AAPS PharmSciTech **2006; 7 (4) Article 102 (http://www.aapspharmscitech.org).**

Scale-up of a Pan-Coating Process

Submitted: April 17, 2006; Accepted: June 29, 2006; Published: December 28, 2006

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ABSTRACT

The purpose of this work was to develop a practical scale-up model for a solvent-based pan-coating process. Practical scale-up rules to determine the key parameters (pan load, pan speed, spray rate, air flow) required to control the process are proposed. The proposed scale-up rules are based on a macroscopic evaluation of the coating process. Implementation of these rules does not require complex experimentation or prediction of model parameters. The proposed scale-up rules were tested by conducting coating scale-up and scale-down experiments on 24-inch and 52-inch Vector Hi-coaters. The data demonstrate that using these rules led to similar cumulative drug release profiles (f2 >> 50; and P Analysis of Variance [P_{ANOVA}] >> 0.05 for cumulative percentage of drug released after 12 hours [Cum12]) from tablets made at 24- and 52-inch scales. Membrane characteristics such as opacity and roughness were also similar across the 2 scales. The effects of the key process variables on coat weight uniformity and membrane characteristics were also studied. Pan speed was found to be the most significant factor related to coating uniformity. Spray droplet size was found to affect the membrane roughness significantly, whereas opacity was affected by the drying capacity.

KEYWORDS: Pan coating, scale-up, scale-down, similarity, solvent coating, drug release, opacity.

INTRODUCTION

It has been estimated that mixing problems related to pharmaceutical process scale-up and process development cost more than $500 million per year.[1] While pan-based coating processes have been used for several decades, the scaleability of the process still remains a challenge. It is foreseeable that the pharmaceutical industry will be faced with more new chemical entities (NCEs) and new biomolecules that will come in short supply during development. It is therefore crucial to be able to conduct most of the experiments at a small scale and then apply the learning to the commercial scale.

Coating Process Conditions

Aqueous and solvent coating processes are extensively used in the pharmaceutical industry to apply functional and/or nonfunctional coats to tablets. Final product performance, including coating uniformity and drug release, is a strong function of these coatings. In addition to functionality, the texture and opacity of the coatings also affect bulk flow characteristics as well as overall aesthetics of the finished product. Opacity of the membrane can affect downstream processes such as laser drilling, Near-infrared (NIR) detection, or vision inspection systems. In addition, opacity could also be an indicator of membrane morphology.

The literature is rich with experimental studies that researchers have performed. Stetsko et al[2] developed a mathematical model for an aqueous film coating process in a 48-inch Acela Cota (Thomas Engineering Inc, Hoffman Estates, IL). Water removal efficiency (WRE) was selected as the key response variable, which was defined as the percentage of water sprayed on the tablet bed per minute. It was suggested that WRE could serve as a tool to assist in the scale-up process. Liu et al[3] studied the effects of spray rate, inlet air temperature, and pan speed on process efficiency and dissolution in an aqueous film coating process. In these experiments, changes in efficiency as a result of the process conditions did not significantly affect in vitro and in vivo performance. Porter et al[4] studied the effects of process conditions on an aqueous colorcoat Opadry (Colorcon, West Point, PA) process in a 24-inch O'Hara Technologies coater (O'Hara Technologies Inc, Richmond Hill, Ontario, Canada). The variables studied were percentage solids in the sprayed suspension, inlet air temperature, spray rate, atomizing air pressure, pan speed, and number of spray guns. The pan load and drying airflow rate was kept constant. The main response variables were coating uniformity, process efficiency, exhaust temperature, and moisture content. It was found that a change from 1 spray gun to 2 directly reduced weight gain variation. Pan speed was found to have the largest effect on coating uniformity followed by spray rate, inlet temperature, and number of spray guns. Rege et al[5] studied the effects of airflow, pan speed, inlet air

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temperature, coating time, atomization pressure, and fan pressure on coating uniformity and percentage recovery in a 24-inch Acela Cota coater. Atomizing pressure was identified as being the most influential variable with respect to coating uniformity. This was not in agreement with the findings from Porter et al,[4] who estimated the pan speed to be the most significant variable with respect to coating uniformity.

In most of these earlier works, the investigators identified a matrix of pertinent system variables and performed fractional factorial tests on them. This information was then used to derive a model by curve-fitting techniques. These models can predict how a change in process parameters (within the range that was studied) can affect a response variable that was studied. However, they do not provide a fundamental means for scale-up.

