In-line Measurement of Moisture Using an NIR Filter Photometer in Rotor Processor for Dry Powder-layering: Part III

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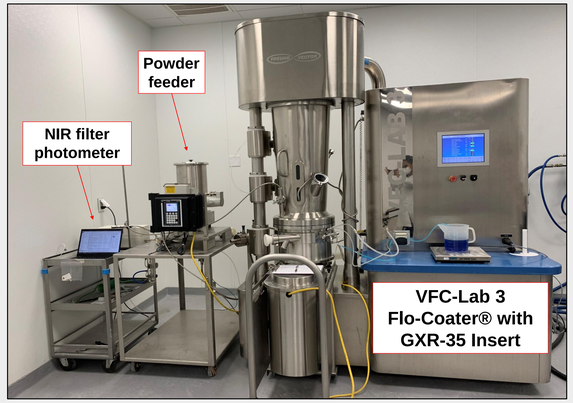
PURPOSE

- It is very critical to maintain a ratio of binder solution to powder feed rate during dry powder-layering processes. In many instances, there is only a narrow window of opportunity available to start a powder feeder when inert cores or substrate become sufficiently wet. The offline conventional LOD (Loss-On-Drying) measurements do not provide feedback quickly enough to adjust the process parameters. It is, therefore, very crucial to continuously monitor moisture directly or related absorbances to achieve a successful process.
- The main purpose of this investigation was to demonstrate the use of an NIR filter photometer as an *in-line* process analytical tool to monitor and characterize absorbances for various events (binder addition, powder addition, equilibrium state, etc.) throughout the dry powder-layering process.

METHODS

- A mixture of micronized acetaminophen (96.8%w/w), micronized talc (3%w/w), and fumed silica (0.2%w/w, Aerosil® 200) was used as a powder blend. Sugar spheres (Suglets® 25/30 mesh) were used as inert cores. A 5% polyvinyl pyrrolidone (Plasdone™ K-29/32) aqueous solution was used as a binder.
- Dry powder-layering was performed using a fluid bed with rotor insert (VFC-Lab 3 Flo-Coater® with GXR-35 insert, Freund-Vector Corporation) and a powder feeder.
- Absorbance values of the moving product bed were recorded using an NIR fiber optic photometer (RS1000, Innovative Technologies Group) located approximately four inches above the product surface.
- Samples were withdrawn from a sample port throughout the process and LOD measurements were performed.

METHODS



Process Parameter:	Set Point:
Slit Airflow	13 CFM
Slit Air Temperature	60-65 °C
Rotor Speed	300 RPM
Solution Flow Rate	7-10 g min^{-1}
Nozzle Air Pressure	27 psi
Powder Feed Rate	10 g min^{-1}
Eductor Air Pressure	15 psi
Product Temperature	24-27 °C
Chamber Pressure	-0.5 inWC

- Initial Batch Size = 1800 g
- The process was considered complete once >120% of weight gain on the sugar spheres was achieved.

RESULTS

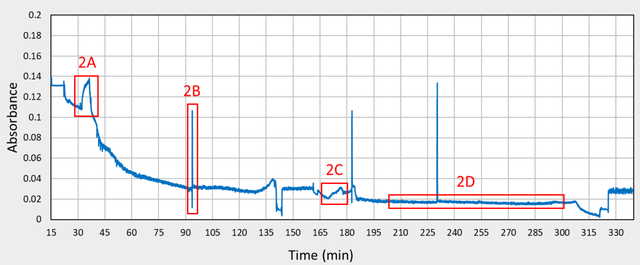


Figure 1. *Absorbances values recorded by an NIR filter photometer during the acetaminophen powder-layering process. Various process events in Figure 1 are labeled as 2A, 2B, 2C, and 2D. The same sections are magnified in Figure 2.*

RESULTS

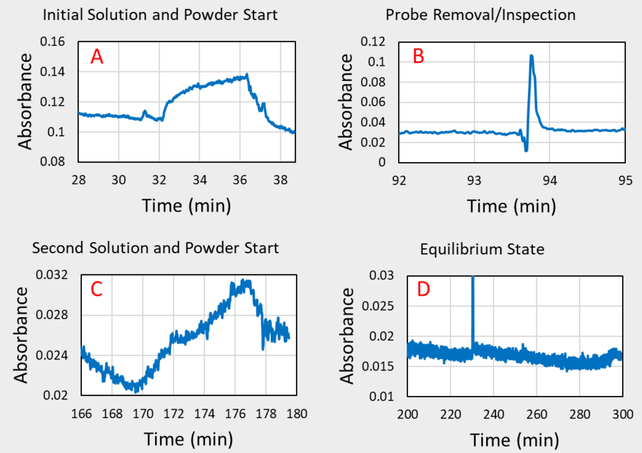


Figure 2. *Various process events from Figure 1: A) the absorbance pattern with starting of solution spray and powder; B) the absorbance pattern upon removal of an NIR probe for inspection; C) the absorbance pattern with starting of second phase of solution spray and powder; and D) the absorbance pattern during an equilibrium or steady state.*

Figure 2A- The absorbance values decreased initially and then steadily increased after starting spraying the binder solution. The absorbance values started decreasing as soon as soon powder was added. The absorbance values decreased gradually with continuous powder addition until an equilibrium was reached.

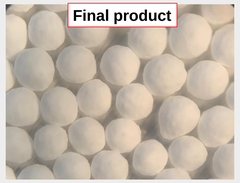
Figure 2B- After reaching the equilibrium, the NIR probe was removed for inspection and the event was observed in Figure 2B as a spike in absorbance values.

Figure 2C- Depiction of the same patterns of change in absorbances like Figure 2A when the addition of binder solution and powder occurred.

Figure 2D- The process is in equilibrium where the ratio of binder addition rate and powder feed rate resulted in a successful powder-layering process. The spike shows the similar event as Figure 2B where we took out the NIR probe for inspection.

RESULTS

- The powder-layering process was very reproducible (n=3) with comparable absorbance patterns for specific events.
- Yield: >96% with < 1% agglomerates (>1.4 mm)
- The final product showed very narrow size distribution (X10: 836 µm; X50: 1050 µm; X90: 1252 µm) and sphericity of 0.78 at X50.



- The moisture content values obtained from the moisture analyzer did not correlate directly to the NIR absorbances. This apparent non-correlation is because as the powder-layering process progressed, the absorbance values reflected the powder layered surface's moisture, whereas the LOD measurement showed the total moisture content including the inner core. However, the change in LOD values can be observed in the NIR absorbance values.

CONCLUSIONS

- NIR filter photometer was successfully demonstrated to explain the changes (binder addition, powder addition, equilibrium condition, etc.) occurring during the API powder-layering process.
- NIR filter photometer can serve as a versatile process analytical tool to monitor process changes with high sensitivity in real time.

ACKNOWLEDGEMENT

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REFERENCE

1. Smith, T.J., Crawford, M., Alfred, G., Boesen, A, Shah, A. (2019). "Detection of Moisture Using a NIR Filter Photometer on Dynamically Moving Particles in a Rotor Processor," AAPS PharmSci 360, San Antonio, TX.