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Mixing Efficiency in Side-Vented Coating Equipment

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ABSTRACT

The purpose of this study was to evaluate tablet mixing within side-vented coating equipment by assessing the development of color uniformity during coating. A colorimetric method was used to evaluate the time for uniform coating for different mixing baffle systems at different scales of equipment. The influence of tablet size was also determined. The inclusion of rabbit ear baffles in the small-scale equipment reduced the time to achieve color uniformity by 20 minutes. The design of baffle influenced the time for uniform color with a mixing efficiency rank order of tubular > ploughshare > rabbit ear. Upon scale-up, the efficiency of mixing seen at development scale remained equivalent in terms of the influence of baffle design. The study into the influence of tablet size revealed the importance that the total batch surface area has on the time taken to achieve color uniformity, with 7-mm diameter tablets having a higher surface area for an equivalent volume of product and taking 15 to 20 minutes longer to achieve color uniformity than 16-mm diameter tablets.

KEYWORDS: mixing, baffle design, color uniformity, film coating, tablets

INTRODUCTION

Tablet mixing within side-vented coating equipment contributes significantly to the efficiency of the coating process. Mixing efficiency is of great importance when one considers recent developments in the materials used for tablet coating or where the active material is included in the coating. The introduction of Opadry II HP (Colorcon, Dartford, UK), which is based on polyvinyl alcohol and can be used at solid contents up to 25% wt/wt, highlights the necessity for improved mixing efficiency. The high solids level reduces the amount of time to apply the desired theoretical weight of coating material and subsequently the time for mixing to take place. The inclusion of active materials in the coating to be applied[1] necessitates the requirement to have a uniform film application in thickness and weight. However, weight variations of 24% have been reported for conventional film coating operations.[2]

The movement of tablets during the coating process will determine the amount of coating material deposited and the tablet-to-tablet variation in coating thickness and weight. Previous studies in this area have examined factors that influence the tablet movement and the properties of the coated tablets. Individual tablet movement was studied[3] for different batch and tablet sizes by measuring the time spent by a marker tablet at the tablet bed surface (spray zone). The influence of tablet shape was studied[4] by measuring the variation in the thickness of coating on the tablet. Tobiska and Kleinebudde[5] used the temperature difference between the spraying zone and the drying zone as a measure of mixing efficiency in a Bohle Lab.Coater (BLC) pan coater. Bhagwant et al[6] measured the variability and loading of a model drug, FD&C yellow #6, in assessing process parameters that affected mixing and loading.

Although tablet properties such as shape and size affect mixing, equipment design may also have an important impact. The influence of drum speed and baffle position was studied by Signorino and Forcellini[7] using a colorimetric method to detect differences in the amount of coating applied. The present study assesses the mixing within a coating process using differential colorimetric measurements as a measure of the coating (color) uniformity. The performance of different baffle systems in achieving color uniformity, the effect of

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Table 1. Coating Process Parameters*

Coating Parameter	XL	Premier 200	Accelacota 350
Inlet temperature (°C)	60	60	60
Airflow (m^3/h)	450	2500	6000
Flow rate (g/min)	40	400	940
Drum speed (rpm)	10	5	4
Atomizing air pressure (bar)	1.2	2.5	3.0
Spray width pressure (bar)	1.5	3.0	3.0
Cabinet depression (Pa)	–100	–100	–100
Gun to bed distance (cm)	20	26	30

*XL indicates Manesty XL model.

equipment scale-up, and the influence of tablet size were studied.

MATERIALS AND METHODS

Normal concave 16-mm, 14-mm, and 7-mm diameter tablets consisting of microcrystalline cellulose (Avicel PH102, 66.0% wt/wt, FMC, Brussels, Belgium), lactose (Tablettose 80; 33.3% wt/wt, Meggle, Wasserburg, Germany), colloidal silicon dioxide (Aerosil 200, 0.2% wt/wt, Degussa Huls, Dusseldorf, Germany), and magnesium stearate (0.5% wt/wt, BDH, Poole, UK) were compressed on a rotary tablet press (Unipress Diamond, Manesty, Knowsley, UK). The mean tablet weights were 1280 mg, 750 mg, and 100 mg, respectively (n = 20, all within ±1% of the mean), and all tablets were compressed to give a mean tablet breaking load of 120 ± 10N (n = 20, Schleuniger, Model 2E, Solothurn, Switzerland).