Scale-up Principles

There have been numerous efforts in the past to propose scale-up principles for the pan coating, and especially mixing processes. Levin[6] has applied the dimensional analysis approach for granulation scale-up. This involves identifying all variables crucial to process analysis. Buckingham's pi theorem is then used to identify the number of dimensionless groups that need to be identified in order to define and scale the process. Ding et al[7] developed scaling relationships for rotating drums by nondimensionalizing the differential equations governing the behavior of solids motion. The analysis does not account for the spray-related processing parameters. Qualitative insight into the different factors that affect the coating process has been provided by several researchers.[8,9] Avis et al[10] and Turton and Cheng[11] proposed some scale-up rules for pan coating, where parameters such as pan loading, pan speed, number of spray guns and distance between them, coating time, and spray rates were discussed. The batch size of solids was scaled on the basis of ratio of pan volumes and the pan speed on linear velocity. The spacing between guns and the number of guns were used to scale the spray rate. No discussion was provided on the "drying" kinetics of the system. Porter[12] has discussed the scale-up problem in more detail. The scale-up variables considered included pan loading, pan speed, number of spray guns, spray rate, and inlet airflow. However, the approach was somewhat qualitative. For example, spray rate was scaled using an inlet airflow that was decided by recommendations from the vendor of the equipment to meet the negative-pressure pan setting.

In the current study, similar nondimensional groups were investigated and experiments were conducted to validate them. The drying kinetics inside the coater are also addressed. Critical process variables are identified and a practical scale-up methodology is proposed. The intention of this work was to develop fundamental and broadly applicable scale-up rules. Scale-up was considered successful when identical drug release characteristics (predominantly dependent on coating morphology) and coating texture (roughness and opacity) were achieved using the proposed rules.

MATERIALS AND METHODS

Scale-up experiments were performed at pilot and commercial scales. The pan coaters used were 24-inch Vector HC-60 (Vector Corp, Marion, IA) with 2 spray guns and 52-inch Vector HC-130 with 4 spray guns. Freund spray guns (VectorCorp, Marion, IA) (2-fluid nozzle) were used for all experiments. The tablets used were capsule-shaped longitudinally compressed tablets. The target weight gain for all runs was 42 to 45 mg per tablet. An acetone-based cellulose acetate membrane coating formulation was used. Five individually marked active tablets from each coating run were tested for drug release profiles. The individual tablets were marked using a permanent marker before coating. Since the coating was clear, the marked tablets could be identified easily after coating. The membrane weight gain on each tablet was known a priori, and hence the drug release rate could be corrected for individual membrane weight gain. Drug release testing was performed using United States Pharmacopeia (USP) type VII apparatus over a period of 24 hours. The amount of drug released was measured in 2-hour increments. The cumulative drug release profiles as well as the cumulative amount of drug released at the 12-hour time point were examined. In order to measure coat weight variability, 100 individually marked tablets were weighed before and after application of the membrane coating. The opacity was gauged using a semiquantitative scale. A visual rating scale of 1 to 5 with 1 representing a clear membrane and 5 representing a highly opaque membrane was developed in an effort to gauge the opacity and roughness of the membrane. Samples from each lot were presented to 10 independent (not involved in the scale-up experiments) process and formulation scientists along with the rating guidelines. An average from the 10 ratings was used.

RESULTS AND DISCUSSION

A typical pharmaceutical tablet coating process in a pan coater is shown in Figure 1. The coating process can be split into coat application (spray-related) and tablet handling (pan- and tablet-related) processes, as shown in Figure 2. It is acknowledged that this separation is a simplification because some of these process parameters are interrelated and, under extreme conditions, the tablet factors will affect the spray and vice versa. In typical pharmaceutical applications, the target coat weight is governed by non-process-related factors (eg, desired drug release). The coating formulation

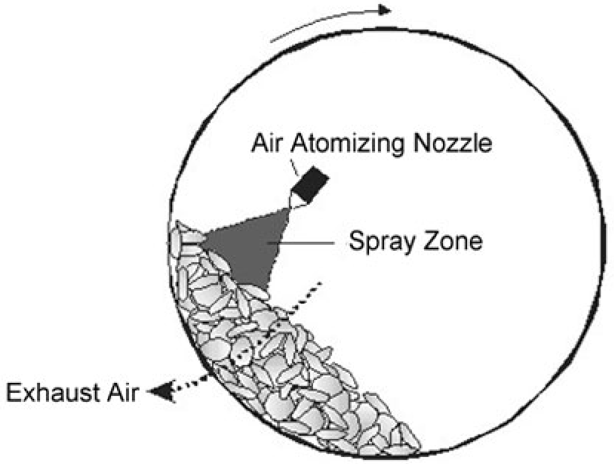

Figure 1. Representation of a typical pan coating process.

