Factors affecting coating efficiency

Tablet film coating is a rather complex operation for which the coating efficiency may be affected by many factors. A wide range of tablets in different weight, shape, and size were incorporated into this study, which built in a rare opportunity to evaluate the coating efficiency in a broad spectrum in terms of the physical appearance of the core tablets. For a given core tablet type coated in a predetermined design of the perforated pan coater and spray nozzle, if categorized by the functionality, the variables that may affect the coating efficiency can be divided into several groups. They include material variables such as pan load (batch size) and solid concentration of the coating suspension; equipment variables such as pan speed; environmental variables such as inlet air temperature, dew point, and flow rate; spray variables such as atomization and pattern air flow rate, and liquid spray rate. These variables with their ranges are described in Table 2.

A multivariate analysis tool was utilized in attempting to understand the impact of the rather extensive material or process variables on coating efficiency. The correlation coefficients between the coating efficiency values and the studied process parameters were obtained. The correlation coefficient is a measure of the statistical relationship between the two variables, coating efficiency and process parameter, in terms of the covariance of the variables divided by their standard deviation. Shown in Table 3, the input variables for the coating process were divided into individual and composite parameters. Examples of the former included pan load, pan speed, inlet air flow rate, and spray rate, while the latter included the ratios of the suspension spray rate/atomization air flow rate (SR/AA), suspension spray rate/pattern air flow rate (SR/PA), and atomization air flow rate/pattern air flow rate (AA/PA). The correlation coefficients of the resulting parameters, such as spray droplet particle size, velocity, and EEF, of the coating operation are also listed in Table 3. A corresponding graphical representation for the information shown in Table 3 is provided in Fig. 1.

The coating efficiency of the 24 batches in this study ranged from 86 to 99%. Among the input individual process variables, only the spray rate, pattern air flow rate, and pan load showed more pronounced effects on coating efficiency with correlation coefficients of $r = 0.87$, $r = -0.82$, and $r = 0.68$, respectively (highlighted in Table 3). Individual input process variables demonstrating the least impact on coating efficiency included the coating suspension concentration ($r = 0.27$), pan speed ($r = -0.28$), atomization air flow rate ($r = 0.08$), tablet velocity ($r = 0.03$), exhaust air temperature ($r = 0.17$), and length of coating time ($r = -0.17$). The impact of the inlet air flow rate on coating efficiency was marginal ($r = 0.58$). Overall, it appeared that the efficiency of the active film coating process was strongly affected by factors affecting spray quality such as spray rate and pattern air flow rate. The correlation coefficients of the individual spray process variables, SR, AA, and PA, were 0.87, 0.08, and −0.82, respectively. In contrast, the composite spray process variables, such as the SR/AA, SR/PA, and AA/PA, demonstrated significant correlation coefficients of 0.89, 0.96, and 0.91, respectively, with the coating efficiency. In fact, these were the highest positive correlation values between the coating efficiency and the variables evaluated in this study. A graphical example of the relationship between the coating efficiency and these composite spray variables, such as AA/PA, is shown in Fig. 2 to further illustrate this

Table 3
Correlations between material and process variables and coating efficiency.

Parameter		Correlation coefficient
Individual input parameter	Pan load	0.68
	Pan speed	−0.28
	Inlet air flow rate	0.58
	Exhaust air temperature	0.17
	Coating suspension concentration	0.27
	Atomization air flow rate (AA)	0.08
	Pattern air flow rate (PA)	−0.82
	Spray rate (SR)	0.87
	Spray zone width	−0.51
	Gun-to-bed distance	−0.47
Composite input parameter	Spray rate/atomization air flow rate (SR/AA)	0.89
	Spray rate/pattern air flow rate (SR/PA)	0.96
	Atomization air flow rate/pattern air flow rate (AA/PA)	0.91
Resulting parameter	Spray droplet particle size D_{10}	0.59
	Spray droplet particle size D_{50}	0.53
	Spray droplet particle size D_{90}	−0.30
	Spray droplet particle size D_{32}	0.58
	Spray droplet particle size D_{43}	0.39
	Total particle concentration	0.15
	Spray volume flux	0.60
	Spray droplet velocity	−0.82
	Tablet velocity	0.03
	Actual coating time	−0.17
	Environment equivalency factor	−0.68

