Impact of Bottom Spray Fluid Bed Processing on Barrier Membrane Coated Drug Layered Pellets Using an Aqueous Ethylcellulose Pseudolatex

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Purpose

To evaluate the effect of several process parameters on the barrier membrane coated chlorpheniramine maleate (CPM) beads with Aquacoat® ECD-30, an aqueous ethylcellulose pseudolatex dispersion, using a star design of experiment (DOE).

Methods

800 g of drug layered, and seal-coated CPM sugar spheres (Suglets®) were used as the base for the application of Aquacoat dispersion. Triethyl citrate (TEC) was added to the dispersion and mixed for 1 hour. The final solid content of the dispersions was diluted to 15% w/w and coated to 30% w/w weight gain using a GPCG-2 bottom spray fluid bed processor.

Table 1: Coating Formulation

Formulation	% w/w	Amount (g)
Drug layered CPM Beads	76.92	800.00
Aquacoat ECD-30 Dispersion (dry basis) *	18.97	197.28
TEC (@ 24% w/w to EC polymer content)	4.11	42.72
Total Batch Size (@30% WG)	100.00	1040.00

Key: *Aquacoat ECD-30 (675.6 g), TEC (42.72 g), and DI Water (899.68 g) were weighed to achieve 15% w/w solid content. This dispersion, when applied on beads was equivalent to 240 g coating (i.e. 30% weight gain).

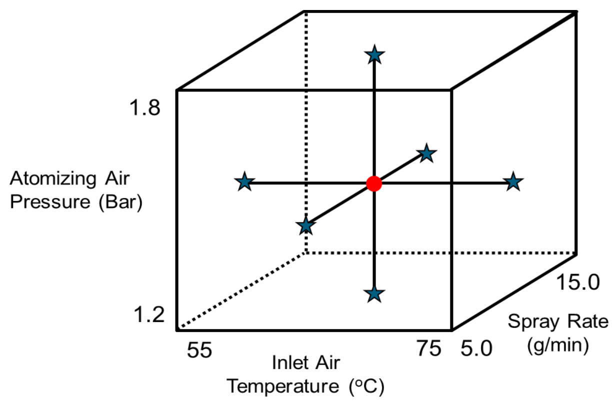
The air volume was maintained at around 65 m^3/h. A 9-run star design was generated to evaluate the effect of each process parameter (Figure 1, Table 1). The center point was repeated 3 times. Coated beads were divided into two groups, one was left without post coating heat treatment (uncured), whilst the other group was cured at 60°C for 2 hours in a convection oven. All samples of coated beads were characterized for particle size distribution and sphericity using Camsizer (Retsch) and SEM (Phenom). Around 1g (equivalent 32.6 mg of CPM) of coated bead samples were tested for dissolution behavior in 1000 ml DI water at 37°C using Apparatus I at 100 rpm for 24 h. Samples were collected using an autosampler (Distek) and analyzed spectrophotometrically (Cary) at 262 nm.

Table 2: Experimental Design

Run No.	Inlet Air Temperature (°C)	Spray Rate (g/min)	Atomizing Air Pressure (bar)
1	65.0	10.0	**1.8**
2	65.0	10.0	1.5
3	65.0	**15.0**	1.5
4	65.0	5.0	1.5
5	65.0	10.0	1.2
6	**55.0**	10.0	1.5
7	65.0	10.0	1.5
8	65.0	10.0	1.5
9	**75.0**	10.0	1.5