Table 1. Dimensional Analysis Approach to Pan Coating Scale-up*

Independent Process Variables			
Spray-related		Pan-/tablet-related	
Spray rate (g/s)	Y	Pan diameter (cm)	Y
Viscosity (g/cm/s)	N	Pan depth (cm)	Y
Surface tension (g/s^2)	N	Pan speed (s^{-1})	Y
Atomization air (cm^3/s)	Y	Baffle efficiency	N
Pattern air (cm^3/s)	Y	Core size (equivalent d) (cm)	N
Pan air flow rate (cm^3/s)	Y	Bulk density (g/cm^3)	N
Inlet air temperature (°C)	Y	Gravitational acceleration (cm/s^2)	Y
Inlet air dew point (°C)	N	Pan load (g)	Y
Gun to bed distance (cm)	Y	Number of guns	N
Coating time (s)	Y		
Total	10	Total	9
Total relevant	7	Total relevant	5
Dimensions	4	Dimensions	3
Dimensional groups required	3	Dimensional groups required	2

*Y indicates yes; N, no. Denotes whether the parameter is considered relevant for the scale-up analysis.

and solution properties are optimized during formulation development, and it is preferred to keep them constant through scale-up.

A dimensional analysis of the coating process is presented in Table 1. The number of dimensionless groups required to completely describe the system is given by Buckingham's pi theorem. Though the required number of dimensionless groups can be defined for the process, establishing a scale-independent relationship is not as straightforward in the case of a pan-coating process for functional coatings because the permeability of the coating is the key dependent variable. However, the permeability is typically measured indirectly after a few other processes such as drying and laser drilling have been performed. Therefore, a simple practical approach to the scale-up problem is presented in this work. Several researchers have proposed ways to scale particle size with pan diameter for rotating drums using dimensionless analysis,[7,13] but during a scale-up operation in industry, the tablet size must be kept constant. It has also been proposed that spray rate per spray gun should be kept constant (if the distance between the guns is constant on different scales) to achieve similar microscopic coating characteristics.[11] This strategy will work only if scale-up is achieved by elongating the pan in order to maintain geometric similarity and is not practical given the pan depths required to maintain this type of similarity.

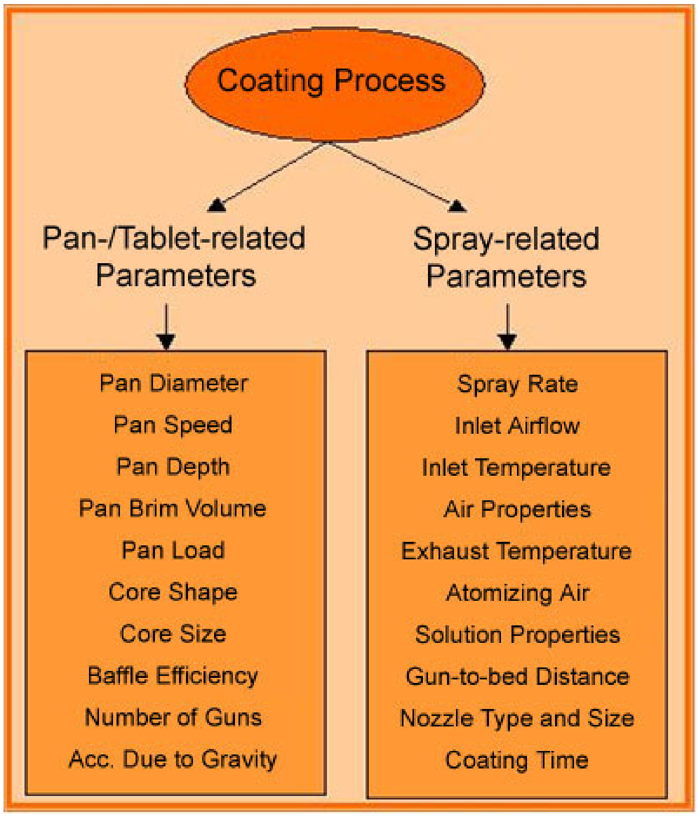

Figure 2. List of variables affecting the pan-coating process.