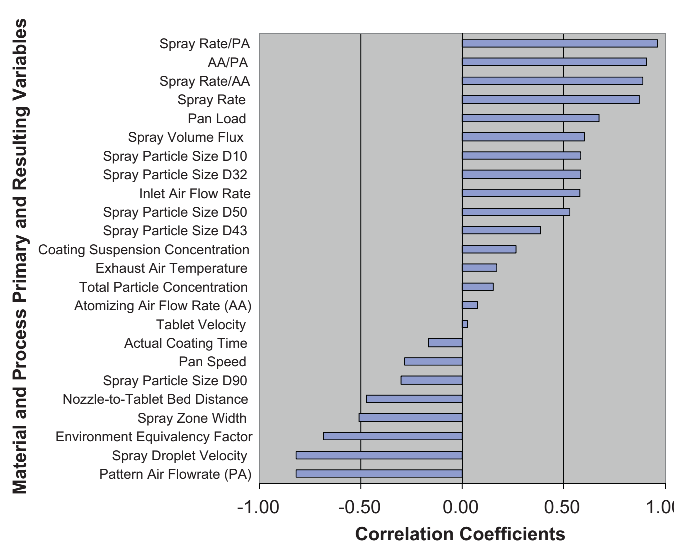

Fig. 1. Coating efficiency correlation coefficients relative to the material and process variables.

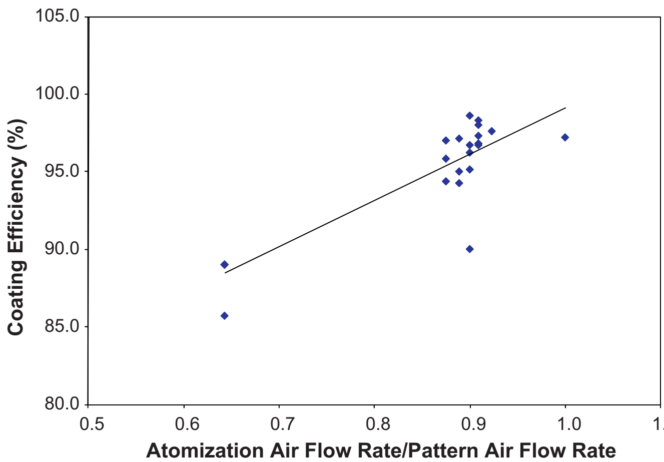

Fig. 2. The relationship between the composite spray parameter, ratio of atomization air flow rate to pattern air flow rate (AA/PA), and coating efficiency.

point for all 24 coating runs in this study. The results suggested that high AA/PA ratio was critical for coating efficiency improvement. To be discussed later in this article, the SR, AA, and PA were the individual process parameters that most affected spray characteristics such as the shape of the spray plume, droplet size and distribution, and droplet velocity. These parameters turned out to be the most influential factors on the coating efficiency.

