

# Influence of Process Parameters on Properties of Instant Release Tablet Coatings

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## Introduction

- Newly developed color coating systems based on PVA-PEG grafted copolymer provide important benefits of low-viscosity suspensions and high film flexibility that result in more robust coating processes over a broad range of coating conditions.
- Design of Experiments (DoE) method was applied to refine and optimize the process parameters.
- The optimization responses were focused on overall coating quality, tablet surface roughness, and coating efficiency.
- A novel non-destructive optical method, the Optical Coherence Tomography (OCT) was used to evaluate the tablet surface smoothness.

## Materials

- Instant release coating systems Kollicoat® IR White II and Kollicoat IR Carmine (BASF SE, Germany)
- Placebo tablets contain 70% Ludipress® LCE (BASF SE, Germany), 19.25% Kollidon® VA64 (BASF SE, Germany), and 0.25% Magnesium Stearate (Fisher Scientific)

## Methods

Tablets were coated using an Accela-Cota/Compu Lab System with a 15" fully-perforated pan insert.

Parameters	Setting
Batch size	1 kg
Theoretical Weight Gain	4%
Pan Speed	18 rpm
Air flow	165 cfm
Atomization air pressure	35psi
Solid concentration	20%

Table 1. Fixed coating process parameters

Variable process factors include spray rate and tablet bed temperature.

Normalized Levels	X <sub>1</sub> : Spray Rate (g/min)	X <sub>2</sub> : Tablet Bed Temperature(°C)
-1.41421	2.00	14.99
-1	3.66	20.12
0	7.67	32.50
1	11.67	44.88
1.41421	13.33	50.01

Table 2. Factors and normalized levels of the Central Composite Design (a = 1.41421)

Minitab software<sup>1</sup> was utilized to establish a polynomial model for each response in the form of  $Y = b_0 + b_2X_1 + b_2X_2 + b_3X_1^2 + b_4X_2^2 + b_5X_1X_2$  where Y is the response,  $b_0$  is the constant, and  $b_2$ ,  $b_3$ ,  $b_4$  and  $b_5$  are the regression coefficients.  $X_1$  and  $X_2$  are the main factors.  $X_1^2$ ,  $X_2^2$  and  $X_1X_2$  are the quadratic and interaction effects.

Response variables tested include:

$Y_1$  = Surface Roughness

$Y_2$  = Overall Coating Quality

$Y_3$  = Coating Efficiency (%)

Surface Roughness ( $Y_1$ ) was evaluated using Optical Coherence Tomography<sup>2</sup> (OCT) technology (Model: OCM1300SS, Thorlabs, Newton, NJ). The OCT scan provides a rapid, real time measurement of surface roughness. Average roughness (Ra) was calculated by<sup>3</sup>

$$Ra = \frac{\sum_{n=1}^N |Z_n - Z^-|}{N}$$

$Z_n$  – the individual height value for one of the measuring points

$Z^-$  – the mean of all height data points

$N$  – the total number of measuring points.

Surface roughness values were determined by taking the average of 4 individual measurements on a single tablet, each containing 950 measurement points. The 2D and 3D images in Figure 1 provided a visual assessment of the coating morphology.

Overall Coating Quality ( $Y_2$ ) in Figure 3 and 5 was visually graded as 0, 1, 2, and 3 for each run<sup>4</sup>.

- 3 (dark green): The best coating quality with a visually smooth surface
- 2 (light green): Visually acceptable coating quality
- 1 (orange): Visually rough surface without damage
- 0 (red): Tablets stick together or on coating pan, causing defects or film removal

Coating Efficiency (%) ( $Y_3$ ) = (Actual weight gain / Theoretical weight gain) x 100

## Results and Discussion

Experiment	Levels of Factors		Responses		
	$X_1$ Spray feed rate (g/min)	$X_2$ Tablet Bed Temperature (°C)	$Y_1$ Surface Roughness	$Y_2$ Overall Coating Quality	$Y_3$ Coating Efficiency (%)
1	3.66	44.88	1.999	2	82.5
2	11.67	20.12	4.169	1	92.2
3	3.66	20.12	2.060	3	85.3
4	7.67	32.50	3.038	2	90.5
5	7.67	32.50	2.622	3	91.3
6	7.67	32.50	2.611	3	90.2
7	11.67	44.88	3.051	2	88.8
8	13.33	32.50	3.328	1	91.8
9	2.00	32.50	1.888	2	81.5
10	7.67	14.99	3.357	1	91.9
11	7.67	32.50	2.834	2	90.4
12	7.67	50.01	3.240	3	89.5
13	7.67	32.50	2.615	3	89.6
14	7.67	32.50	2.528	3	88.1

Table 3. Central composite design comprised of 14 runs with three observed responses

