Evaluation of Film Coating Weight Uniformity, Tablet Progression and Tablet Transit Times in a High Throughput Continuous Coating Process

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The developmental film coating from this study was commercially launched in April 2016 as:

Opadry® QX
Quick and FleXible Film Coating System

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Purpose

Compared to batch coating processes, continuous film coating processes allow for fast coating times and have been shown to provide excellent color uniformity due to a shallower tablet bed depth and increased frequency of tablet presentations to the spray zone.[1] It has also been shown that high solids concentration (≥20%) coating systems may be well suited to maximize the efficiency of continuous processes.[2]

Interest in continuous coating for pharmaceutical products is increasing and there is a need to more fully understand how these processes compare to traditional batch coating processes in terms of actual coating weight uniformity rather than just color uniformity. This study evaluates the effect of tablet residence time and uniformity of tablet progression on coated tablet weight variation in a high throughput continuous coating process. In addition, the coating uniformity values obtained in the continuous coating process were compared to coating uniformity in a typical production scale batch coating process.

Methods

Trials were conducted in a 24" diameter continuous tablet coater (Model CTC, Thomas Engineering, USA) equipped with 22 spray guns (ABC type, Schlick, DE) (Figure 1).

Figure 1. Exterior and Interior Views of Thomas CTC

Colorcon placebo tablets (300 mg, 10 mm, round with debossed logo) were used as the substrate. An innovative, pigmented coating formulation developed by Colorcon based on Kollicoat IR (polyvinyl alcohol-polyethylene glycol graft copolymer) (BASF, Florham Park, NJ) was used in the study. The formulation was prepared at both 20% or 25% solids concentration and applied to a target weight gain (WG) of 3.0% at tablet throughput rates of both 680 kg/hour or 850 kg/hour using the process parameters shown in Table 1.

Table 1. Coating Process Parameters

CTC Parameters	Trial 1	Trial 2
Inlet air temperature (°C)	75	72
Inlet airflow rate (cfm / m^3/hr)	6700 / 11383	6600 / 11213
Target exhaust temperature (°C)	47	47
Target bed temperature (°C)	45	45
Solids concentration (%)	20	25
Dispersion spray rate (g/min)	1700	1700
Atomizing air pressure (psi/bar)	35 / 2.4	35 / 2.4
Pattern air pressure (psi/bar)	30 / 2.1	30 / 2.1
Pan speed (rpm)	12	12
Resultant EEF*	3.26	3.25
Tablet feed rate (kg/hr)	680	850
Target resident pan load (kg) (quantity of tablets in the pan at any given time)	120	120
Coating weight gain (%)	3.0	3.0

* Environmental Equivalency Factor (Thomas Engineering TAAC Program)

Individually marked tracer tablets were used to determine tablet transit times and coating weight variation. Each tracer tablet was marked with a unique letter and number. The marked tablets were dried to constant weight in a 50°C oven. After drying, the weight of each individual tablet was recorded. At the start of each trial, groups of 100 marked tablets were added to the in-feed side of coating process every 30 seconds for 2.5 minutes for a total of 500 marked tablets in each trial. The time of addition for each group of marked tablets was recorded.

As the coating progressed, all coated tablets were captured from the discharge side of the pan in individual bags at 30 second intervals. After completion of each coating trial, the tracer tablets were sorted from each bag and the time of discharge for each tablet was recorded. This allowed tablet transit times through the coater to be determined with an accuracy of ± 30 seconds. The coating formulation used a low level of Yellow #10 pigment to allow for visual assessment of color uniformity but still allow for the markings on the tracer tablets to be clearly seen (Figure 2).

Figure 2. Example of Marked Tracer Tablets Before and After Coating

The recovered tracer tablets were then re-dried to constant weight and re-weighed to determine the actual coating WG applied to each tablet as well as coating weight variation amongst each set of marked tablets. Drying the tablets to constant weight before and after coating ensured that any moisture gain or loss as a result of the coating process would not impact the accuracy of coating weight gain determination.

Comparative trials were conducted using marked tablets in a 48" fully perforated batch pan at the same 3.0% target WG, coating solids concentrations, and appropriate process scale-out factors to maintain similar thermodynamic conditions (EEF) and linear pan velocity. The process conditions used for these trials are shown in Table 2.