Based on the results from the multivariate analysis, the coating efficiency was more affected by the coating suspension spraying process related variables than core tablet, coating pan, or coating environment related variables. The condition of the spray is most influenced by the process parameters SR, AA, and PA for a given spray nozzle structure. Ultimately, these influential factors impact the coating efficiency by affecting the droplet velocity ($r = -0.82$) and droplet size ($r = 0.53$) at the droplet-tablet interface. The main function of the atomization air during spraying is to break up the liquid jet and deliver the droplets to the tablet bed. Pattern air impinges on the spray plume to redirect the atomized droplets away from the radial axis of the spray, inducing a symmetric elliptical spray projection which increases the spray coverage on the tablet bed. The atomization air is mainly responsible for delivering the spray to the tablets and is the dominant factor in determining the droplet velocity. Pattern air, on the other hand, slightly hinders the delivery of the spray to the tablets. It, however, has more significant impact than the atomization air on the droplet size. Fig. 3 illustrates how the droplet size (represented by D_{50} where 50 wt% of the droplets have a larger equivalent diameter (Rawle, 2006)), changes with the atomization air flow rate or pattern air flow rate in the ranges studied. The results suggested that either higher atomization air flow rate or pattern air flow rate resulted in lower droplet size; the impact on droplet size reduction caused by the pattern air flow rate was more pronounced. In general, higher AA leads to higher droplet velocity and smaller droplet size; higher PA leads to lower droplet velocity and smaller droplet size; and higher SR leads to lower droplet velocity and larger droplet size. The overall impact of spray conditions on droplet characteristics, such as droplet velocity and droplet size, is summarized in Table 4.

The reasoning of why the composite coating liquid spraying process variables, such as SR/AA, SR/PA, and AA/PA, significantly affected the coating efficiency is further explained below. High SR in combination with low PA, contributed to a larger droplet size. The spray droplet velocity may not have been affected in any significant way due to the cancelling out effects of high SR and low PA. As a result of this, a high ratio of SR/PA is beneficial for the coating efficiency by collectively increasing the spray droplet size ($r = 0.96$).

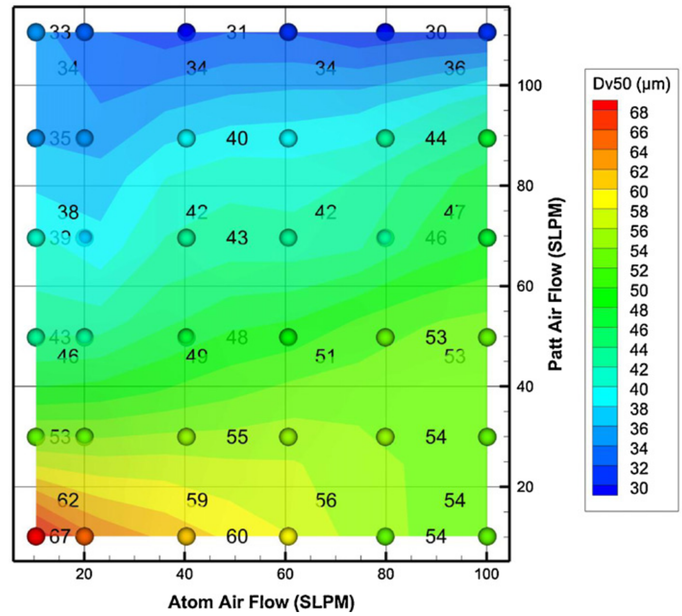

Fig. 3. Typical spray droplet size (D_{50}) as a function of atomization and pattern air flow rates for a 10.0% (w/w) coating suspension with a spray rate of 80 g/min at a 20-cm gun-to-bed distance.

In the case of SR/AA, high SR and low AA have the collective effects of decreasing droplet velocity and increasing droplet size, which is beneficial for the coating efficiency ($r = 0.89$). The larger droplet size minimizes the spray drying, resulting in better efficiency. Finally, the most complicated effect on coating efficiency comes from AA/PA. On one hand, an increase of AA and/or a decrease of PA would increase spray droplet size due to the stronger impact from PA. On the other hand, an increase of AA and a decrease of PA will synergistically increase droplet velocity. Qualitatively, it can be deducted that increased droplet size is the dominant effect caused by high AA/PA, resulting in a higher coating efficiency ($r = 0.91$). Overall, increasing SR/AA, SR/PA, or AA/PA has beneficial effect on the coating efficiency. In practice, it is most efficient to increase the AA/PA value whenever possible in order to achieve a high coating efficiency as the spray rate is often limited by the aforementioned requirements of the coating environmental conditions in the pan coater.

