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IDENTIFY RIBBON DENSITY USING NEAR-INFRARED SPECTROSCOPY

Ahammed Basheer P K M[1], Dr.Shrikant Sharma[2]
Department of Biotechnology
[1,2]Shri Venkateshwara University, Gajraula (Uttar Pradesh)

Abstract

There have been two separate ways attempted to monitor ribbon density in real time using near-infrared spectroscopy data. The roll compactor was used to create varied densities of microcrystalline cellulose ribbons (MCC). Some of this could be explained by using spectral slope as a measure of density shift in the ribbon. An in-line PCA (principal component analysis) model was used to find the optimal roll pressure range for the manufacture of ribbons. Qualitatively, the density scans demonstrated that the model was able to represent the density responses to changes of the process parameters It is possible to monitor process control using in-line sampling by determining density changes.

Keywords: Density distribution; NIR; PAT; quality by design; roller compaction

1. Introduction

Many companies employ dry granulation because it is affordable and can process heat- and moisture-sensitive pharmaceuticals [1]. Roll compaction can be used to produce dry granulation. Compression from the rollers reorganises particles and causes a denser product to be formed when powder is delivered past two counter-rotating rollers. Compactors are designed to maintain a constant pressure level regardless of the flow rate of material being supplied to the rolls. Another benefit of roller compaction is that it requires far less room, equipment, energy, and time than traditional methods do. In addition, the size of the manufacturing equipment does not determine the amount of product that can be produced. By varying the amount of time the equipment is run, it is possible to change the lot size while minimising costs associated with long-term product storage.

When utilising a roller compactor, you may run into issues with the compact's density dispersion [2]. In order to reduce the fluctuation in the created "ribbons," the feeding mechanism must ensure a constant and uniform flow of material. The ribbon's density is highest in the middle, while the density near the edges is lowest. Granules are also affected by feed stress. The powder in the feeder becomes denser when subjected to increased feed stress. Using a screw feeder is inefficient in maintaining a constant feed stress at greater entry angles. Tablets with low hardness and high friability can be produced as a result of over-densification. As a result, tablets with a significant degree of weight variations may be produced by using low-density ribbons. The feed screw has been shown to affect the granulation characteristics by managing the roll gap

Ribbon thickness and product quality are both influenced by the roll gap. The greater the roll spacing, the lower the average density of the ribbons generated. As a result of the increased compaction pressure required to densify when the roll gap is substantial, this relationship between density and roll gap is explained [3]. If density dispersion along ribbon needs to be minimised, roller compactors with controllable roll gaps should be used. Compaction material is subject to constant shear deformation between the rolls, which Johanson predicted using one of the most well-known models. This model assumes that the material has a cohesive and compressible effective yield function while also being isotropic, frictional, and cohesive.. Due to the large range of density fluctuation that can occur, the Johanson model is unable to accurately characterise the final product[4]. Compression pressure is higher in the middle of a ribbon's breadth, according to recent studies [5]. Ultrasonic testing and X-ray tomography have recently been used to study the density fluctuations in roller compacts [6]. Researchers recently used chemical imaging to obtain near-infrared (NIR) images of MCC ribbons to show the density distribution along the ribbon in an off-line investigation [7].

A calibration approach links the pixel intensity to the ribbon's porosity in this method. As the results of the off-line investigation demonstrated, the low-density regions of the ribbons were concentrated towards their margins. NIR spectra can be influenced by the physical properties of the materials being investigated, hence it has been stated that this can be used to determine density in roll compacts [8]. Relative humidity, concentration, and compression pressure all have a positive impact on roll-compacts' density. Predictions of roll-compact density in real time were made using a correlation between the NIR spectrum slope and thickness in previous investigations [9]. After achieving uniform feeding, the density variation was measured.

Developing manufacturing processes based on existing quality assurance concepts is one goal of this research. Work began with the process analytical technology project and has progressed through Quality by Design and investigations into pharmaceutical process materials science to this point.