### Surface Roughness ( $Y_1$ ):

- The spray rate and squared tablet bed temperature ( $p=0.022$ ) terms were important for surface roughness.
- Surface roughness increased at tablet bed temperature < 20°C and spray rate >12g / min. (Figure 2)
- Higher smoothness was achieved at a lower spray rate.
- For most runs, the surface smoothness was excellent with Ra <3.5 µm.
- Regression equation:  
 $Y_1 = 2.07741 + 0.415136X_1 - 0.0837934X_2 - 0.00519975X_1^2 + 0.00170878X_2^2 - 0.00532957X_1X_2$

## Overall Coating Quality ( $Y_2$ ):

- The large area of light and dark green color in the contour plot (Figure 3) indicated the wide operating conditions that can be used with Kollicoat IR coating systems.
- A good quality coating could be achieved at a very low tablet temperature of 15°C with a moderate spray rate. Similarities were found between the overall coating quality and the roughness contour plot.
- The green area (best coating quality) matched those with less roughness in Figure 2.
- The red area (tablets with coating defects) in Figure 3 coincided with the red area (for extremely rough surface) in Figure 2.
- Figure 4 provided the Overall Coating Quality prediction by the regression equation  

$$Y_2 = 1.29321 + 0.0634767X_1 + 0.0661235X_2 - 0.0324709X_1^2 - 0.00176710X_2^2 + 0.0100843X_1X_2$$
- By defining process time as a function of spray rate, Process Time =  $\frac{\text{Core mass [g]} \times \text{Weight Gain}}{\text{Spray Rate [g/min]} \times \text{Solid Concentration}} = \frac{1000 \times 4\%}{\text{Spray rate [g/min]} \times 20\%}$

The coating quality contour in Figure 3 can be plotted against the process time in Figure 5, showing the same broad process conditions as shown by the parameter charts.

## Coating Efficiency (%) ( $Y_3$ )

- The spray rate and spray rate squared ( $p=0.002$ ) terms might be important.
- The coating efficiency > 90%, as the tablet bed temperature < 45°C and the spray rate > 8g / min. (Figure 6)
- Regression equation:  $Y_3 = 78.0656 + 2.92619X_1 - 0.062196X_2 - 0.127935X_1^2 + 0.00001767X_2^2 - 0.00302530X_1X_2$

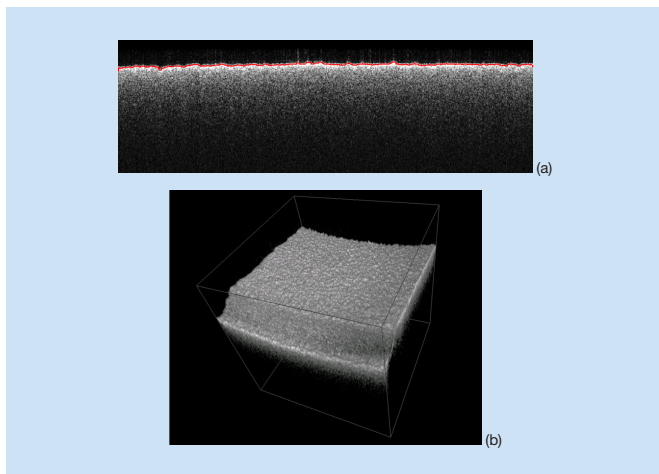


Figure 1. Typical screen observations of tablet roughness in OCT (a) 2D image (b) 3D image

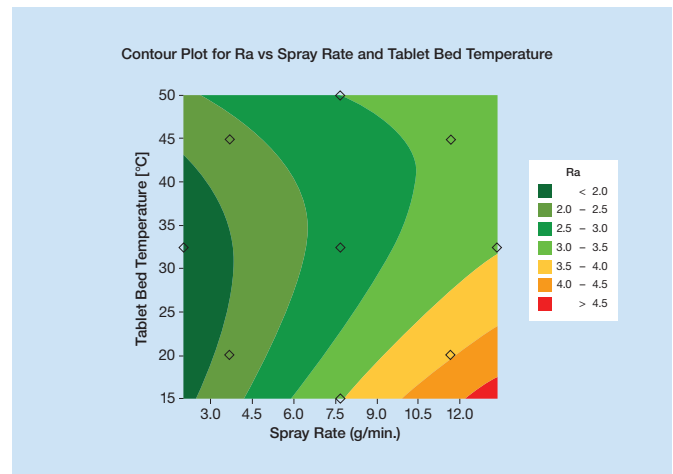


Figure 2. Contour plot of spray rate / tablet bed temperature effect on Surface Roughness Ra

