Application note

Material identity verification

Fast, efficient, reliable verification of different Opadry film coatings using TruScan RM Handheld Raman Analyzer with TruTools

Authors

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Introduction

Pharmaceutical companies that manufacture tablets, capsules, and other solid dosage forms use film coatings on their products to differentiate appearance and improve palatability by masking unpleasant tastes or odors. Film coatings also protect tablets from light, moisture, and environmental gases, reduce breakage and chipping, and prevent cross contamination. Colorcon® produces a range of Opadry® film coatings that are widely used by pharmaceutical manufacturers and are available in diverse formulations suitable for various API and excipient characteristics and release profiles. Traditional material identity verification uses wet chemistry or Fourier transform infrared (FT-IR) spectrometry and necessitates opening of secondary packaging, sampling the raw materials, transporting samples to a central laboratory, and expert sample preparation and analysis of results.

There exists an urgent to identify all different Opadry raw materials in the warehouse in a fast and efficient way. Different Opadry have very similar formulations with small differences in the addition of colorants which making discrimination among them even more challenging. The Thermo Scientific™ TruScan™ RM handheld Raman analyzer

can authenticate materials anywhere in the pharmaceutical manufacturing plant, without sample preparation and have nearly fully substituted conventional testing methods. Thermo Scientific TruTools™ is an embedded chemometrics package which runs on TruScan RM and expands its analytical capabilities. TruTools, leverages Solo, a chemometrics software package from Eigenvector Research Inc, provides advanced pre-processing of spectra, and a platform to implement customized chemometric models, qualitatively and quantitatively, including Principal Component Analysis (PCA), Partial Least Square (PLS), and Partial Least Square Discrimination Analysis (PLSDA) on board the handheld device. All the results will be shown on the device in minutes.

In this application, Five Opadry Colorant (Opadry Blue, Opadry Pink, Opadry Purple, Opadry White and Opadry Yellow) and three types of Opadry white (Opadry II White, Opadry White Ys-1-7000, and Opadry White Ys-1-7068) and were analysed using TruScan RM with TruTools, by employing different chemometric models to achieve a good separation and specificity to discriminate them.

Principal Component Analysis (PCA) models for discriminating five Opadry colorants.

All the raw spectra were collected on TruScan RM (785nm laser excitation) by using optimised acquisition parameters at 250mW laser power, 2000 ms exposure time and 10 coadds as shown in Figure 1. Representative spectra of the five groups show unique Raman features, however, the difference between spectra for the Opadry formulations is still relatively small. There are clearly three dominant peaks of Titanium(IV) oxide, anatase (TiO_2) used as the primary pigment, represented by three strong peaks in the spectral region below 800 cm-1.

In order to discriminate these five different Opadry materials, the raw spectra have been pre-processed by SNV (standard normalized variate, 1st derivate and mean centre) before further chemometric analysis. The PCA analysis plot in figure 2 shows excellent separations between classes with greater than 96% of the data contained in the first two principle components of the analysis.