****Green: Low Limit* ***Black: Center Point*** ***Red: High Limit***

Figure 1. Star Design

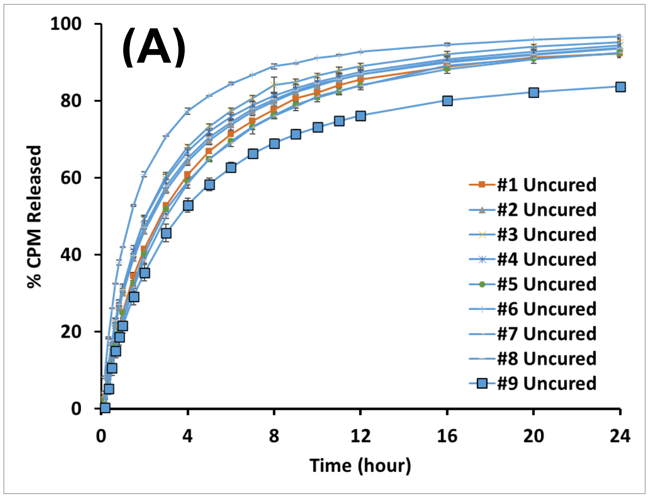


Results

Table 3: Summary of Ranges of Dependent Variables

Dependent Variables	Range
1. Product Temp. (°C)	33.8 – 47.4
2. Exhaust Temp. (°C)	31.9 – 41.8
3. Coating Process Efficiency	97.41 – 98.76
4. Agglomeration	0.12 – 1.44
5. Assay	101.5 – 103.1
6. D50 (Uncured) (µm)	1058 – 1061
7. D50 (Cured) (µm)	1056 – 1061
8. Drug Release (Uncured) (%)	83.7 – 96.7
9. Drug Release (Cured) (%)	61.2 – 75.2

Figure 2. Dissolution Data for All Runs Uncured (A) and Cured (B)