2. Experimental Materials and Methods

The ribbons examined using "MCC Avicel PH 200 and 102 (FMC, Philadelphia, USA)."

2.1Monitoring of Ribbons

Flat and diamond-knurled rollers of 12 cm in diameter and 4 cm wide were used in the lab roller compactor "(Alexanderwerke®, Remsheid, Germany) " to manufacture the ribbons. The roll gap control was disabled during the experiment. As a result, operator-selected roll pressure and screw speed influenced the final density. For the experiments, the vacuum option was used to reduce powder loss. Within the next two minutes, a set of in-line measurements using real-time ribbons had been completed. To make these ribbons, a roll pressure of 25 to 70 bar was applied to the rollers. Three different roll pressures were studied (25, 40, and 70 bar). A 1.3cm thickness was the norm. Table I shows the ribbons' features and production settings.

	MCC 200	MCC 102	Flat surface models	In-line
Feeding system	Screw	Piston	Screw	Screw
Roller type	Rough	Rough	Flat	Rough/flat
Roll pressure (bar)	15, 20, 25, 35, 45	15, 25	25, 33, 40, 48, 55, 63, 70	Varied
Inlet pressure (bar)	n/a	1.5, 2.0, 2.5, 3.0	n/a	n/a
Screw speed (rpm)	35	n/a	35	35
Roll speed (rpm)	9	9	9	9
Vacuum option	On	Off	Off	On
Roll gap control	Off	Off	Off	Off

Table I. Creation of Ribbon's conditions

2.2Determination of Envelope Density

A GeoPyc 1360 pycnometer was used to measure the envelope density (Micromeritics, Norcross, GA). The measurements were taken in a 12.7-mm-diameter chamber with combine pressure of 0.1284 and 28 N, respectively. The measurements were taken with Dry Flo® as the medium. The GeoPyc instrument handbook recommends a sample size greater than 250 mg for appropriate measurements. Samples of roughly 1 cm in length and 0.8 cm in width were evaluated three times for the offline ribbons.

2.3Thickness Measurements

The samples' thickness was measured using a computerised calliper. A cheap laser sensor, the optoNCDT 1402, was used to measure the ribbon thickness in-line (micro-epsilon, UK). It was necessary to place the laser 8 cm behind the NIR probe in order to acquire the most accurate thickness measurement. A high-precision balance was used to weigh the samples. A calliper and a laser were used to change the sample's thickness, yielding two unique volumes. To produce ribbons with a smooth surface, just the two reference methods described here were employed.

2.4Acquisition of Near-Infrared Spectra

The fibre optic probe was positioned 7.5 centimetres above the samples in order to capture NIR spectra. The integration time was calculated using an average of eight spectra, resulting in a value of 69.9 ms. The CDH 50 Standard White disc was made from an Albrillon disc, a highly reflective organic microcrystalline fluorinated polymer. A MATLAB 7.1 technique was utilised to transport the samples in parallel with and over a linear transverse's moving stage (The Math-Works, Natick, MA). We used two distinct sampling approaches to gather the data About 0.8 cm in width separated each of the four rough surfaces. NIRS sampling areas are around 0.5 cm broad, hence this was the width that was selected. Figure 1 shows how the spectra were collected using a four-section sampling method that spans the ribbon's length. The density and thickness of the reference envelope were determined by slicing an approximately 1 cm-long sample. A 28 cm long ribbon was utilised to collect the spectra. Eight spectra were acquired for each of the test conditions.