Table 2. Process Conditions Used for 48" Batch Coating Trial

48” Batch Pan Parameters	Trial 1	Trial 2
Inlet air temperature (°C)	62	62
Inlet airflow (cfm / m^3/hr)	1800 / 3058	1800 / 3058
Target exhaust temperature (°C)	48	47
Target bed temperature (°C)	47	45
Solids concentration (%)	20	25
Dispersion spray rate (g/min)	400	400
Atomizing air pressure (psi/bar)	25 / 1.7	25 / 1.7
Pattern air pressure (psi/bar)	25 / 1.7	25 / 1.7
Pan speed (rpm)	6	6
Resultant EEF	3.23	3.22
Pan load (kg)	130	130
Coating weight gain (%)	3.0	3.0

Results

Coated Tablet Appearance – Continuous Coating Process

All coated tablets were uniform in appearance with no visually apparent defects. Excellent logo definition was noted for all samples (Figure 3).

Figure 3. Coated Tablet Appearance

Tablet Residence and Transit Times

Tablet transit times through the continuous coater averaged 15 min at 680 kg/hr and 14 min at 850 kg/hr respectively. For each trial 50% of all marked tablets exited the coater within a span of ~2-3 minutes while the remaining 50% of the marked tablets exited the coater in an elapsed coating time as short as 11.5 minutes.

In the case of a few tablets, 27 minutes of coating time elapsed. Statistical representations of tablet transit times are shown in Figures 4 and 5.

Figure 4. Tablet Progression Through the CTC at 680 kg/hr (20% Solids Concentration)

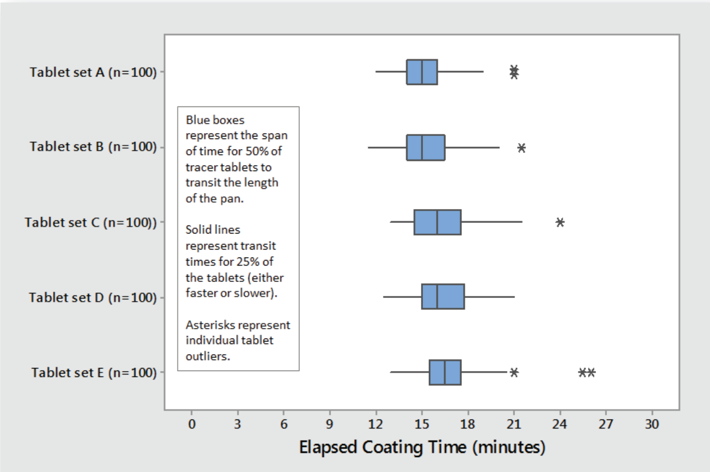
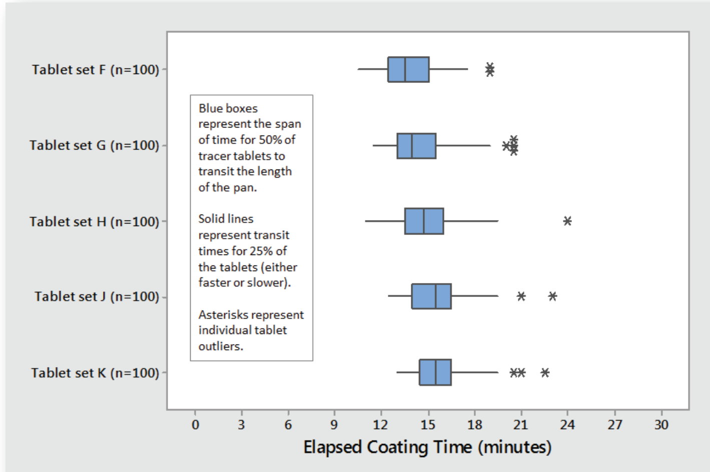


