Evaluation of a Simple Fluid Bed Dryer Sampler Modification for On-line Profiling and Endpoint Using Effusivity

Patrick Okoye[1*], Michael Emanuel[1], Timothy J. Smith[2]
1. Mathis Instruments Ltd, Fredericton, NB, Canada; 2. Vector Corporation, Marion, IA, USA

*Corresponding author's email: Patrick@mathisinstruments.com

ABSTRACT (T3308)

PURPOSE: To evaluate the capability of a simple modification to an existing sampling port on a fluid bed dryer for monitoring moisture uptake and loss using effusivity sensor. The goal was to provide a method to profile a typical granulation and drying process in a fluid bed and to develop the criteria for end-point determination.
METHOD: A sampler was designed to extract material from the fluid bed, bring it in contact with the effusivity sensor, and then discharge it back into the fluid bed. This sampler enabled effusivity measurements on-line and real-time. Binary mixtures of Microcrystalline cellulose (MCC) and Lactose monohydrate (LAC), at a ratio of 20:80, were granulated in a fluid bed granulator/dryer using a granulation (binder) solution consisting 5% w/w polyvinylpovidone (PVP) in Purified Water. Moisture samples were extracted and analyzed at intervals using the in-line effusivity sensors. Additional samples were also analyzed using an offline moisture analyzer.
RESULTS: Effusivity profiles depicted repeatability of process when the binder addition rate remained the same over three trials. The profile shifted upward when the binder liquid addition rate was increased, consistent with the higher moisture producing higher effusivity values. In each case, effusivity increased with the addition of binder, and proportional to the addition rate. During the drying phase, effusivity values dropped, as expected, in relation to the moisture decrease.
CONCLUSION: The online effusivity measurement showed similar trend as off-line moisture analyzer. The study also showed that modification of an existing sampler was sufficient to introduce a representative and reproducible sample to the effuvsivity sensor, thus facilitating on-line profiling and monitoring of fluid bed granulation and drying process.

INTRODUCTION

Powder-moisture interactions are one of the fundamental issues in the pharmaceutical manufacturing. The state of moisture in a powder material may be characterized using thermal analysis, x-ray diffraction, or vibrational spectroscopy. Traditionally, in fluid bed drying (FBD) process, moisture content of granulation is monitored offline with Karl Fischer volumetric titremetry or at-line with thermogravimetric loss-on-drying (LOD) methodology. Karl Fischer and LOD methods may require the operator to in some instances and to avoid over-drying, stop the process, use a sample thief/port to collect a sample, and then analyze the sample off-line. As such, it is not possible to obtain real-time moisture trends. In addition, Karl Fischer analysis is costly, time-consuming, and uses chemical reagents that require purchase and proper disposal.
This study furthers earlier work on the application of thermal effusivity as an on-line, real-time tool for moisture analysis. This work introduces the ability to use an existing sampler on the fluid bed dryer with minor modifications. The current application does not require modification

to the FBD equipment but uses the existing sample port for on-line integration with the effusivity sensor.

Thermal effusivity is a material property that depends on the relationship between thermal conductivity, heat capacity, and density of materials. Effusivity is also sensitive to the amount of moisture in samples. Since water has an effusivity of 1600 $Ws^{1/2}/(m^2K)$, a small percent change in moisture in a typical powder during granulation or drying, results to change its effusivity value.

METHODOLOGY

Four (4) batches, Trials 45, 46, 47, and 48, are presented here to evaluate the repeatability of process and the capability of on-line moisture analysis using effusivity sensor with an existing sample port. Granulation process was performed with the FL-M-15 unit equipped with 20 Liter container having a Vector manual sample valve with air purge for effusivity sensor (see picture below in Figure 1); and spray gun equipped with 1.2 mm nozzle located in middle gun port. The filter system consisted of polyester cartridge filters. Effusivity sensor (B86) with additional weight of 417 grams (total weight with sensor = 565 grams) was mounted on the sample valve. Powder materials consisted of 80% lactose monohydrate (LAC) and 20% microcrystalline cellulose (MCC). The granulation (binder) solution was 5% PVP (K30). The drying process was controlled using Inlet Air Temperature of ~ 40 °C and fluidization airflow of ~ 250 CFM. For Trial 48, and in order to evaluate the change of a process variable with effusivity sensor, the granulating solution spray rate was increased from 100 g/min to 150 g/min after 10 minutes of granulation.