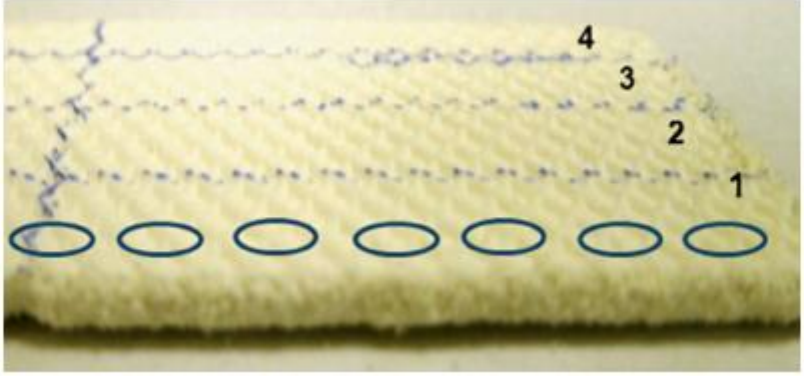

Figure 1Model MCC 200 accuracy assessment experiments employed the sectioning approach.

With the help of diamond knurl and flat rollers, pure MCC 200 was created in real time. At the roller compactor's exit, the NIR probe is positioned in-line as shown in Figure 2. Two independent sets of Spectra were required. Variations in roll pressure were made in 15-bar steps for about a half-hour to obtain the spectrum of ribbons with rough surfaces. For flat-surface ribbon spectra, the roll pressure was changed from 25 to 70 bar for two minutes.

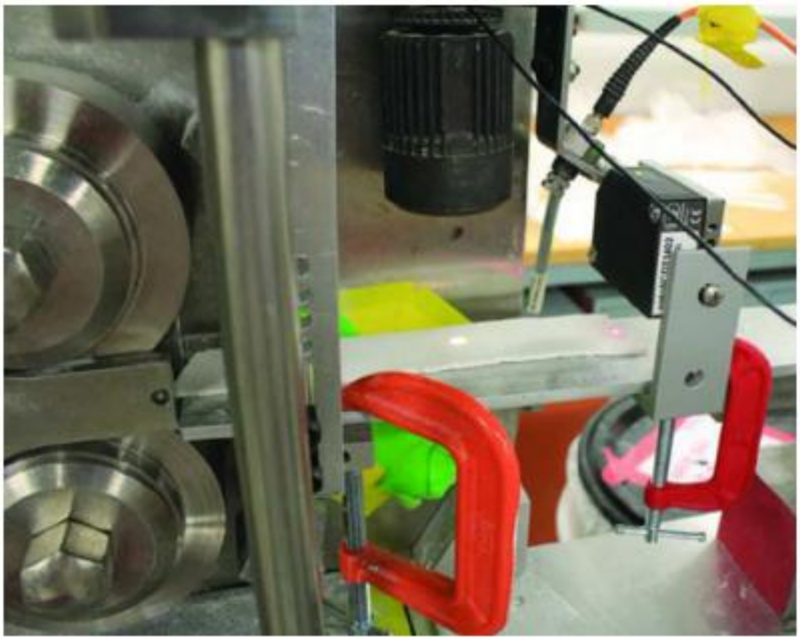

Fig. 2. Experiment setup

"Pirouette 4.0 (Infometrix, Bothell, WA)" software was used to create multivariate calibration models for PCA and PLS regression. PCA and in-line spectral data were used to create qualitative models for detecting changes in ribbon density. After increasing the roll pressure in an in-line experiment, spectra were used to generate a PCA model. It was developed in the 1,305-2,205 nm wavelength range when the PCA model was first conceived. The process of using the data to create precise and accurate models included several stages. The unprocessed NIR spectra are shown in Figure 3. A calibration model was developed for the wavelength range of 1,120-1,310 nm.

The maximal penetration depth of NIR radiation is predicted to be at these shorter wavelengths [10] because of the low molecule absorption. Low-wavelength NIR density investigations may be fruitful due to the higher amount of material that link with the light. In the2nd calibration sample, the 1,305–2,205 nm range was explored. To calibrate the linear transverse, off-line spectral data from ribbons was employed. The calibration model required to include an evaluation of spectral pre-treatments. The subtract process was used to lower all spectra in the 1,120–1,310 and 1,305–2,205 nm models to zero at 1,121 and 1,306 nm. Slope values were then calculated from the readings at 2,100nm following subtraction. Even when the baseline is reset, the remove pre-processing has no effect on the spectra's slope. In the PLS calibration model, the two PLS factors were generated using mean centering.