Pink Opadry OY 35018 (Colorcon, Dartford, UK) was used as the coating material and was applied under the conditions shown in **Table 1** using a Manesty XL coater fitted with a 610-mm diameter coating drum for development studies. A Manesty Premier 200 (1200-mm diameter coating drum) or an Accelacota 350 (1525-mm diameter coating drum) were used to investigate the effect of scale-up. The process was run with no baffles in the drum or with the inclusion of tubular, ploughshare, or rabbit ear baffles as shown in **Figure 1**. The coating parameters chosen were based on those typical for each scale of equipment and selected to give equivalent values for peripheral speed of the drum and suspension application rate. Thus, the influence of the baffles could be fully evaluated. Where different sizes of tablets were examined in the same apparatus, the batch size (in kilograms) was varied to maintain a constant volume of product. For the XL coater, these were 13.7 kg for the 7-mm tablets, 12 kg for the 14-mm tablets, and 11.1 kg for the 16-mm tablets. For the Premier 200, the batch sizes for the 7- and 16-mm tablets were 146 kg and 120 kg, respectively, and a batch size of 300 kg was used in the Accelacota 350 for 16-mm tablets.

Spraying was started and 5 (small scale) or 15 (large scale) samples of 100 tablets were removed from different areas of the tablet bed at set time intervals. The difference in the sample size used (at different scales) was to avoid removal of samples having a large impact at the small scale. From these samples, the most uniformly and the least uniformly coated tablets were removed (by visual inspection) and the delta (Δ)E was determined as described. The remaining tablets were returned to the batch. This sampling technique was repeated at regular intervals until a uniform color (determined visually) was achieved throughout the tablet batch.

A colorimetric method was used to determine the time point for achieving a uniform coating. The Internationale de l'Eclairage method for expressing color difference correlates with a basic 3-dimensional nature of color. ΔE, the total color difference, was selected for indicating the color uniformity during the coating run because it considers the influence of lightness, chroma, and hue.

For each of the samples removed at the various time points, the most and least uniformly coated tablets were chosen and the ΔE value (equivalent to the total color difference of the 2 samples) obtained using a spectro-

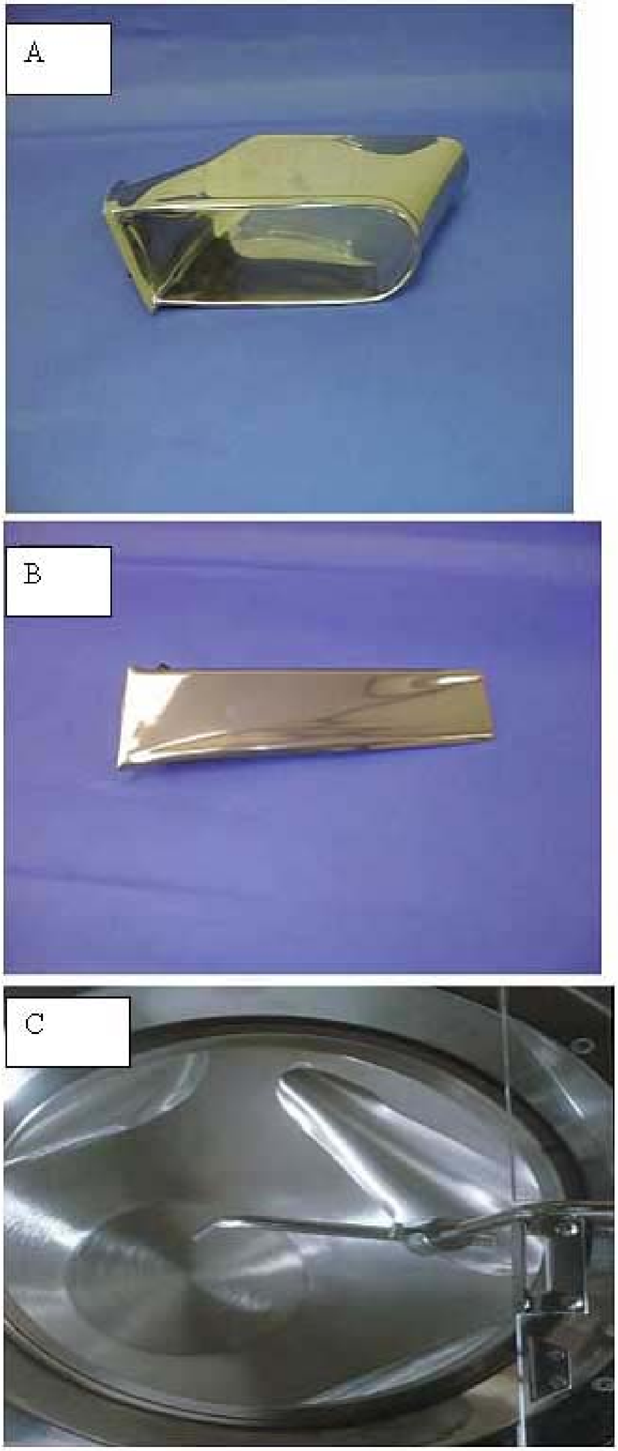

Figure 1. The (A) tubular, (B) ploughshare, and (C) rabbit ear baffles used in the study.

photometer (Datacolor International Spectraflash 600, Lawrenceville, NJ). This technique allowed ΔE with time and time for complete mixing (t_{mix}) (taken as the time point where ΔE was less than 2.5) to be determined.

