TECHNICAL NOTE

No. 2107

Stearates verification using a handheld Raman analyzer

Ensure material quality at the point of need

Key Words
Qualitative analysis, Raman spectroscopy, PCA, pharmaceutical manufacturing, excipients, magnesium stearate, calcium stearate, zinc stearate, chemometrics

Introduction

Magnesium stearate is a white powder that becomes solid at room temperature. In the pharmaceutical manufacturing process, magnesium stearate is the most commonly used lubricant for capsules and tablets, and is used to help prevent pharmaceutical ingredients from adhering to manufacturing equipment. Calcium stearate, and to a lesser extent, zinc stearate, are also used as pharmaceutical excipients in manufacturing, primarily for tablet and capsule lubrication.

Magnesium stearate, calcium stearate and zinc stearate share a similar chemical compound structure and are more challenging to verify during the incoming raw material inspection process. While the Thermo Scientific™ TruScan™ RM handheld Raman analyzer has a built-in multivariate residual analysis decision engine to identify most materials, more complex materials analysis requires users to build custom, advanced methods.

Thermo Scientific TruTools™ is an embedded chemometrics package for the TruScan RM analyzer. It enables users to create customized predictive applications, including classification, semi-quantitative and quantitative methods. TruTools leverages Solo, a chemometrics software package from Eigenvector Research Inc., which allows users to develop models that can be deployed onto the TruScan RM analyzer.

In this application, a Principal Component Analysis (PCA) method was found to be successful in identifying the various stearates. A TruTools PCA method produces a Pass or Fail result screen, based on the logic selected in the TruScan RM analyzer's WebAdmin functionality.

PCA method setting in WebAdmin allows users to make a decision based on either normalized hoteling (T^2), normalized residual (Q), both or combined. Thus the user can control the PCA method's selectivity. For example, if normalized Q value will be used for the Pass/Fail criteria to identify raw materials, then any Q values higher than 1 will be considered as Fail. Usually, normalized Q value is more common than normalized T^2 as the criteria for pass/fail indication, as Q value reflects the unusual variations outside the model.

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Calcium Stearate

- Acquisition Parameters:
  - Laser Power: 250 mW
  - Exposure Time: 500msec
  - Number of Coadds: 20
- Number of Scans: 34

Eigenvector Solo Settings:

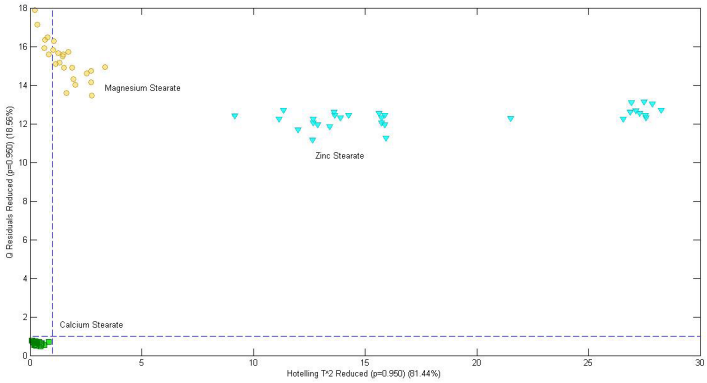
- Wavelength: 302-2175.3cm^{-1}
- Pre-processing: SNV, 1st Derivative (order: 2, window: 13 pt, incl only, tails: polyinterp), Mean Center
- Number of PCs: 2
- Cross validation: venetian blinds w/ 8 splits and 1 sample per split

Magnesium Stearate

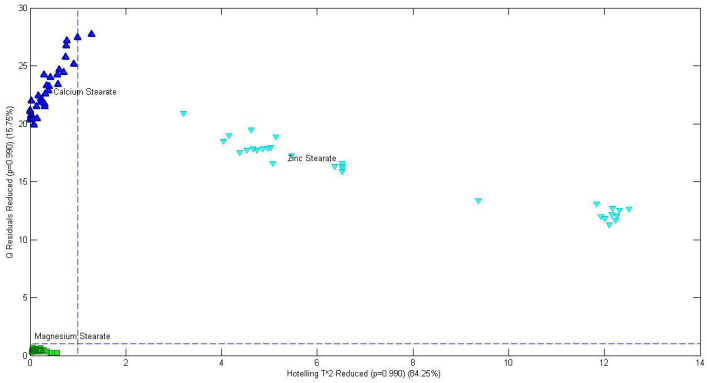
- Acquisition Parameters:
  - Laser Power: 250 mW
  - Exposure Time: 500msec
  - Number of Coadds: 20
- Number of Scans: 23