3. Results and discussion

Variation in Spectral Power is Dependent MCC-produced ribbons had NIR spectra taken both offline and lives. Figure 3 depicts the spectra that resulted from varying the roll pressure on the powder. Previous studies have demonstrated that fluctuations in roll pressure can produce changes in ribbon characteristics, which were detected using NIR spectroscopy. As a result of the ribbons being manufactured from a single material, these spectral property differences are the result of physical rather than chemical modifications (MCC 200). As the slope changes, the ribbon's physical properties alter as well. After subtracting the pre-treatment values from all spectra, which were then baseline corrected to zero at 1,121 or 1,306 nm, the slope values were computed by subtracting the pre-treatment values. Increasing the roll pressure causes the NIR spectrum's slope to increase. A typical spectral slope and envelope density for ribbons generated from 20 to 45 bar is depicted in Figure 4. Correlation coefficients for these ribbons indicated a linear link between density and spectra slope. The latest findings [11] corroborate prior observations by Gupta.

3.1Qualitative Modelling

Variations in the roller compaction operating parameters resulted in spectrum variations that were evaluated using PCA (Principal Component Analysis). An inline experiment with rough surface ribbons was conducted using a PCA model having variation in roll pressure between 30 and 35 bar..

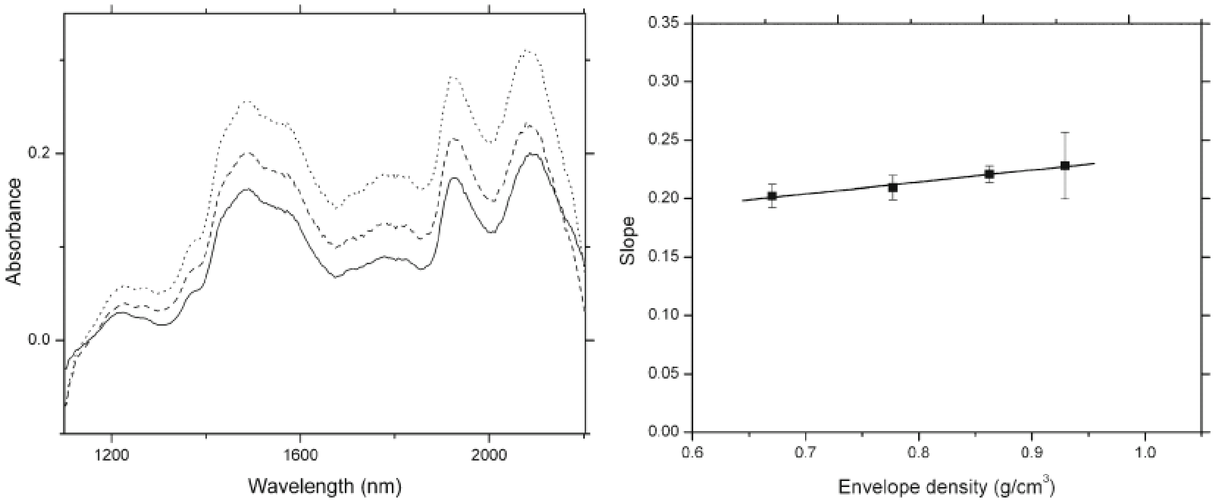

Fig. 3. NIR spectra from MCC 200 ribbons that were created at 15 (straight), 25 (dashed), and 45 bar (dot).