RESULTS AND DISCUSSION

Influence of Baffles on Mixing

Initial experiments were performed using the development scale coater (Manesty XL) to establish the reproducibility of the method and to examine the influence of baffles. Rabbit ear baffles were chosen because 8 could be successfully fitted to this apparatus. For this experiment, 14-mm tablets were used. **Figure 2** shows the influence of baffles in a 610-mm coating drum on the time to achieve uniformity of color. The results show that for this capacity of coating drum, the inclusion of mixing baffles had a positive effect on mixing. The inclusion of 4 baffles led to a reduction of 20 minutes in the time to achieve color uniformity in comparison to when the coating pan was run with no baffles fitted. The results also show a slight benefit in using 8 baffles over 4 baffles as suggested by Signorino and Forcellini[5]: there was a further reduction of approximately 6 minutes. These experiments were repeated at least 3 times to assess the reproducibility of the methodology. The standard errors of the ΔE values varied from 2.76 at the early time points to 0.04 at the later time points. This was considered acceptable and allowed single runs to be performed in the larger-scale equipment.

Influence of Scale-Up and Baffle Design on Mixing

Further experiments were performed with 7-mm and 16-mm diameter tablets to examine a wide difference in tablet size. **Figures 3A** and **3B** show the relationship between process time and ΔE when 16-mm round tablets were processed in different scales of equipment using either ploughshare or tubular baffles. (These are the only baffle types available for the Premier 200 and the Accelacota 350 equipment.) The times to achieve complete mixing (t_{mix}) are summarized in **Table 2**. These relationships show an increase in time to achieve coating uniformity as the volume of product increases, either 15 or 20 minutes on moving from the small scale to the large scale, depending on the baffle system used. There is often believed to be a dead zone in the center of the tablet bed—a zone relatively untouched by the spray. This increase in time with volume would support

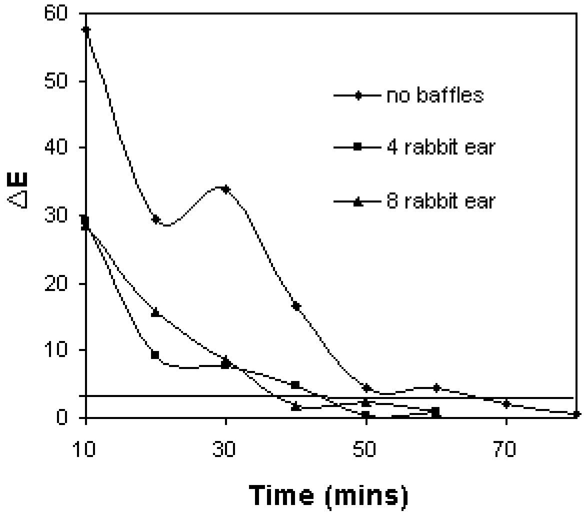

Figure 2. The relationship between ΔE and coating time for 0 (n = 4), 4 (n = 3), and 8 (n = 3) rabbit ear baffles. (The horizontal line represents a ΔE of 2.5, the value used to indicate complete mixing.)

the suggestion that as the volume of product increases, the dead zone in the center of the drum increases, thus making it increasingly difficult to uniformly pass all the tablets through the spray zone and achieve uniform color. The increase in time to achieve complete mixing with an increase in volume was evident for both baffle systems, with the tubular design appearing to be more effective in achieving color uniformity in a shorter time.

Influence of Tablet Size on Mixing Efficiency

Figure 4 shows the relationship between spraying time and ΔE for 16-mm and 7-mm round tablets processed in a Premier 200 coater with the same batch volume. The results show an increase in the time to achieve color uniformity for 7-mm tablets (90 minutes) compared with 16-mm tablets (45 minutes). This difference can be attributed to the increased surface area of the smaller tablets and the different movement of the tablets within the drum. The surface area of an individual 7-mm tablet is 117 mm^2 and that of an individual 16-mm tablet is 753 mm^2. The total surface areas of the 2 tablet types in the batches coated were 171 m^2 for the 7-mm tablets and 71 m^2 for the 16-mm tablets. These factors affect the time tablets spend in the spray zone and hence how long color development takes.