3.2. Modeling of the droplet spray drying

Ideally, the aqueous coating suspension travels through the spray zone to reach the tablet bed in the form of droplets after leaving the spray nozzle. The droplets absorb the heat from the inlet air supplied to the coating pan, resulting in the evaporation of the water from the coating suspension. The water evaporation process of a single spray droplet in a stagnant flow field,

Table 4
General impact of the spray conditions on the droplet velocity and size.

Spray condition		Wet spray droplet characteristics	
Spray rate (SR)	↑	Droplet velocity	↓
		Droplet size	↑
Atomization air flow rate (AA)	↑	Droplet velocity	↑↑
		Droplet size	↓
Pattern air flow rate (PA)	↑	Droplet velocity	↓
		Droplet size	↓↓

↑ and ↓ symbolize an increase and decrease effect, respectively.
↑↑ and ↓↓ symbolize the stronger increase or decrease when comparing the effect caused by atomization air and pattern air.

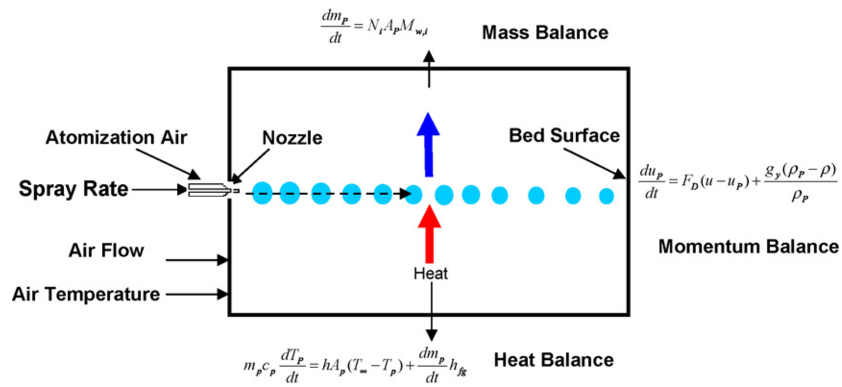

Fig. 4. A spray droplet evaporation process involving heat, mass, and momentum transfer processes.

determined by the heat transfer, mass transfer, and momentum transfer processes, is illustrated in Fig. 4. Described in Appendix I, the heat, mass, and momentum equations were solved to obtain the relationship between the spray characteristics and process parameters using the Fluent® computational fluid dynamics simulation software. Illustrated in Fig. 5, the results indicated that larger droplets have lower velocity while smaller droplets have higher velocity when initially leaving the spray nozzle. This negative association was further supported by the fact that the correlation coefficient between the droplet velocity and droplet size (D_{50}) was −0.56. In the meanwhile, it was demonstrated that the droplets decelerated over a very short distance, with the larger droplets showing slower and less decay, after leaving the spray nozzle. As illustrated in Fig. 6, the smaller spray droplets experienced greater size reduction during spraying than the larger droplets. The reduction in size caused by the spray drying process for the droplets in the 1 μm, 5 μm, and 10 μm diameter range were >100%, 33%, and 7.5%, respectively, for a 20 cm gun-to-bed distance. The results suggested that droplets smaller than 10 μm are partially or completely spray dried with disappearance of the wet droplets before they reach the tablet surface and that they leave the pan coater in the exhaust air. Therefore, reducing the percentage of the smaller droplets in the spray, especially those smaller than 10 μm, will