When the roll pressure was increased from 30 to 35 bar, NIR spectra were used to train the PCA model. Normal process variation was defined by shifting operating pressures from 30 to

35 bar using the NIR spectrum and PCA model. Figure 4 depicts predictions for in-line trials with various roll pressures. We were able to determine the Mahalanobis distance after doing an in-line experiment with a roll pressure range of 25–30 bar (the distance from the multivariate mean). The pressure change is shown by an arrow. The density of the material changes when the roll pressure is increased. The 95 percent confidence interval (Mahalanobis distance critical value) shown in Figure 4 does not include 25-bar spectra, which is a significant omission. In order to maintain the gradient, the system must attain a pressure of 30 bar before the model's 95% confidence interval can be deemed accurate for all spectra (30 to 35 bar). Figure 4b shows what happens when you go from a roll pressure of 35 to 40 bar. Figure 4b shows that the initial spectra did not fit within the model's 95 percent confidence interval. Sub-feeding occurred early on in the system's development, resulting in final measurements that were outside of the 95 percent confidence interval for the other spectrum. The model predicts that material properties will change as pressure is raised from 35 to 40 bar

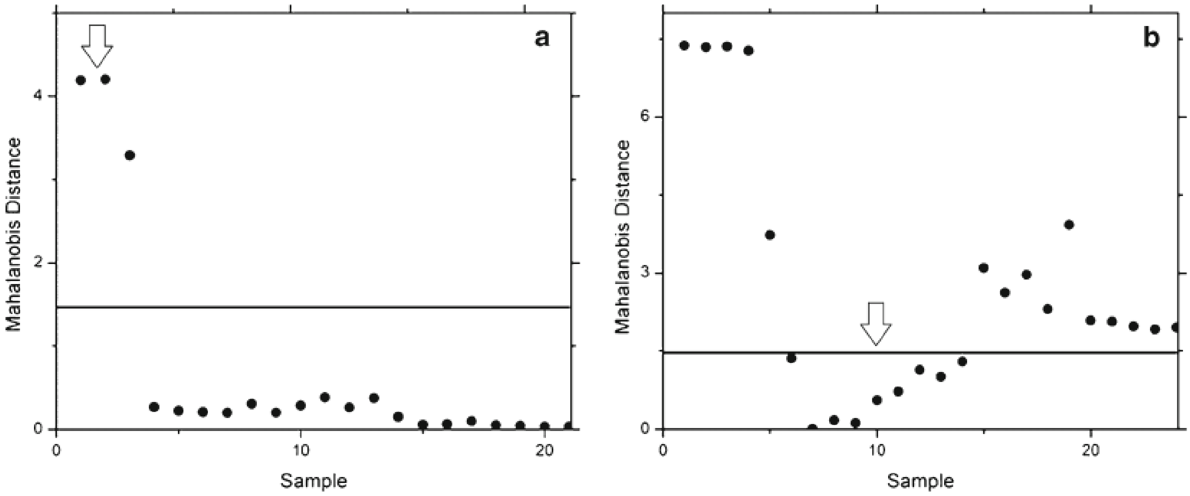

Fig. 4. Roll forces ranging from 25 to 30 bar to 35 to 40 bar, As shown by the horizontal line, the Mahalanobis distance critical value is above which a sample is determined to be distinct from the calibration set.

4. Conclusion

The density and dispersion of the roll compact can be monitored using the techniques provided in this study. NIR spectra fluctuation density is affected by operational parameters such as roll pressure. Ribbon density rises in tandem with the slope of the spectra, which is influenced by roll pressure. Roll pressure at 15 bar did not correlate with NIR spectral slope for "real-time" monitoring. To keep tabs on variations in ribbon quality due to adjustments to operational parameters, the PCA method can be employed. PCA and slope approaches, which employ spectrum data instead of density measurements, can be used to avoid sampling error.

A weakness in PCA and slope is the lack of density values. The PCA model looks to be the most appropriate in this situation for monitoring changes in density distribution in real time.

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