The macroscopic parameters that need to be defined include spray rate, airflow, inlet air temperature and dew point, atomization air, pattern air, pan load, and pan speed. It was assumed that mixing efficiency is constant across scales. The effect of dew point of the inlet air would be negligible for a solvent-based coating process and was therefore ignored. The liquid properties were maintained constant. The number of spray guns was scaled according to the length of the pan (pan depth), in order to ensure complete coverage. In order to keep the design of experiments manageable, 4 variables were selected for this study: pan load (kg), pan speed (s^{-1}), total spray rate (mL/min), and inlet airflow (cm^3/s). All other parameters were kept constant. It is understood that most of these variables will have some influence on the coating process but have not been included for simplicity.

There are 3 types of similarities required for successful scale-up: geometric, dynamic, and kinematic.[6,14] Maintaining geometrically similar systems gives the best chance to attain dynamic and kinematic similarities, as depicted in Figure 3. In the case of a pan coater, both pan and spray related factors need to be maintained "similar" across the scales.

Geometric Similarity

Geometric similarity means that the shape and dimensions of the pan coater are proportional across various scales[15,16] and can be achieved by having systems with similar aspect ratios (ratio of pan length to diameter). Equipment manufacturers need to ensure that the aspect ratio of pans across scales is constant. The height, width, and shape of passive baffles should also be proportional across the different scales in order to achieve similar mixing. The geometric similarity can further be achieved by keeping the pan load to pan volume ratio constant. This in turn keeps the h/D ratio constant, where h is the closest distance from the center point of the pan to the bed surface (h can be considered as the characteristic length of the system from a tablet handling perspective) and D is the pan diameter.

$$\frac{\text{Pan Load}}{\text{Pan Volume}} = \text{constant} \tag{1}$$

Equation 1 can be used to estimate the pan load that can be used in the bigger pan during scale-up. The pan volume in Equation (1) is the brim volume of the pan and is typically provided by the equipment manufacturer.

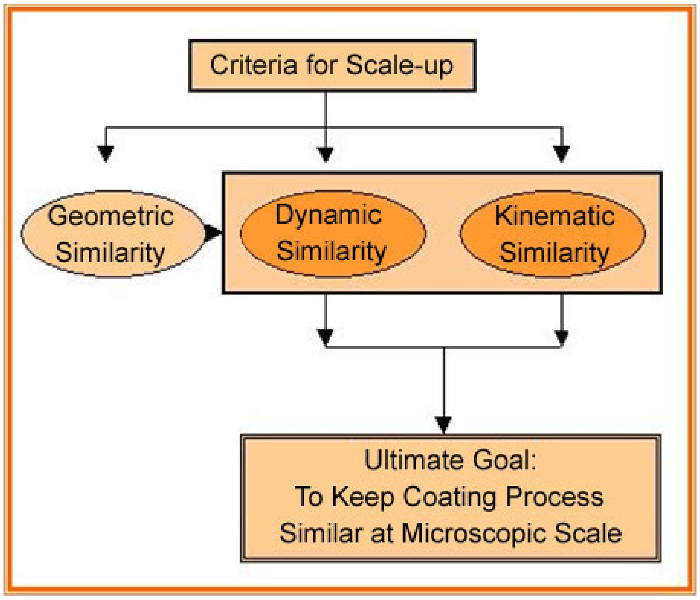

Figure 3. Types of similarities required across scales for achieving successful scale-up.

Dynamic Similarity

Dynamic similarity ensures that the ratio of forces at corresponding points in the pan coater is similar across various scales. The 2 main forces in a rotating pan are the inertial and gravitational forces. A balance between these 2 forces is important to achieve a desirable motion of tablets. The ratio of inertial to gravitational forces (Froude, Fr) is a commonly used dimensionless number that dictates the dynamics of the system.[7,11,13,17] It has also been proposed that during scale-up, the linear velocity of the pan must be kept constant.[9,18] However, Fr number scaling offers a more fundamental rationale and is therefore used in the current work.

$$Fr = \frac{\omega^2 D}{g} = \text{constant} \tag{2}$$

where ω is the pan speed. Equation (2) can be used to predict the pan speed for the larger pan, given the small-scale conditions to achieve similar dynamics.