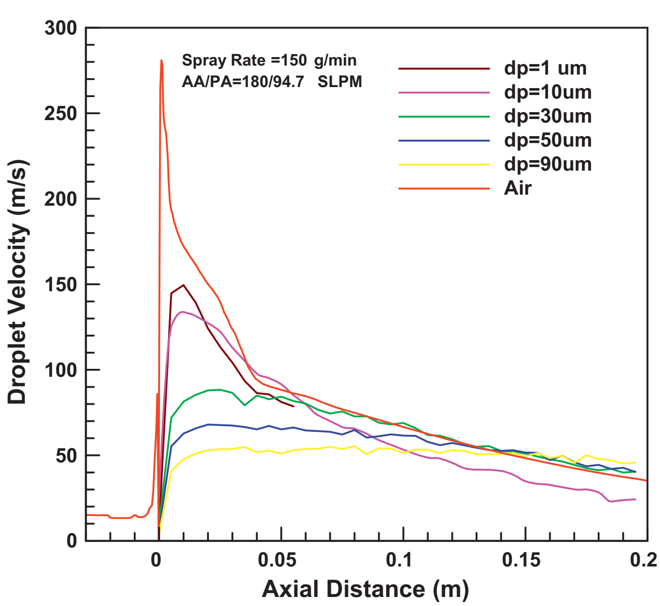

Fig. 5. Relationship between spray droplet velocity decay and axial gun-to-bed distance from the center of a spray plume.

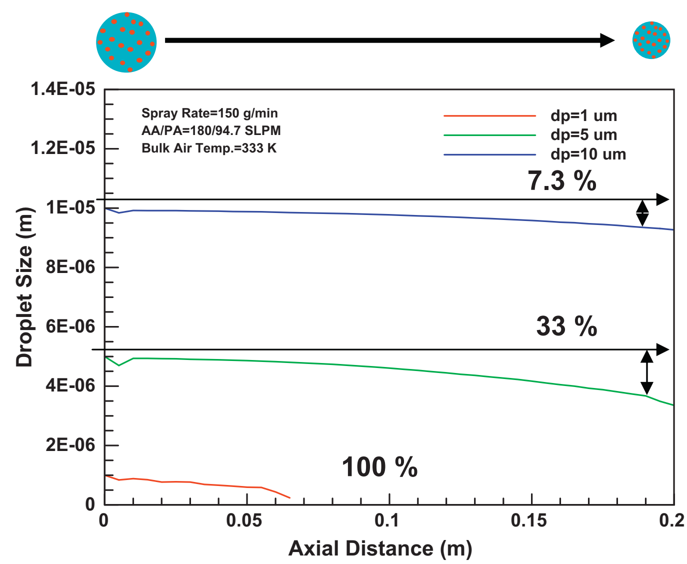

Fig. 6. Droplet size reduction as a function of its travelled distance.

improve the coating efficiency. As a result, it was again verified that larger droplet size, associated with lower droplet velocity, was beneficial for improved coating efficiency by the modeling work.

4. Conclusion

The results of this study have shown that while maintaining a stable processing environment is important to obtain film coated tablets with satisfactory physical appearance, the most effective way to improve the efficiency of an aqueous tablet active film-coating in a perforated pan coater is to control the coating liquid delivery process itself. Large droplet size to reach the core tablets while the droplets are still in the liquid state were necessary for improved coating efficiency. The optimization of the input composite spraying process parameters is most important in order to maximize coating efficiency. High ratios of the suspension spray rate/atomization air flow rate (SR/AA), suspension spray rate/pattern air flow rate (SR/PA), and atomization air flow rate/pattern air flow rate (AA/PA) had the most positive impact on the coating efficiency. Other material and process variables such as coating suspension solids concentration, pan speed, tablet velocity, exhaust air temperature, and the length of the coating time had much less impact on the coating efficiency in the perforated pan film coating process.

Acknowledgment

Mr. Rick Falk from Bend Research Inc. is sincerely thanked for his contribution to the spray characterization work.

Appendix I. Modeling of the droplet spray drying

Ideally, the aqueous coating suspension travels through the spray zone to reach the tablet bed in the form of droplets after leaving the spray nozzle. The droplets absorb the heat from the inlet air supplied to the coating pan, resulting in the evaporation of the water from the coating suspension. The water evaporation process of a single spray droplet in a stagnant flow field, determined by the heat transfer, mass transfer, and momentum transfer processes.

