In-Line Measurement of Moisture Using an NIR Filter Photometer in Rotor Processor: Part II

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PURPOSE

Moisture is a very critical process parameter for wet granulation processes and therefore, needs continuous monitoring. Due to the growing interest in continuous processes and related FDA's initiatives, process analytical technologies have gained lot of attention in monitoring various unit operations continuously. Previously, we conducted studies to test the feasibility of using an NIR (near infrared) filter photometer on dynamically moving material in a rotor granulator to continuously measure moisture. The method was established and validated with widely used excipients (lactose, microcrystalline cellulose, starch, and their binary blends) and the results were very promising (R^2=0.92-0.99)[1]. The main purpose of the present study was to continue the investigation using placebo blends and commonly used active pharmaceutical ingredients to further ascertain the suitability of the NIR filter photometer for the *in-line* measurement of moisture during rotor granulation.

METHODS

Three granulation formulations were used: a placebo blend of lactose (Lactose 312, Foremost™); pregelatinized starch (Pure-Dent® Starch B815, Grain Processing Corporation); microcrystalline cellulose (MCC, Emcocel® 50M, JRS Pharma), acetaminophen (semi-fine powder, Mallinckrodt), and ibuprofen (ibuprofen 25, BASF). For each granulation process, 5% polyvinylpyrrolidone (PVP, Plasdone™ K-29/32, Ashland™) aqueous solution was used as a binder. Granulations were performed using a fluid bed rotor granulator (VFC-Lab 3 Flo-Coater® with GXR-35 insert, Freund-Vector Corporation). Absorbance values (using Putty software) 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. Granulation samples were withdrawn from the sample port throughout the granulation process and LOD (Loss-On-Drying) measurements were determined using a moisture analyzer (Mark 3 LTE, Sartorius). Absorbance values and LOD measurements were correlated to make corresponding calibration curves.

RESULTS

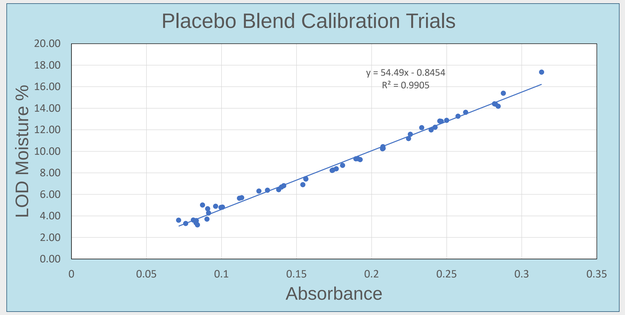

Figure 1

Figure 2

Time Stamp	LOD %	Moisture %	Error
8:56	3.45%	3.39%	0.06%
9:03	3.50%	3.06%	0.44%
9:09	4.76%	4.35%	0.41%
9:17	6.02%	5.63%	0.39%
9:24	7.11%	6.94%	0.17%
9:32	8.18%	8.29%	0.11%
9:49	9.56%	9.88%	0.32%
9:59	10.33%	10.43%	0.10%
10:08	11.62%	11.50%	0.12%
10:17	12.29%	12.52%	0.23%
10:28	13.77%	13.68%	0.09%
10:38	15.29%	14.82%	0.47%
10:48	13.64%	13.80%	0.16%
10:59	8.01%	7.87%	0.14%
11:07	5.00%	3.85%	1.15%
11:14	3.65%	4.23%	0.58%

