Investigating the Use of Absolute Exhaust Humidity Control as a Control Parameter for Multiparticulate Coating

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Introduction

Applying coatings to multiparticulates utilizing fluid bed technology is a widely used method for a variety of pharmaceutical processes, including drug layering, delayed release, barrier membrane polymer coatings for extended release and taste-masking applications. Controlling agglomeration is one of the key drivers in developing a successful coating process. A combination of several parameters such as airflow, inlet and exhaust temperature, spray rate and equipment set-up are commonly used to develop a processing range that minimizes particle to particle agglomeration.

Absolute humidity, which is the measurement of moisture in air, regardless of temperature, has the potential to simplify the development of the spray process and offer a single safe threshold for processing without the risk of agglomeration.

This study examines the use of absolute exhaust humidity as a control parameter for developing reliable process ranges for multiparticulate fluid bed coating processes.

Methods

To develop a baseline absolute humidity measurement, lab-scale placebo trials were completed in a Bosch Hüttlin Unilab fluid bed system. Using the data recorded in the lab-scale trials, this process was scaled up utilizing a Freund-Vector VFC-60 FLO-COATER fluid bed equipped with a Compu4 control system, fitted with an 18-inch Wurster insert. Processing methods/parameters are shown in Table 1.

All trials began with conservative spray rates, and appropriate process conditions were used to maintain the manufacturer's recommended product temperatures. After an initial period of spraying, the spray rate and inlet temperatures were increased, and the system conditions were allowed to reach equilibrium. Once equilibrium was reached, samples were screened for agglomeration. This process was continued until significant agglomeration was observed. Corresponding specific humidity, dewpoint and temperature readings were recorded; the absolute humidity was calculated from those values.

Differences between the lab scale and pilot scale process system humidity monitoring were:

Lab Scale

Inlet: Built-in sensor measuring specific humidity; manually recorded

Exhaust: Built-in sensor measuring specific humidity; manually recorded

Pilot Scale

Inlet: External Sensor measuring dew point and temperature; manually recorded

Exhaust: Built-In sensor measuring dew point and temperature; automatically recorded

Table 1: Material and Processing Methods

	Lab Scale	Pilot Scale
Product	45/60 Mesh Suglets, Sugar Spheres (Colorcon)	
Batch Size (kg)	5	50
Coating Material	Surelease, Aqueous Ethylcellulose Dispersion (Colorcon) Diluted to 15% solids	
Air Flow	Adjusted to provide proper product movement	
Spray Conditions		
Rate @ start (g/min)	12	70
Time at initial rate (min)	20	20
Rate Increase Frequency (min)	5	10
Inlet Temperature	Increased as needed to maintain product temperature	
Product Temperature (°C)	42-45	42-45

Results

The lab scale trials showed that agglomeration started occurring at absolute humidity levels exceeding 10 g/m^3, with increasing agglomeration as the humidity climbed beyond 12 g/m^3, reaching 5.65% agglomeration at 17 g/m^3. During the pilot scale trials, agglomeration began at absolute humidity levels exceeding 10 g/m^3, with increasing agglomeration as the humidity exceeded 12 g/m^3. Agglomeration reached 5.88% at 17.24 g/m^3, which is very similar to the lab-scale trials (Figure 1).

Figure 1: The Effect of Exhaust Air Absolute Humidity on the Formation of Agglomerations Coating Suglets with Surelease