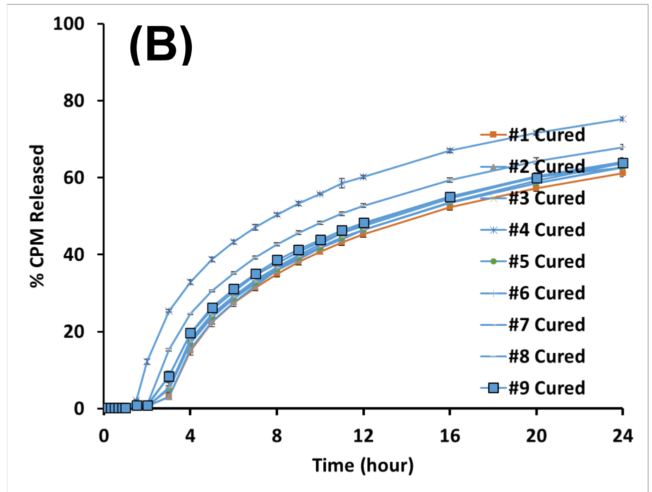


Figure 3. Fastest Drug Release vs. Slowest Drug Release

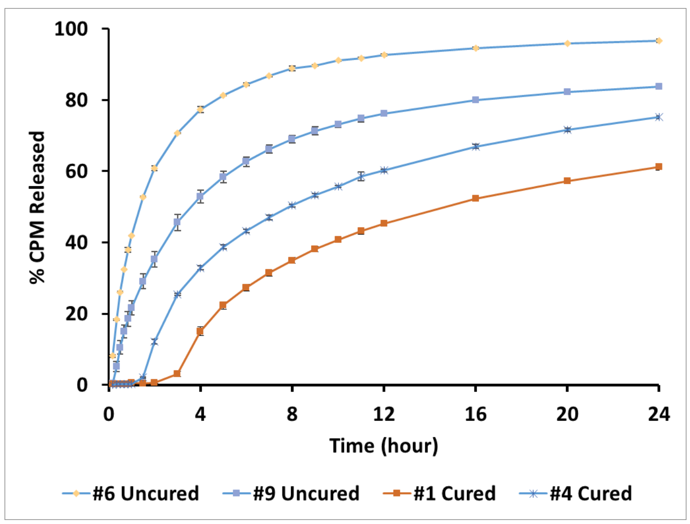


Figure 4. SEM of Coated Beads: (A) Uncured, (B) Cured

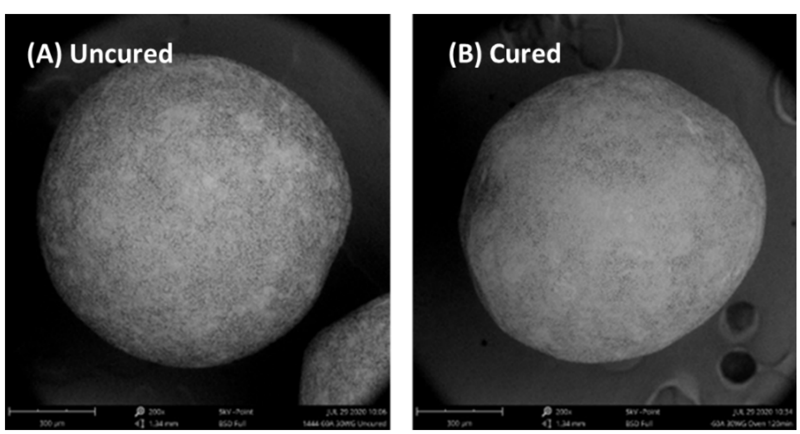
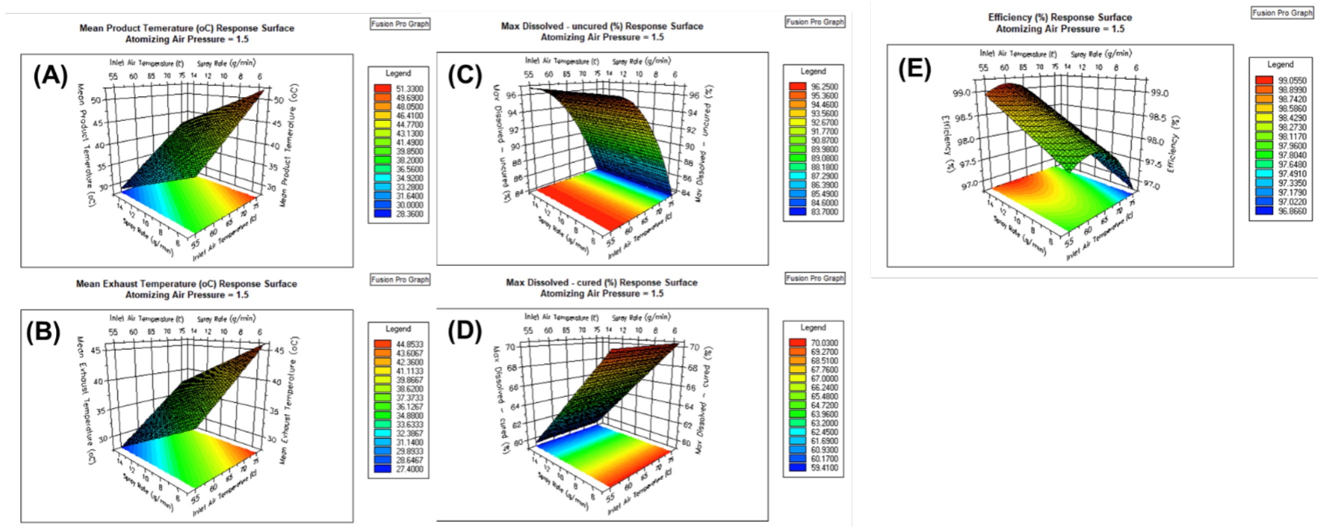


Figure 5. Response Surface Plots for Product Temperature (A); Exhaust Temperature (B); Drug Release from Uncured Beads (C); Drug release from Cured Beads (D); Coating Efficiency (E)



- Lower spray rate and higher inlet air temp. had a positive effect on product and exhaust temp.
- Higher inlet air temp. reduced drug release of uncured beads. Higher spray rate reduced drug release of cured beads.
- Coating efficiency is highest at ~ 60°C inlet air temp.

Conclusions

This study evaluated the effect of several process parameters on CPM beads barrier membrane coated with Aquacoat ECD-30. Atomization pressure of 1.5 psi, spray rate of 15 g/min and inlet air temperature of 60°C were found to be optimal to provide product bed temperature of 31.75°C, uniform coating consistency and drug release. The study provided insight into selecting process parameters for the application of Aquacoat ECD-30.

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