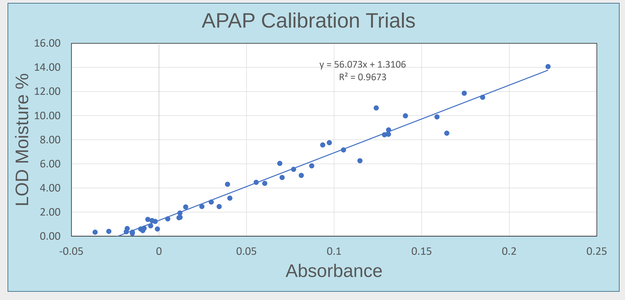

Figure 3

Figure 4

Time Stamp	LOD %	Moisture %	Error
1:05	0.37%	1.64%	1.27%
1:13	0.53%	0.93%	0.40%
1:19	1.49%	0.73%	0.76%
1:25	2.05%	0.86%	1.19%
1:30	2.52%	1.89%	0.63%
1:35	4.52%	3.87%	0.65%
1:40	6.06%	5.26%	0.80%
1:46	7.02%	6.47%	0.55%
1:54	9.52%	8.27%	1.25%
2:06	9.75%	9.01%	0.74%
2:13	6.30%	6.22%	0.08%
2:24	1.13%	1.13%	0.00%
2:32	0.56%	1.64%	1.08%

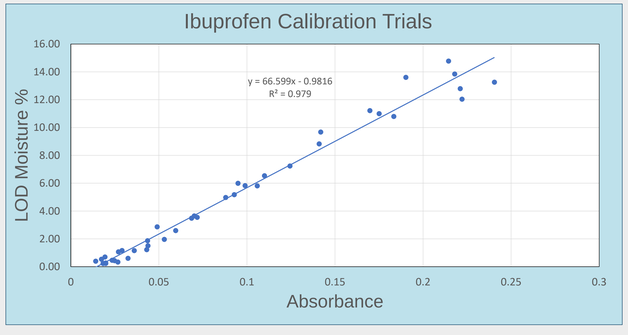

Figure 5

Figure 6

Time Stamp	LOD %	Moisture %	Error
9:10	0.19%	0.59%	0.40%
9:10	0.22%	0.59%	0.37%
9:10	0.22%	0.59%	0.37%
9:20	0.36%	-0.10%	0.46%
9:24	0.75%	0.48%	0.27%
9:28	1.09%	0.89%	0.20%
9:33	2.00%	1.57%	0.43%
9:38	2.69%	1.86%	0.83%
9:43	3.32%	3.25%	0.07%
9:48	4.23%	3.76%	0.48%
9:53	5.19%	4.78%	0.41%
9:59	6.44%	5.83%	0.61%
10:05	5.70%	5.21%	0.49%
10:11	7.06%	6.50%	0.56%
10:17	9.05%	8.38%	0.67%
10:23	11.48%	10.85%	0.63%
10:32	14.55%	13.68%	0.87%
10:41	12.73%	12.12%	0.61%
10:51	13.88%	13.77%	0.11%
11:00	14.21%	14.33%	0.12%
11:09	9.89%	8.74%	1.15%
11:17	4.61%	4.04%	0.57%
11:23	1.18%	1.69%	0.51%
11:28	0.43%	0.99%	0.56%
11:31	0.36%	1.28%	0.92%
11:35	0.37%	0.66%	0.29%

RESULTS

Figure 1 shows the data used to generate the calibration equation for the placebo blend material. Figure 2 depicts the difference between the measured LOD moisture and the moisture calculated from the absorbance using the calibration equation. The average error is only 0.31% for the placebo blend.

Figure 3 shows the calibration trials for the acetaminophen material. Figure 4 is the validation data. This trial also had low error values, with an average of only 0.72%.

Figure 5 is the data for the ibuprofen material calibration trials. Figure 6 shows the validation trial data. The average error for this trial was 0.50%.

CONCLUSION

We successfully established a process analytical tool for an *in-line* measurement of moisture during wet granulation using an NIR filter photometer. It is necessary to create a new calibration equation for each formulation/process for accuracy; however, the user-friendly filter photometer allows for straightforward calibration.

Although we have not done much testing with it yet, we expect to be able to use this technology to measure *in-line* moisture for other product lines, such as fluid bed top and bottom spray, fluid bed drying, and continuous granulation on our Granuformer. We plan on doing more testing with *in-line* moisture measurements on future R&D projects. If you are interested in more NIR research, please see our poster on powder layering.

ACKNOWLEDGEMENTS

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