Eigenvector Solo Settings:

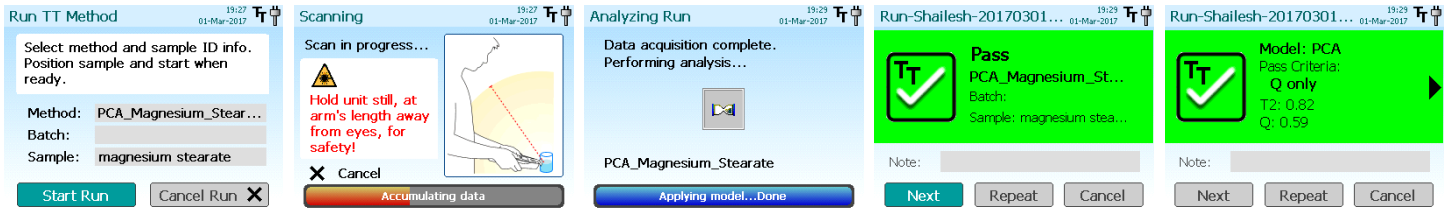
- Wavelength: 556.8-1980.3 cm^{-1}
- Pre-processing: 1st Derivative (order: 2, window: 15 pt, incl only, tails: polyinterp), Mean Center
- Number of PCs: 2
- Cross validation: venetian blinds w/ 6 splits and 1 sample per split



Cross Validated Calcium Stearate PCA method against Zinc Stearate and Magnesium Stearate



Cross Validated Magnesium Stearate PCA method against Zinc Stearate and Calcium Stearate



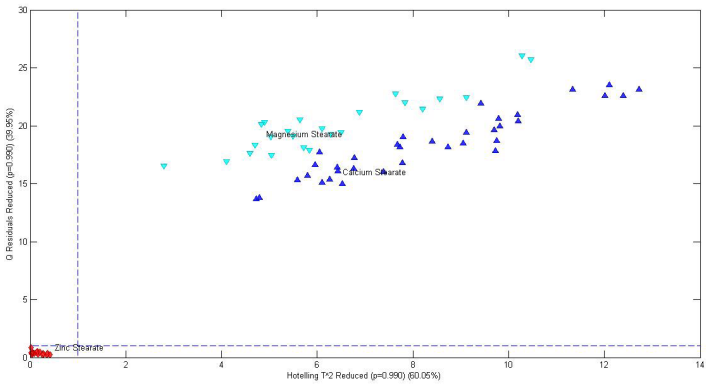
Operator selects TruTools PCA Magnesium Stearate method, analyzes material, result produces Pass screen.

Zinc Stearate

- Acquisition Parameters:
  - Laser Power: 250 mW
  - Exposure Time: 500msec
  - Number of Coadds: 20
- Number of Scans: 21

Eigenvector Solo Settings:

- Wavelength: 320.2-2060.9cm^{-1}
- Pre-processing: SNV, 1st Derivative (order: 2, window: 15 pt, incl only, tails: polyinterp), Mean Center
- Number of PCs: 2
- Cross validation: venetian blinds w/ 4 splits and 1 sample per split



Cross Validated Zinc Stearate PCA method against Magnesium Stearate and Calcium Stearate

Summary

Due to global supply chains and increased regulatory scrutiny, pharmaceutical manufacturers must ensure the quality of materials throughout the production process, as well as increase productivity and efficiency. The TruScan RM analyzer provides manufacturers with fast and accurate material verification, minimizing the need for time-consuming laboratory sampling tests. With the addition of the TruTools chemometrics package, the TruScan RM becomes a more powerful spectrometer, capable of identifying and quantifying more complex materials at the point of need.

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