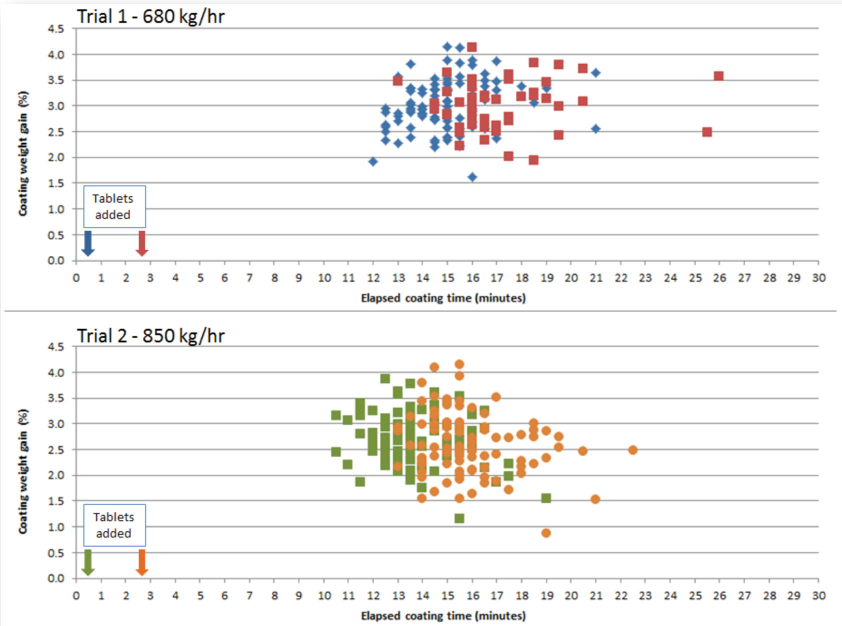
Figure 5. Tablet Progression Through the CTC at 850 kg/hr (25% Solids Concentration)



Coated Tablet Weight Gain and Variability – Continuous Coating Process

For Trial 1, coated tablet WG averaged 3.0% as targeted. For Trial 2, the average WG was slightly below target at 2.7% WG. It is suspected that there was a slight increase in the resident pan load at the higher throughput rate of 850 kg/hr compared to the previous trial at 680 kg/hr. Surprisingly, it was found that coated tablet weight gain was independent of residence time despite some tablets remaining within the coater for a substantially longer period of time than others. It is likely that some tablets appear more frequently in front of the spray zone while others appear less frequently, similar to typical tablet movement in traditional batch coating. This relationship between elapsed coating time and coating weight gain is shown with 4 sets of marked tablets in Figure 6.

Figure 6. Effect of Tablet Residence Time on Coating Weight Gain in the CTC



Coated tablet weight variation ranged from 15.25% relative standard deviation (RSD) to 22.37% RSD. Increasing throughput rates and higher coating solids concentration resulted in increased weight variability as shown in Table 3.

Table 3. Coating Weight Gain and Variability

Trial	Tablet Set	Throughput Rate (kg/hr)	Solids Conc. %	Avg. Weight Increase (mg) (n=100)	St. Dev. (mg)	Actual Weight Gain (%)	% RSD
1	A	680	20	10.57	1.74	3.02	16.49
	B			10.75	1.60	3.07	14.93
	C			10.70	1.62	3.06	15.25
	D			10.39	1.72	2.97	16.66
	E			10.46	1.67	2.99	16.14
2	F	850	25	9.49	1.82	2.71	19.11
	G			9.21	2.05	2.62	22.19
	H			9.49	1.99	2.71	21.22
	J			9.28	1.95	2.65	20.82
	K			9.15	2.02	2.61	22.37

Coating Uniformity Comparison with Traditional Batch Coater

Reference trials in the 48" batch pan exhibited higher coated tablet weight variation than trials conducted in the CTC. This is especially significant given the much longer actual coating time in the batch coater vs. the CTC. A comparison between coating uniformity in the CTC vs. the traditional batch coater is shown in Table 4.

Table 4. Coating Time and Coating Uniformity Comparison – CTC vs. Batch Coating

Parameters	CTC	48" Batch	CTC	48" Batch
Solids conc. (%)	20		25	
Pan load (kg)	120 (resident)	130	120 (resident)	130
Total coating time (min)	15 (average residence time)	49	14 (average residence time)	39
Coated tablet weight variability (% RSD)	15.90	18.74	21.10	23.90

Conclusions

Coating variability and tablet movement in a production scale continuous coating process were quantified. Tablets progressed through the continuous process with relatively small variability in transit times and exhibited superior uniformity compared to tablets coated in a traditional batch coater. Higher productivity coating systems (≥20% solids) are better suited for continuous processes where coating weight variability is reduced relative to traditional batch coating processes. Further work is ongoing to assess the effects of changing pan speeds and even higher solids concentration coatings in continuous coating processes.

Acknowledgements

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References

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2. Neely C, Cunningham C, Rajabi Siahboomi AR (2014). Evaluation of a high productivity developmental aqueous coating formulation in a high throughput continuous coating process. Poster presentation, AAPS Annual Meeting and Exposition, San Diego, CA.

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