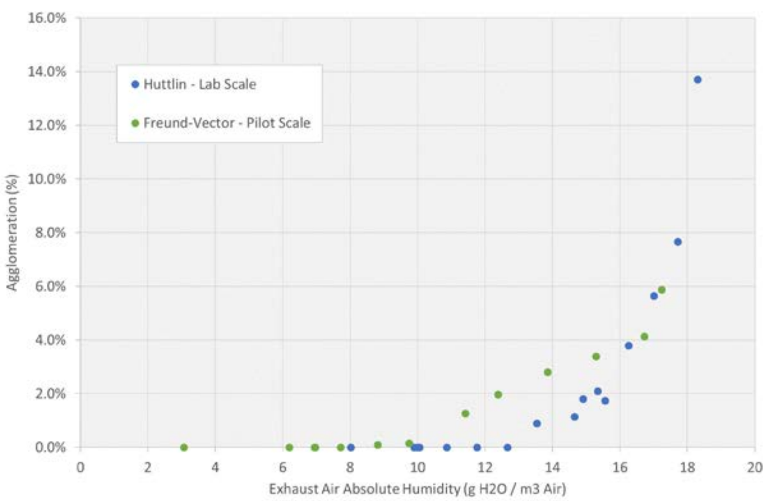


Image: Freund-Vector VFC-60 FLO-COATER with Wurster Insert

When tracking spray rate on the pilot scale trials, initial data showed a discrepancy in maximum achievable spray rate without agglomeration, with Trial 1 reaching 148 g/min before agglomeration occurred, and Trial 2 only reaching 88 g/min before recording agglomeration. When the data was normalized for absolute humidity, it showed that agglomeration occurred at the same humidity level, with the difference in the two trials being due to a higher inlet dew point for Trial 2 at 10.0°C, versus Trial 1 at 8.0°C (Figure 2 and 3).

Figure 2: Comparison of Agglomeration Rates to Spray Rate

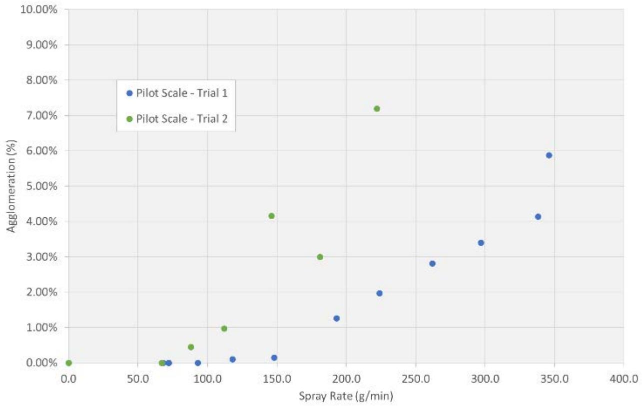
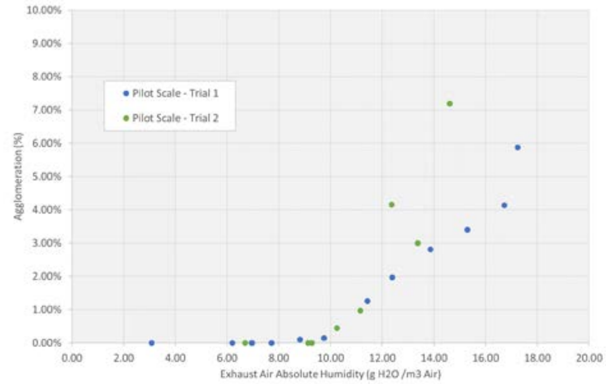


Figure 3: Comparison of Agglomeration Rates to Exhaust Absolute Humidity



Conclusions

The results of this study show that absolute exhaust humidity can be used as a control parameter for developing reliable operating parameters when coating multiparticulates in a fluid bed. Consistency was observed across different equipment manufacturers' lab scale and pilot scale trials, which could be advantageous for scaling up across different pieces of equipment in the industry. These trials show absolute humidity is a critical parameter for scale-up and consistent processing.

The Compu4 control system used in this study can directly monitor and report exhaust air moisture conditions and has the advantage of being programmed to adjust operating parameters to control exhaust humidity. Measurement could potentially be accomplished manually with simple modifications to the equipment. Further investigation is needed to explore the impact of substrate particle size, various coating systems and equipment design on maximum absolute humidity levels. However, this research suggests the potential for using absolute humidity as a control variable along with integrated sensors and automated feedback to achieve a more consistent process.

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