Kinematic Similarity

Kinematic similarity ensures that the ratio of velocities (kinetics) at corresponding points in the pan is similar across scales. In order to achieve this, velocity of the tablets and spray kinetics should be kept the same. It is known that tablet velocity changes as a function of the length along the cascading bed.[19] Therefore, it is proposed that the location of the spray along the cascading length of the bed is maintained constant. The spray kinetics will be a function of the droplet size coming out of the spray gun, which in turn is dependent on atomizing air, pattern air, spray rate, nozzle type and size, and solution properties. The drying of the droplet before it reaches the tablet is dependent on inlet airflow, inlet air temperature, and gun-to-bed distance. In order to achieve similar membrane morphology, the droplet size of the spray hitting the tablet should remain the same, provided that the tablets move at the same speed across scales. If τ_{dry} is characteristic drying time for the droplet and $\tau_{surface}$ is the time the tablet spends on the bed surface, then for scale-up

$$\frac{\tau_{dry}}{\tau_{surface}} = \text{constant} \tag{3}$$

The time spent on the bed surface will be a function of tablet velocity and pan size. The characteristic drying time can be determined by heat and mass transfer correlations for droplet drying. To do so, the dependence of droplet size on spray rate, inlet airflow, atomizing pressure, fluid properties, and nozzle type should be known. Various models for droplet size variations have been proposed in the past for aqueous-based systems[20,21] but are not suitable for the solvent-based solutions used in this study. In the absence of droplet size distribution data for the current experimental conditions, a macroscopic approach of the drying kinetics was employed.

Airflow Calculation

A macroscopic mass and energy balance for an aqueous coating process was first reported by Ebey.[22] Recently, such analysis was extended to both organic and aqueous film coating by Ende and Berchielli.[23] Neglecting the heat loss from pan to surroundings and assuming that the outlet air temperature is equal to the tablet bed temperature, it can be shown that if the airflow-to-spray rate ratio (drying capacity, Equation 4) and the inlet temperature are held constant, the exhaust temperature will also remain constant.[22,23] This information can be used to predict inlet airflow during scale-up, while maintaining similar overall drying capacity.

$$\text{Drying Capacity} = \frac{\text{Airflow}}{\text{Spray Rate}} = \text{constant} \tag{4}$$

Spray Rate Calculation

The probability of a tablet being in the spray region can be given by $p = n/N$, where n is the number of tablets in the spray zone at any instant and N is the total number of tablets in the pan. While scaling up to a bigger coater, pan load and spray area both increase, but the increase in N is many folds bigger than that of n. Therefore, the overall probability of a tablet being in the spray zone decreases for a larger coater. Furthermore, this probability is inversely proportional to the time it takes for a tablet to reappear in the spray zone. Therefore, the lower the probability, the more time it takes before the tablet reappears in the spray region. The time between passes through the spray zone is equivalent to the drying time for individual tablets, though the majority of the drying occurs when the tablet is at the surface. The time between 2 successive coating events on a tablet is defined as the circulation time.[24,25] Hence, for the bigger pan, the circulation time is higher and p is lower. As a result, tablets in a larger coater are allowed more time to dry. The tablet that takes more time to reappear in the spray zone can be sprayed with more solution each time it passes through, since it gets proportionally more time to dry before being sprayed on again. In an equation form,

$$\frac{(\text{SR})(n)}{(N)} = \text{constant} \tag{5}$$

where SR indicates spray rate.

Since it is easy to determine n and N for a given system, the spray rate can be estimated using the above equation. This equation can also be used to predict the effects and changes needed due to changes in the tablet size, which will manifest itself as a change in the value of n and N. For a given spray area, n $1/d^2$ tablet, whereas for a given pan load and tablet shape, $N \propto 1/d^3$.

$$p = \frac{n}{N} \propto d \tag{6}$$

where d indicates the tablet size.

