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In-Line Particle Measurement Using the Viavi MicroNIR PAT-U in Continuous Wet Granulation

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PURPOSE

- Conventionally, granulation of active pharmaceutical ingredients (APIs) and functional excipients relies on offline measurements to determine final particle characteristics, such as loss on drying (LOD) and particle size distribution (PSD).
- By the time results are available, the material in the machine may have already changed. In-line monitoring can reduce reliance on offline testing by providing real-time feedback during processing, helping operators identify critical changes before the process moves beyond the desired endpoint.
- Reliable particle data is essential to determine granulation performance and predict how the powder will behave during high-speed tablet compression.
- The purpose of this study is to demonstrate the Viavi MicroNIR PAT-U as an in-line process analytical tool for monitoring and reporting final particle characteristics of a continuous wet granulation process.

METHOD(S)

- Continuous wet Granulation was performed using the Gf-215 Granuformer® (FREUND Inc.).
- Powder blend consisted of lactose (70% w/w, GranuLac 200, Meggle), microcrystalline cellulose (29.75% w/w, 50M, Emcocel), and magnesium stearate (0.25% w/w).
- An aqueous solution containing 8% polyvinyl pyrrolidone (PVP, Plasdone™ K-29/32, Ashland™) was used as the binder.
- In-line absorbance values were collected with the Viavi MicroNIR at the sample port.
- Samples collected at the discharge port were analyzed for loss on drying (LOD) using the Mark-3 moisture analyzer (Sartorius).
- These offline LOD results were correlated with Viavi MicroNIR absorbance values to develop a model for reporting in-line LOD values during processing.
- To evaluate the model, in-line LOD values reported by the Viavi software were compared with offline LOD measurements collected during the process.

RESULT(S)

Figure 1 shows NIR absorbance values recorded during the calibration process at the same time points when samples were collected. The water moisture absorbance is observed best at a wavelength of ~1450nm as this is where the O-H overtone is. A correlation was shown that as particle size and LOD increased the absorbance also increased. The data was able to be correlated to offline measured data that represented to same trend. A four-factor predictive model was developed, producing an r^2 value of 0.91.

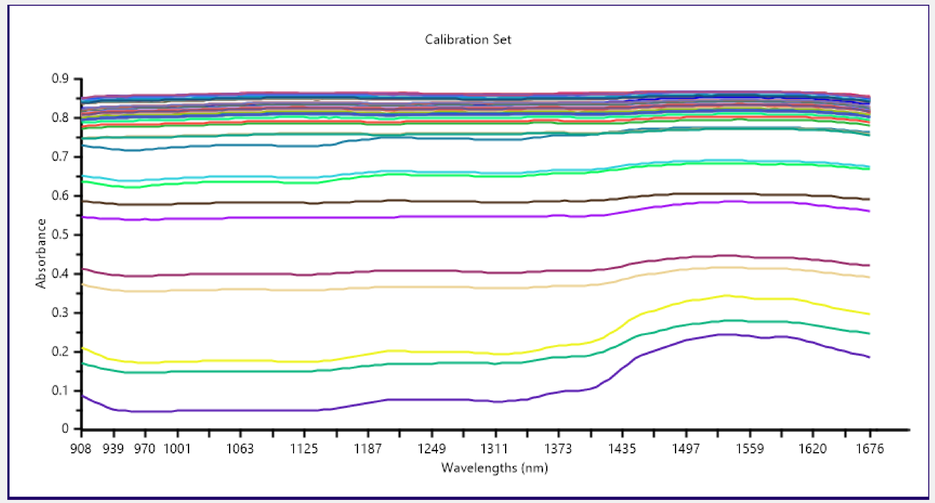


Figure 1: *Absorbance data recorded by the Viavi software during the calibration trial on the Gf-215 Granuformer®*

Table 1 and Figure 2 compare in-line LOD values reported by the Viavi software with offline LOD measurements. The model was developed across a wide parameter range and covered both low and high LOD values. Model performance was highly accurate, with an average absolute difference of 0.69% between the model LOD and offline LOD values. The continuous granulation process was also highly reproducible, with comparable absorbance patterns expected to produce similar LOD values.

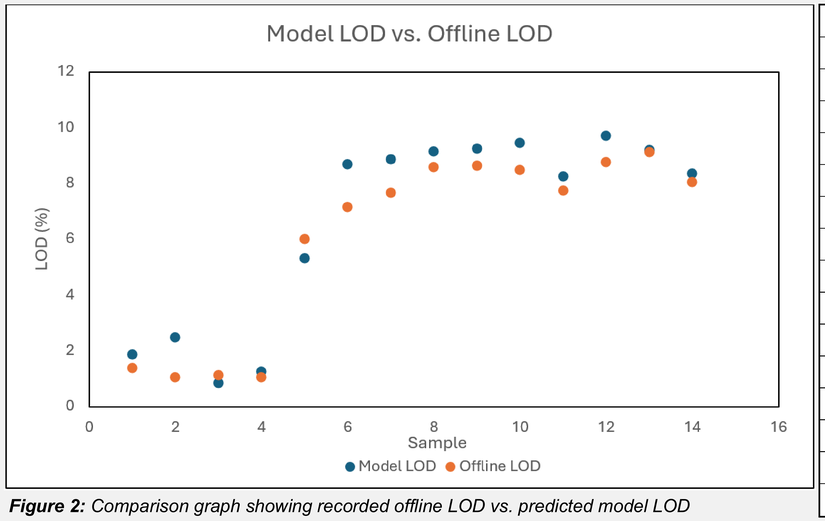


Figure 2: *Comparison graph showing recorded offline LOD vs. predicted model LOD*

Sample #	Model LOD	Offline LOD	ABS Δ
1	1.86	1.4	0.46
2	2.48	1.06	1.42
3	0.86	1.13	0.27
4	1.25	1.06	0.19
5	5.3	6.01	0.71
6	8.7	7.15	1.55
7	8.85	7.68	1.17
8	9.15	8.59	0.56
9	9.25	8.65	0.6
10	9.44	8.49	0.95
11	8.25	7.75	0.5
12	9.72	8.78	0.94
13	9.19	9.11	0.08
14	8.34	8.04	0.3
Average			0.69

CONCLUSION(S)

- The Viavi MicroNIR was successfully demonstrated as an in-line measurement tool for monitoring real-time particle characteristics during continuous granulation.
- It can be concluded from this investigation that the Viavi MicroNIR can serve as a versatile process analytical tool for sensitive, real-time monitoring of material characteristics.



Gf-215 Granuformer®

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