Sample was extracted at the start of addition of binder solution. Additional samples were extracted and analyzed for every 200 grams of binder solution applied. During the drying phase, samples were extracted every two (2) minutes of drying time. For the loss-on-drying using moisture analyzer, approximately 2.5-gram samples were collected from the sample port discharge for off-line analysis.

Figure 1: Sample valve with Effusivity sensor

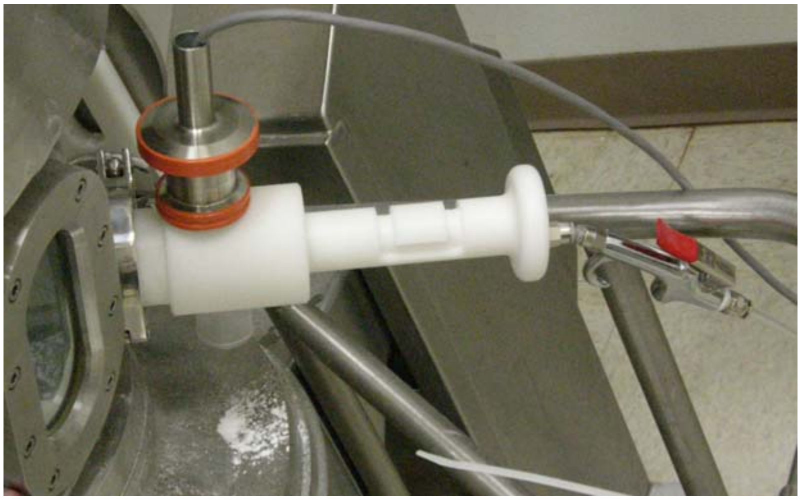


Table 1: Experimental design and Process Variables

Trial Name		Batch Size (Kg)	Solution Delivered (g)	Solution Delivery Rate (g/min)	Inlet Air Temperature (C)	Air Flow Rate (CFM)	Effusivity Reading Frequency
Trial 45	Granulation	8	2000	100	40	250	Every 200 g solution delivered
	Drying	-	-	-	60	250	Every two minutes
Trial 46	Granulation	8	2000	100	40	250	Every 200 g solution delivered
	Drying	-	-	-	60	250	Every two minutes
Trial 47	Granulation	8	2000	100	40	250	Every 200 g solution delivered
	Drying	-	-	-	60	250	Every two minutes
Trial 48	Granulation	8	2000	100/150 *	40	250	Every 200 g solution delivered
	Drying	-	-	-	60	250	Every two minutes
	* 100 g/min for first 1000 grams of solution delivered; 150 g/min for last 1000 grams of solution delivered.						

RESULTS AND DISCUSSION

Figure 1 shows the fluid bed dryer fitted with effusivity sampler unit. Table 1 shows the experimental design with process variables. Figure 2 shows granulation and drying process plot of effusivity versus sample points for trials 45, 46, 47, & 48. The results showed that under similar process conditions, trials 45, 46, & 47 exhibited comparable profiles. For trial 48, an increase in effusivity was observed after 10 minutes of granulation. This was attributed to increase in spray rate of the binder solution from 100 g/min to 150 g/min, as shown in Table 1.

At the end of the process, the four batches have effusivity values of ~250 $Ws^{1/2}/(m^2K)$, indicating similar moisture levels (ranges from 1.14 to 2.17%). When compared to the starting value of ~275 $Ws^{1/2}/(m^2K)$, it indicates that the final material is drier than the original, but effusivity is not only a function of moisture, but also of particle size since the beginning moisture ranged from 0.97 to 1.06%. Larger particles entrain more air in the interstitial space resulting in a lower bulk density and effusivity. As the particles grow during granulation, the dominant influence observed in Figure 2 is the addition of moisture causing the increase in effusivity rather than the particle growth causing a decrease.

Figure 3 shows the plot of on-line effusivity against offline loss-on-drying. The results indicated similar trends with respect to uptake (during granulation) and loss of moisture (during drying) for LOD and effusivity. The data clearly shows the particle size effect. The solid symbols on the Figure are during granulation and the open symbols are during drying. The line on the graph indicates the time component of when the data was generated. At the end of the process, the effusivity was lower (250 versus 275) but the moisture was the same range (1%) for Trial-45, -46, and -47. The lower effusivity is due to the larger particle size after granulation. Batch 48 has the highest moisture level (2%) and highest effusivity. The hypothesis is that batch 48, with the higher spray rate, produced larger granules (lower effusivity) but this was over-compensated by the extra moisture (1%) that was not driven off (higher effusivity). Because of the interaction between particle size and moisture on the effusivity values, correlations between LOD and effusivity were conducted on the granulation and drying phases separately. The correlations are shown on Figures 4 and 5 for the 3 batches that were conducted under the same processing conditions.