It should also be noted that one of the objectives at the larger scale is to maximize the spray rate in order to minimize the batch processing time. When spray rate can be increased, one of the following adjustments needs to be made in order to maintain microscopic spray zone similarity: increase gun-to-bed distance, increase atomizing air, or both. When these parameters change, the gun spacing on the boom might need to be adjusted to ensure full spray coverage across the pan depth. As stated earlier, it is assumed that the coating solution or formulation is optimized at the pilot scale and not changed during scale-up. While that is the case in most practical situations, there can be instances in which the coating solution properties have to be altered. When doing so, the spreading (wettability) and rate of drying have to be balanced for successful scale-up. Two commonly used factors that can help with this are the Weber number (ratio of kinetic energy to surface energy) and Reynolds number (ratio of inertial to viscous force).[26] These 2 factors in combination can be used to account for any change in the solution viscosity or surface tension. However, to accurately use these factors it is essential to know the droplet size distribution.

Coating Time Calculation

The coating time serves as a dependent variable and can be determined by Equation 7 to achieve same weight gain per tablet.

$$\frac{t_{coat} \times \text{SR}}{\text{Pan Load}} = \text{constant} \tag{7}$$

where SR indicates spray rate. Figure 4 illustrates the proposed scale-up rationale.

Another important factor to consider during scale-up is the average number of coating events per tablet constant across different scales. The average number of coatings per tablet can be held constant by keeping the average number of passes under the spray gun (N_c) constant. N_c can be given

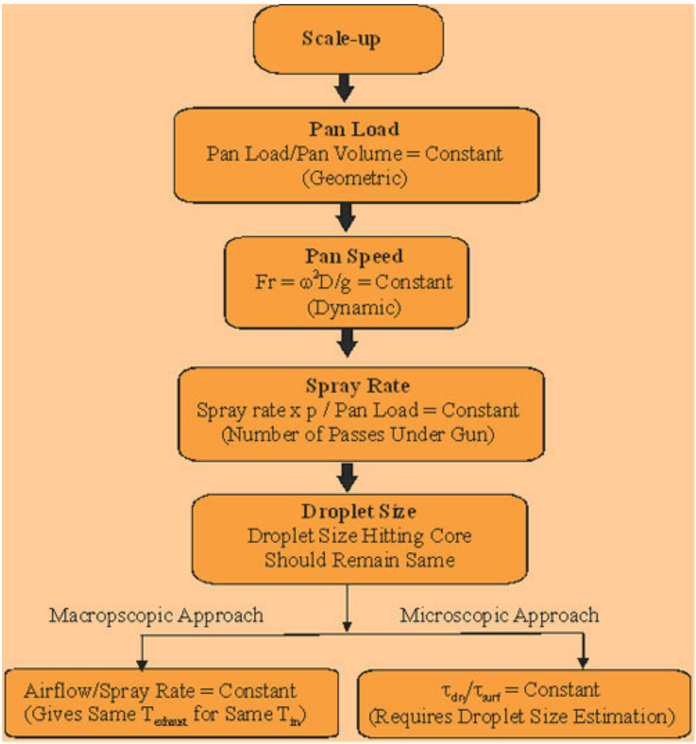

Figure 4. Proposed scale-up methodology for coating process.

by Equation 8 as described in a study by N. Joshi, J. Ergun, Y. Song, and A. Joglekar (unpublished data, 2006).

$$N_c = \frac{VLJt}{aN} \tag{8}$$

where, V is the velocity of tablet in the spray zone, L is the length of spray zone, J is the number of spray guns, a is the projected area of the tablet, and t is the total coating time.

Keeping the average number of coating events per tablet constant will allow maintaining the coat weight uniformity constant. Although this approach was not used as a starting point in the current work, the average number of passes under the gun was evaluated for the conducted experiments.

Four coating experiments were conducted (2 on a 24-inch pan and 2 on a 52-inch pan), as summarized in Figure 5. For the first set of experiments, an optimized 52-inch coater process was scaled down to a 24-inch coater using the proposed rules. The conditions of the optimized 52-inch process are summarized in Table 2. These processing conditions were previously optimized using statistically designed experiments to achieve desired membrane characteristics (in terms of opacity, roughness, and drug release) and were known to result in "smooth" coated membranes. The proposed "scale-up" methodology was used to estimate the corresponding conditions required for the 24-inch coater in order to achieve similar membrane characteristics. The process variables that were scaled-down include pan loading, pan speed, spray rate, and inlet airflow. The following calculations were performed to evaluate the corresponding 24-inch scale parameters:

(1) Pan loading (PL), from Equation 1: $PL_{24\ in} = (PL_{52\ in})$ (Pan brim volume$_{24\ in}$/Pan brim volume$_{52\ in}$) = (110 kg)(30/225) = 14.67 kg

