Drying PAT monitoring by NIR: calibration vs. PCA trend approach

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PURPOSE

To determine the endpoint for drying using NIR technology. To establish the correlation between the Moisture Content of the mixture and the response of the NIR device. To find a mathematical and statistical approach to the in-process control using derivative method, PCA calculation and trend approach.

METHODS

A placebo formulation (shown in table 1) was granulated in this study. The set of processes were performed in high shear mixer (Freund-Vector GMXB Pilot) and then dried using fluid bed (Freund-Vector VFC Lab3) equipped with Viavi MicroNIR PAT U device. The device is connected to the fluid bed with a welded flange.
The load of dry blend was adjusted for each type of equipment to achieve appropriate product movement. The process was replicated with the same formulation and process conditions to demonstrate the robustness of this method. LOD was determined at regular intervals using a thermobalance (Mettler Toledo MJ33). Datas were analyzed and processed by Unscrambler software.

Table 1 - Formulation - Blend		
Component	***Quantity (g)***	***%***
Lactose 200 mesh	1000	50
Pregel. Starch	700	35
MCC	300	15
Total	***2000***	***100***
Formulation - Binding solution		
PVP K30	100	10
DI Water	900	90
Total	***1000***	***100***

RESULTS

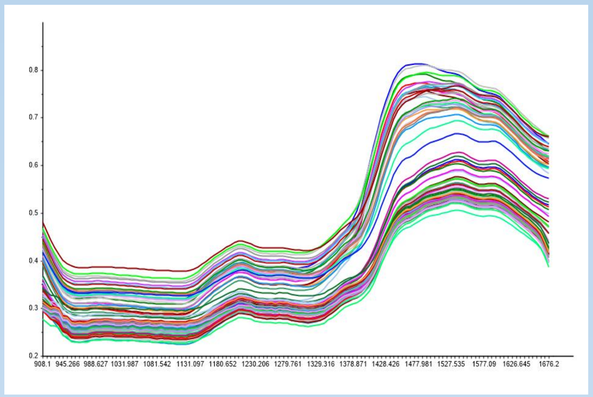

Figure 1

Table 2 - Process Parameters			
Inlet air Temp. (°C)	50	Process time (min)	45
Product Temp. (°C)	22 – 41	Init.l LOD (%)	17
Airflow (m^3/hr)	100 - 110	Final LOD (%)	1.8