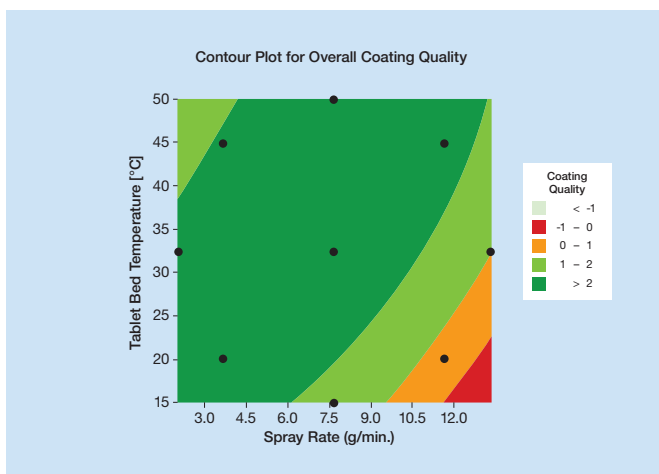


Figure 3. Contour plot of spray rate / tablet bed temperature effect on overall coating quality

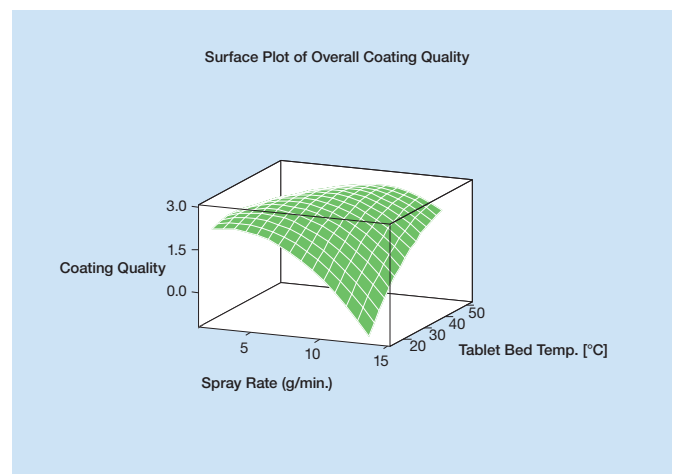


Figure 4. Surface plot of spray rate / tablet bed temperature effect on overall coating quality

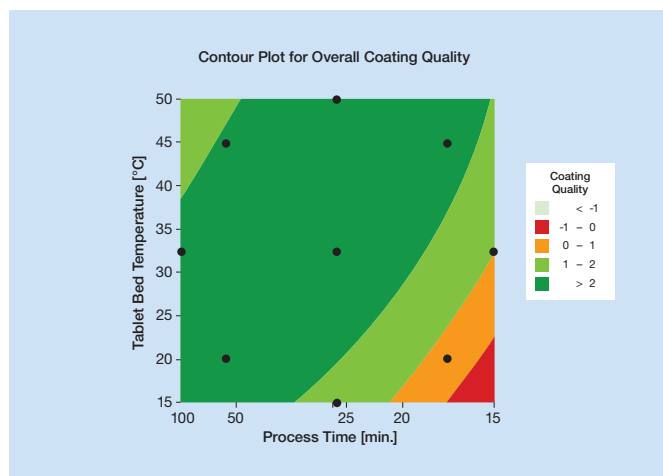


Figure 5. The re-plot of Figure 2 after the spray rate was converted to process time

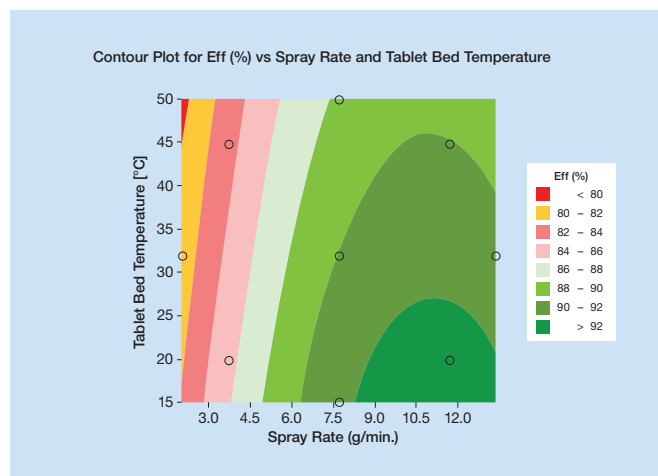


Figure 6. Contour plot of spray rate / tablet bed temperature effect on coating efficiency (%)

## Conclusion

This DoE study showed that Kollicoat IR Coating Systems based on PVA-PEG grafted copolymer provide excellent coating quality across wide coating parameters, which ensures a robust coating process.

Based on the 15" Accela-Cota data:

- A 15°C tablet bed temperature could be achieved when using a spray rate <7.5g /min.
- Coating smoothness increased with decreasing spray rate.
- Coating efficiency increased with higher spray rates.
- The optimum process condition for coating efficiency = 90% and surface roughness = 2.7  $\mu\text{m}$ : Tablet temperature = 40°C, Spray rate = 8g /min.
- OCT provided reproducible and accurate measurements for surface roughness.

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