(2) Pan speed (ω), from Equation 2: $\omega_{24\ in} = \{\omega_{52\ in}{}^2[D_{52\ in}/D_{24\ in}]\}^{1/2} = \{8.5^2(52/24)\}^{1/2} = 12.5$ rpm

(3) Total spray rate (SR), from Equation 6: $SR_{24\ in} = (SR_{52\ in})(p_{52\ in}/p_{24\ in}) = (SR_{52\ in})(n_{52\ in}/n_{24\ in})(N_{24\ in}/N_{52\ in})$

The spray area for the 52-inch coater is about twice that of the 24-inch, hence the ratio $n_{52in}/n_{24\ in} = 2$. The ratio $N_{24\ in}/N_{52\ in}$ will be proportional to the ratio of pan loading for particles with the same diameter. Hence, $N_{24\ in}/N_{52\ in} = PL_{24\ in}/PL_{52\ in} = 14.67/110$. Therefore, $SR_{24\ in}$ = (780 mL/min)(2)(14.67/110) = 208 mL/min. Since 4 spray guns are used in the 52-inch coater, the proposed spray rate per gun = 104 mL/min.

(4) Inlet airflow (AF), from Equation 4: $AF_{24\ in} = (AF_{52\ in})(SR_{24\ in}/SR_{52\ in})$ = 750 cu ft/min (208/780) = 200 cu ft/min.

A coating run was conducted on the 24-inch pan with these proposed operating conditions (Table 2). Some of the calculated parameter values have been rounded off. The same opacity and roughness rating (= 1) was obtained for tablets from both of the scales. Release rate tests confirmed similar drug release characteristics of the membrane on both scales. The cumulative percentage of drug released after 12 hours (Cum12) was used to quantify the drug release characteristics of the membrane and is listed in Table 2. There was no significant difference between the 12-hour cumulative drug release data obtained from 52-inch and 24-inch coater (P_{ANOVA} = .6). In addition, f_2 similarity criteria were calculated for the 2 profiles per scale-up and postapproval changes-modified release (SUPAC-MR) guidelines. The 2 profiles are considered similar if the f_2 similarity factor is greater than 50 and if the difference in drug release at each time point is less than 15%. The f_2 factor for these

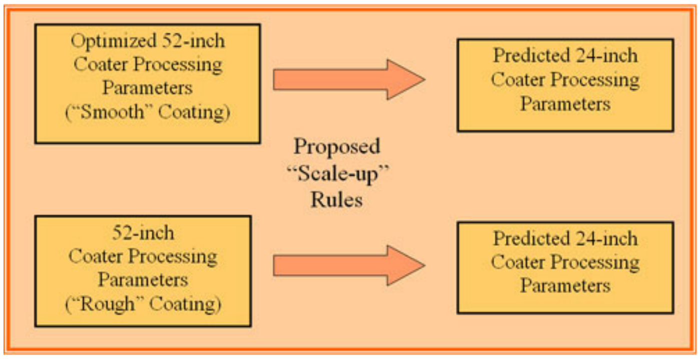

Figure 5. Experimental strategy to test the proposed scale-up methodology.

Table 2. Experimental Conditions and Results from "Scale-up" Experiments

Process Parameters	Optimized 52-inch Process "Smooth" Coating	Scaled 24-inch Process	Optimized 52-inch Process "Rough" Coating	Scaled 24-inch Parameters
Pan load (kg)	110	14.5	110	14.5
Pan speed (rpm)	8.5	13	8.5	13
Air flow (cu ft/min)	750	200	750	200
Spray rate (mL/min/gun)	195	102	195	102
Inlet temperature (°C)	50	50	39	39
Air cap (mm)	025	025	015	015
Average membrane coat weight gain (mg/core)	43.7	42	45.7	44.7
Weight gain (coefficient of variation)	5.2	4.6	-	-
12-hour cumulative drug release (%)	44.6 ± 1.3*	44.5 ± 5.6*	49.6 ± 2.3*	43.1 ± 4.3*

*Error indicates 1 standard deviation.

2 profiles was 92.8 and the largest difference at any time point was 2.3%. These results demonstrate that the coating film formed in both scales had similar membrane characteristics, indicating that the proposed scale-up rules help to scale the process successfully. The average number of passes under the gun for the 52-inch scale coating run was estimated to be 660 (Equation 8), and 840 for the 24-inch scale.