The heat balance in the droplet is related to the convective heat transfer and absorption/emission of the radiation at the droplet surface in a manner described by the following equation (Fluent, 2006):

$$m_p c_p \frac{dT}{dt} = hA_p(T_\infty - T_p) + \frac{dm_p}{dt} h_{fg} + \varepsilon_p A_p \sigma_p(\theta_R^4 - T_P^4) \quad (I.1)$$

where m_p is the mass of the droplet (kg), c_p is the heat capacity of the droplet (J/kg-K), A_p is the surface area of the droplet (m_p), $T_p(t)$ is the temperature of droplet at certain time point t (K), T_∞ is the local temperature of the continuous phase (K), h is the convective heat transfer coefficient (W/m^2-K), h_{fg} is the latent heat of water evaporation (J/K), dm_p/dt is the rate of evaporation (kg/s), ε_p is the Droplet emissivity (dimensionless), σ_p is the Stefan–Boltzmann constant (5.67e^{-8}W/m^2-K), θ_p is the radiation temperature (K).

The heat transfer coefficient, h, is evaluated using the correlation introduced by Ranz and Marshall (Fluent, 2006):

$$\mathrm{Nu} = \frac{hd_p}{k_\infty} = 2.0 + 0.6Re_d^{1/2} Pr^{1/3} \quad (I.2)$$

where Nu is the Nusselt number based on the particle diameter and relative velocity; d_p is the particle diameter (m), k_∞ is the thermal conductivity of the continuous phase (kg), Re_d is the Reynolds number based on the particle diameter and relative velocity, Pr is the Prandtl number of the continuous phase.

The rate of vaporization is governed by gradient diffusion of water, with the flux of droplet vapor into the gas phase related to the gradient of the vapor concentration between the droplet surface and bulk gas. These relationships are described by Eq. (I.4):

$$N_i = k_c(C_{i,s} - C_{i,\infty}) \quad (I.3)$$

where N_i is the molar flux of vapor (kg mol/m^2 s), k_c is the mass transfer coefficient (m/s), $C_{i,s}$ is the vapor concentration at droplet surface (kg mol/m^3), $C_{i,\infty}$ is the vapor concentration in the bulk gas (kg mol/m^3).

The vapor concentration at the droplet surface, $C_{i,s}$, is determined by assuming that the partial pressure of the vapor at the surface is equal to the saturated vapor pressure, P_{sat}, at the droplet temperature T_P

$$C_{i,s} = \frac{P_{sat}(T_p)}{RT_p} \quad (I.4)$$

where R is the universal gas constant.

The water vapor concentration of the total bulk gas is calculated from the transport equation for the droplets:

$$C_{i,s} = X_i \frac{P_{op}}{RT_\infty} \quad (I.5)$$

where X_i is the local bulk mole fraction of droplets, P_{op} is the operating pressure, and T_∞ is the local bulk temperature in the gas.

The mass transfer coefficient is calculated by the Nusselt correlation (Fluent, 2006):

$$Nu = \frac{h_c d_p}{D_{i,m}} = 2.0 + 0.6Re_d^{1/2} Sc^{1/3} \quad (I.6)$$

where $D_{i,m}$ is the diffusion coefficient of vapor in the bulk (m^2/s), Sc is the Schmidt number, $\mu/\rho D_{i,m}$; h_c is the convective mass transfer coefficient (m/s); d_p is the Droplet diameter (m)

Finally, the particle erosion rate, $R_{erosion}$, is defined as follows:

$$R_{erosion} = \sum_{p=1}^{N_{particles}} \frac{m_p C(d_p) f(\alpha) v^{b(v)}}{A_{face}} \quad (I.7)$$

where $C(d_p)$ is a function of the particle diameter, $f(\alpha)$ is a function of the impact angle of the particle path with the wall face, and $b(v)$ is a function of relative particle velocity.

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