Figure 2: Granulation and Drying Profile

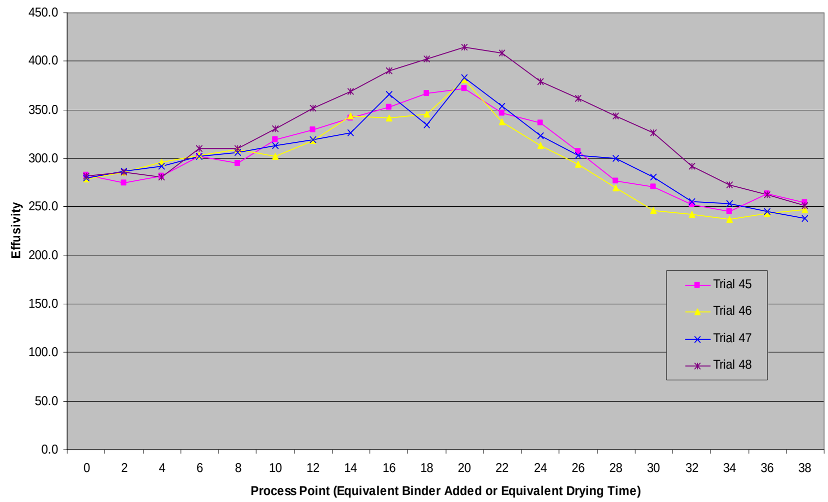
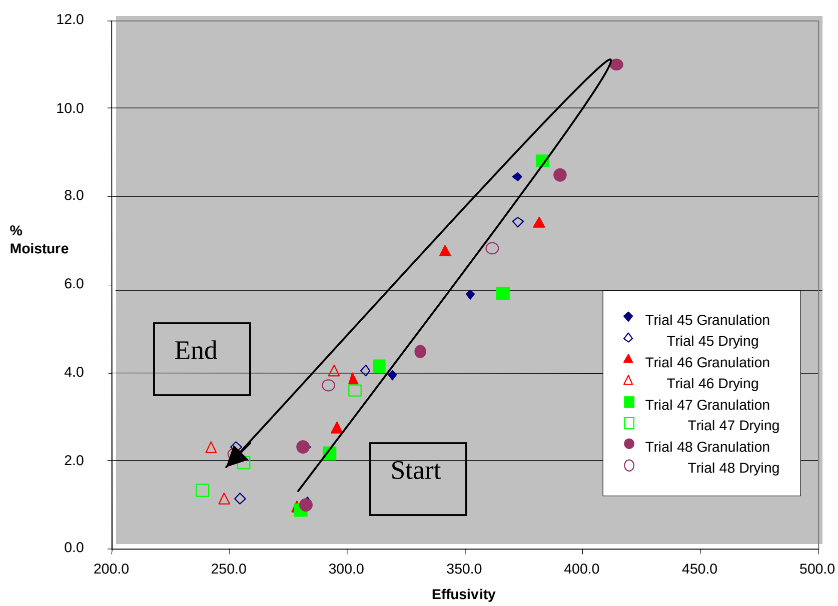


Figure 3: Profile of On-line Effusivity and Off-line LOD



CONCLUSIONS

The on-line effusivity measurement showed similar trends as off-line moisture analyzer during granulation and drying phases. The effusivity sensor distinctively identified process parametric change that occurred when the binder solution spray rate was increased from 100 g/min to 150 g/min, hence, could identify process anomaly in real-time. The study also showed that modification of an existing sampler was sufficient to introduce a representative and reproducible sample to the effusivity sensor, thus facilitating on-line profiling and monitoring of fluid bed granulation and drying process.

CITED ARTICLES

1. Rantanen, J; Jorgensen, A; Rasanen, E; Luukkonen, Pirjo: "Process Analysis of Fluidized Bed Granulation", AAPS PharmSciTech 2001: 2 (4) Article 21.
2. Roy, Y; Nieves, E; Mathis, N; "Thermal Effusivity as a Process Analytical Technology (PAT) to Optimize Fluid Bed Drying", AAPS Journal, Vol. 6, No.4, Abstract W5132, 2004.
3. Kristensen, J; Hansen, V: "Wet Granulation in Rotary Processor and Fluid Bed: Comparison of Granule and Tablet Properties", AAPS PharmSciTech 2006; 7 (1), Article 22.