Another set of experiments was conducted with the intention of further confirming the proposed scale-up rules. A coating run with process conditions known to give rough tablets and a high percentage of twins on the 52-inch coater (Figure 5) was performed. These process conditions were scaled down using the proposed scaling algorithm, as shown for the previous case, and tested on the 24-inch coater. The original process conditions for the 52-inch scale and the proposed process conditions for the 24-inch coater are shown in Table 2. Again, similar membrane characteristics were observed on both scales and the difference between 12-hour cumulative percentage drug release between the 2 scales was insignificant (Table 2). These experiments demonstrate that the proposed scale-up rules work well and membrane characteristics (good or bad) are replicated successfully across the scales. The importance of membrane similarity is underlined for products with controlled release membrane coating such as the osmotic pump solid oral dosage forms manufactured by ALZA (ALZA Corp, Mountain View, CA).

After establishing the scale-up rules from basic similarity principles and testing them, a series of experiments were conducted to study the effect of variables affecting coating uniformity with emphasis on the ones that were selected for this study. For each run, the coating weight gain of individual marked tablets was measured in order to estimate the coefficient of variation during coating. Pan speed was found to have the biggest effect on coating uniformity ($p_{ANOVA} = 0.0004$). The variance decreased with increasing pan speed. This finding suggests that the pan speed should be maintained as high as possible to achieve more uniformity.

Coating efficiency and opacity were most significantly affected by the drying capacity (Equation 4) ($p_{ANOVA} = 0.004$ and $p_{ANOVA} = 0.005$, respectively). The efficiency was found to decrease with the increase in airflow to spray rate ratio. The exhaust temperature was found to affect the opacity significantly ($p_{ANOVA} = 0.017$). Opacity increased with an increase in exhaust temperature, which governs the evaporation rate of the droplets on the surface of the tablets. Thus opacity was directly affected by how dry the process was and the rate of droplet evaporation. No apparent differences in roughness were obtained in any of the coating runs. Thus, no conclusions could be made regarding roughness in this study. It was hypothesized that coating roughness is strongly affected by the balance between droplet spreading (wettability) and drying.[26] The atomization air was increased in order to reduce the droplet size. As predicted, this coating run gave very "rough" tablets confirming that droplet size had a significant role to play in dictating the "roughness" of the tablets.

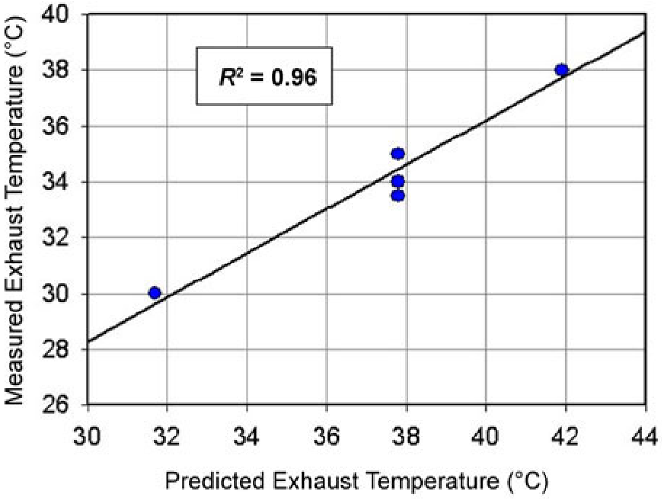

Figure 6. Comparison of predicted exhaust temperature[22] with the experimental exhaust temperature.

The predicted exhaust temperature from the thermodynamic balance suggested by Ebey[22] was compared with the measured exhaust temperature for all the coating runs and is shown in Figure 6. The measured exhaust is always lower than the predicted exhaust as suggested by Ebey but was remarkably close in view of the assumptions made in the model. The simple thermodynamic balance seems to give a fairly good macroscopic picture of the process. It further shows that the macroscopic approach of the drying kinetics (as used in the scale-up section) is a reasonable approach when droplet size data are not available.

CONCLUSIONS

The proposed scale-up rules can be used to achieve similar drug release as well as coating roughness and opacity at the commercial scale to that obtained at the pilot scale. These scale-up rules are based on a macroscopic evaluation of the coating process. Therefore, complex experimentation or prediction of model parameters is not required to use these rules. It is acknowledged that the applicability of these rules will be limited if properties of the coating solution are dramatically different across the 2 scales.

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