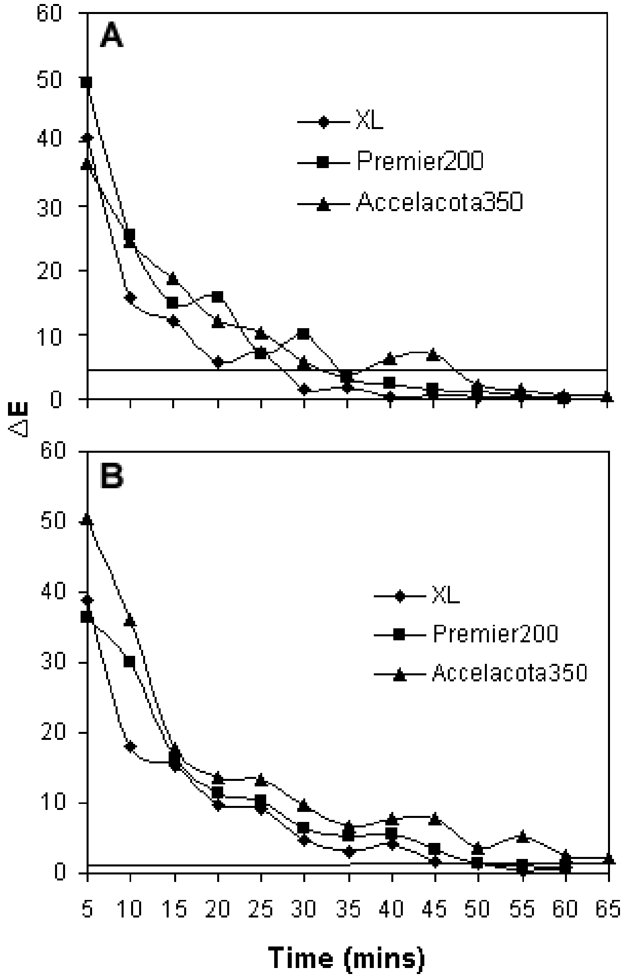

Figure 3. The relationship between ΔE and coating time for 16-mm round tablets processed in different scales of equipment fitted with (A) tubular baffles and (B) ploughshare baffles. (The horizontal line represents a ΔE of 2.5, the value used to indicate complete mixing.)

CONCLUSION

The current studies have shown that the inclusion of baffles improves the mixing performance within the coating drum. Increasing the number of baffles from 4 to 8 also gives an improved performance in mixing for the rabbit ear baffle design tested at the development scale. Different baffle designs show a difference in mixing performance depending on the tablet size tested. Baffles of the tubular design give a greater mixing performance when compared to baffles of the ploughshare design. The difference in mixing performance of these baffle systems remains consistent when the process is scaled up from laboratory scale to pilot scale and onto production scale, with the tubular design giving the more effective mixing.

Table 2. Mixing Times for 16-mm Round Tablets Processed in Different Scales of Equipment Fitted With Tubular or Ploughshare Baffles*

	XL		**Premier 200**		**Accelacota 350**	
	Tubular	**Ploughshare**	**Tubular**	**Ploughshare**	**Tubular**	**Ploughshare**
t_{mix} (min)	30	45	40	50	50	60

*XL indicates Manesty XL model.

Results comparing tablets of the same shape but different size show a difference in mixing performance, with the larger tablet achieving color uniformity more quickly. The difference can be attributed to the effect that increased surface area and decreased tablet movement in the coating drum have on color development.

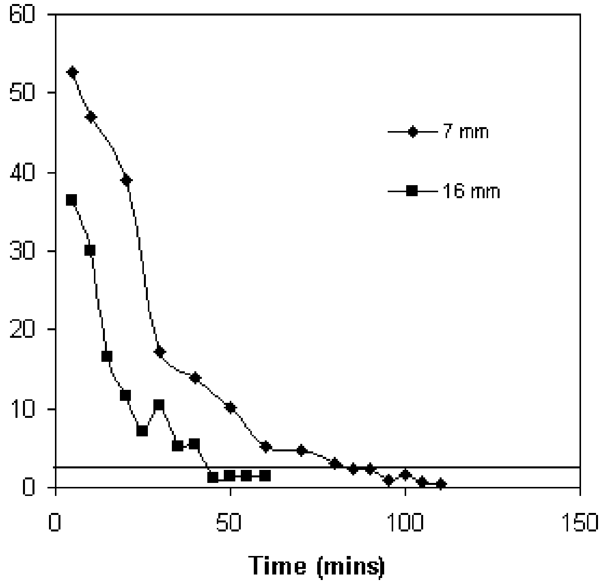

Figure 4. The relationship between ΔE and coating time for 7- and 16-mm round tablets processed in a Premier 200 coater fitted with ploughshare baffles. (The horizontal line represents a ΔE of 2.5, the value used to indicate complete mixing.)

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