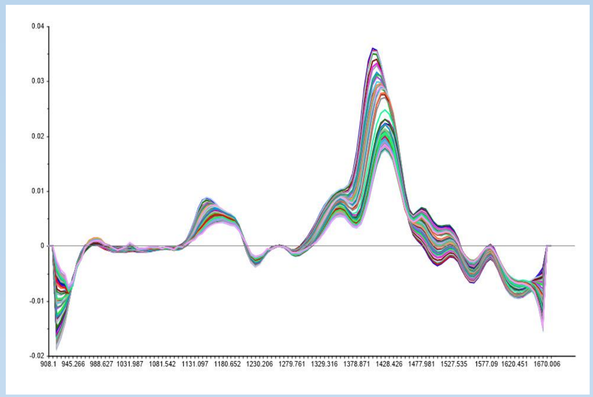

Figure 2

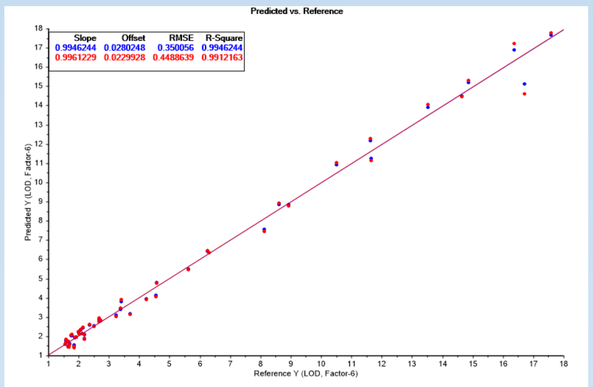

Figure 3

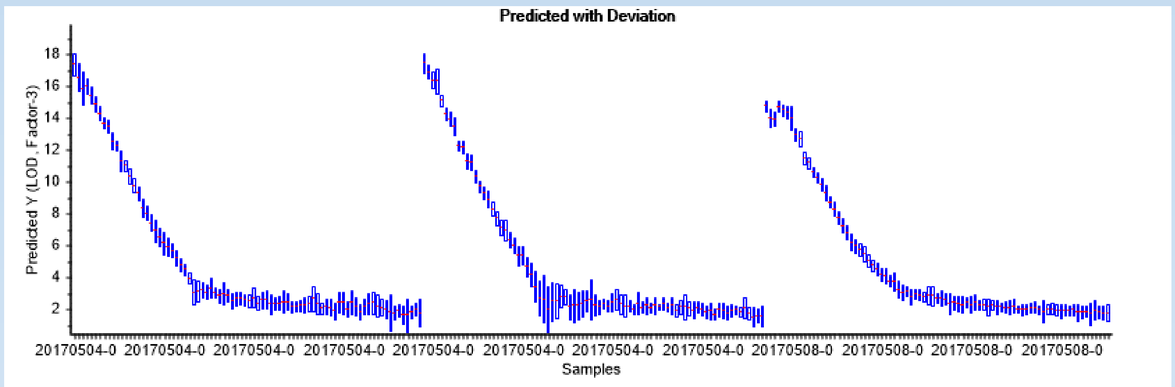

Figure 4

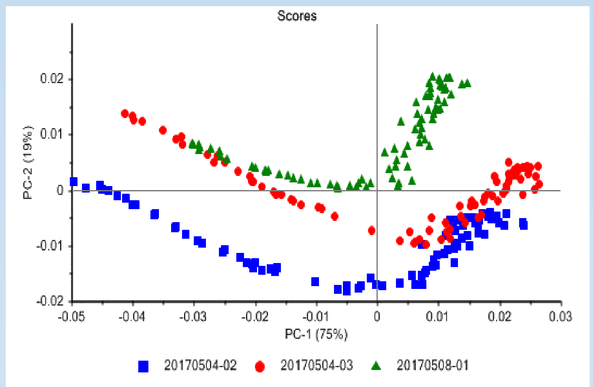

Figure 5

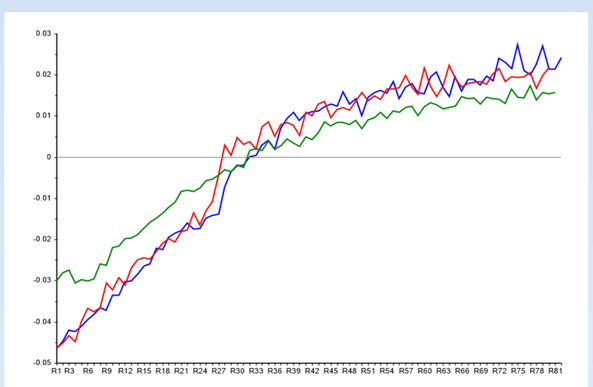

Figure 6

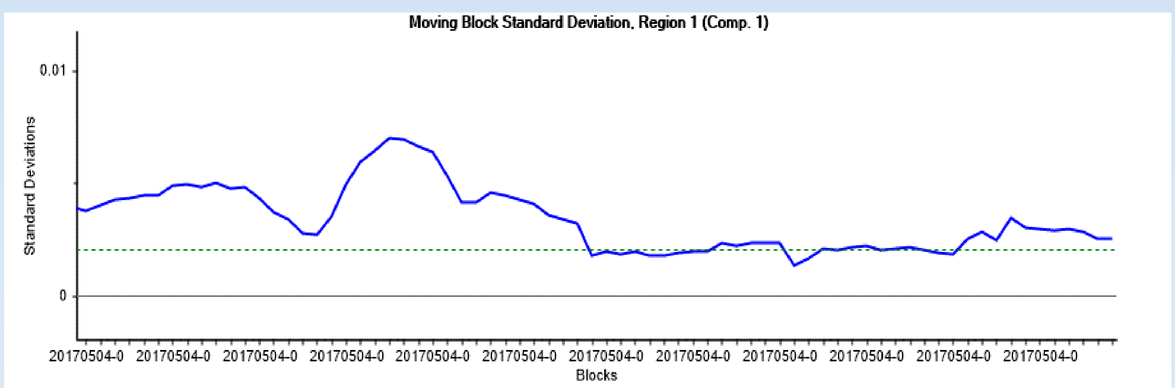

Figure 7

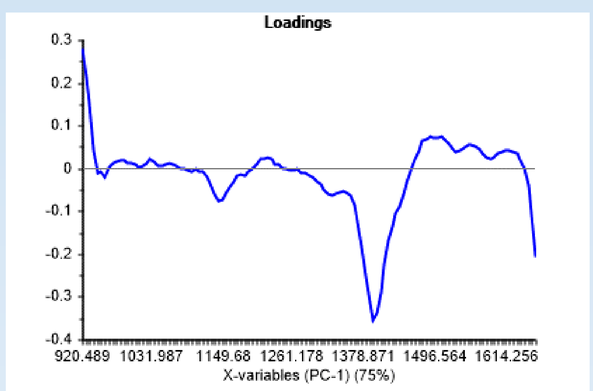

Figure 8

Freund-Vector VFC LAB 3

The Absorbance curve and the 1st derivative are shown in Figures 1-2. The correlation between the measured LOD and the absorbance values is shown in fig. 3. The high R^2 shows that there is a strong correlation between the real datas and the response of the NIR, confirming that the model is robust.
In fig. 4 is shown the calculations of unknown LOD values based on the model created on batch 1. The Principal component analysis confrontation between replicas is shown in fig. 5. In fig. 6 is shown a comparison between the scores of the PCAs of the three batches. In fig. 7 is shown the Standard Deviation of the measures calculated with the moving block method. In fig. 8 are shown the loadings that the system attributes to the spectrum principal component.

CONCLUSIONS

The process shows a very strong correlation between the absorbances read by the NIR instrument and the determined LOD. It is clearly visible the similar trend of the process repetitions. This indicates that the model is reproducible. When the process shows no more changes, the principal component analisys graph tends to a plateau, so it is possible to locate the endpoint of the process in terms of moisture content. The reproducibility of the process in terms of trend and endpoint can allow a process control without the need of a constant calibration. A future developement of this study can lead to a real time control of the process in terms of product carachteristics instead of the process parameters, with the aim of an integration with the automatic control system.

Viavi MicroNIR PAT-U Equipment