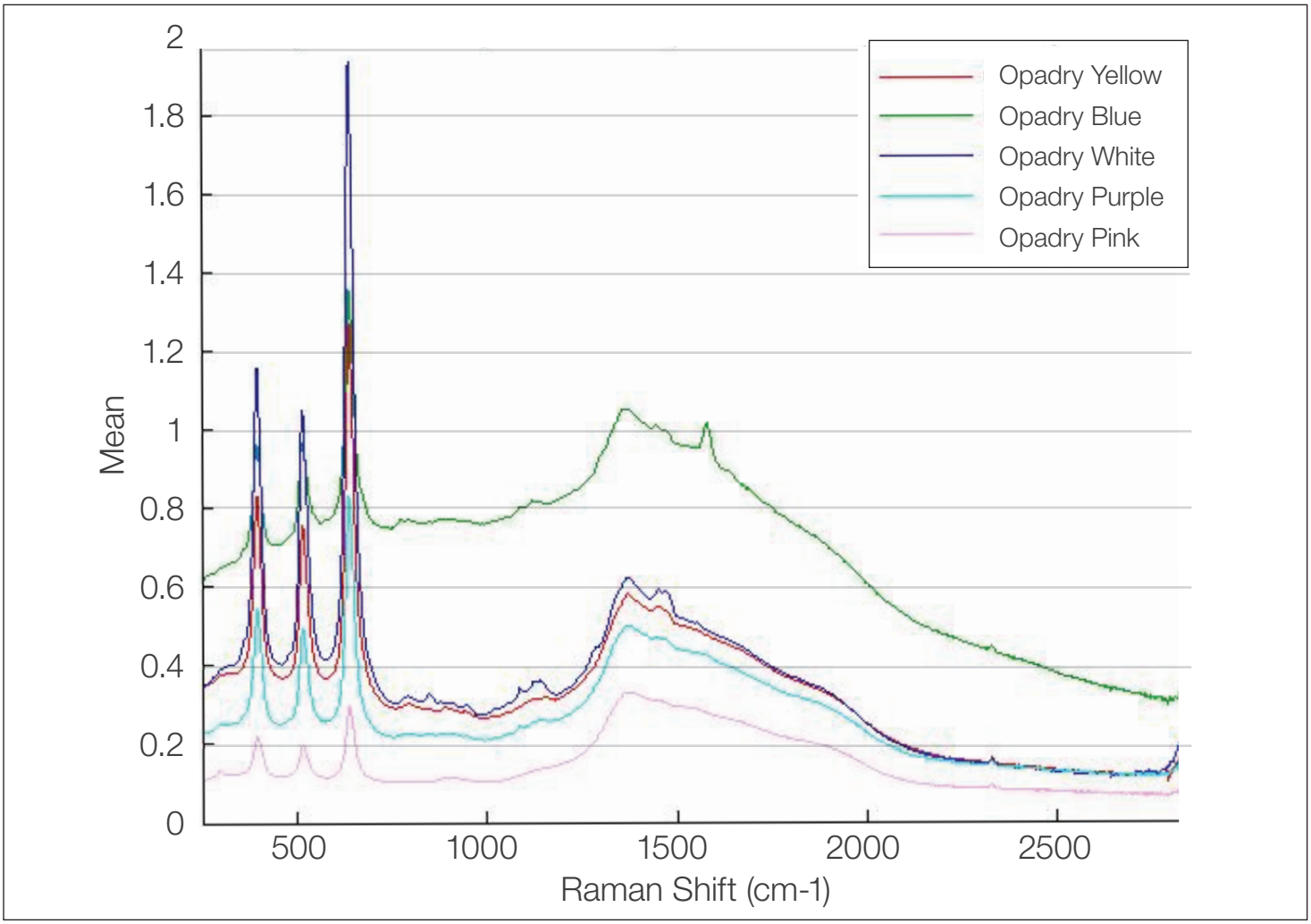

Figure 1: Raman spectra collected from TruScan RM and region of analysis

Good selectivity of the Opadry pink PCA model, as an example, is shown in Figure 3. In the plot of Q residuals and Hotelling T2 plot, only the Opadry pink class sit in the acceptable pass criteria region (T2<1 and Q residuals<1) to identify this material. The other classes are all above Q residuals of 1 indicating a Fail. Typically, normalized Q value is more common than normalized T2 as the criteria for a pass/fail result as Q value may reflect unusual variations outside the model.

After deploying the PCA model of each material to the TruScan RM, the verification results are displayed in minutes after scanning each material. A green screen for "Pass" or red screen for "Fail" may be shown. Figure 4 shows the direct results on the device screen. All five Opadry models exhibit good selectivity, with a false positive rate less than 5%.

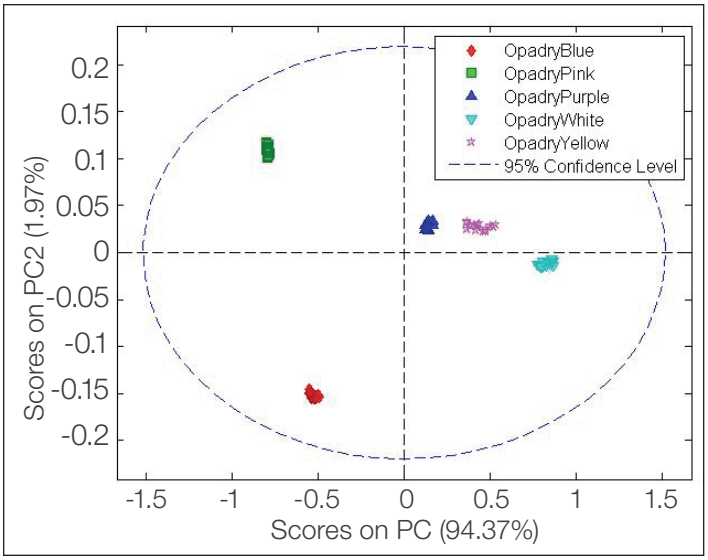

Figure 2: Raman spectra collected from TruScan RM and region of analysis

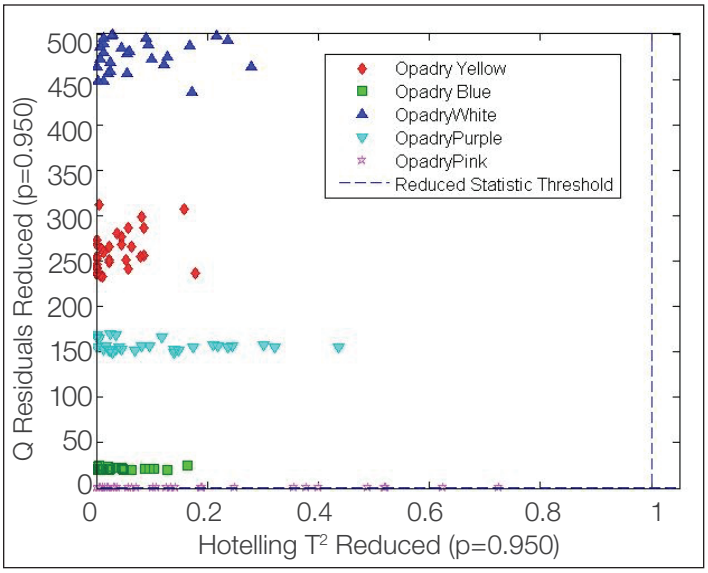

Figure 3: Reduced Hotelling T2 and Q-residuals plot of single class PCA Opadry Pink model, indicating the good selectivity of Opadry Pink method

Partial Least Square Discrimination (PLSDA) models for discriminating three type Opadry Whites.

Three types of Opadry white (Opadry II White, Opadry White Ys-1-7000, and Opadry White Ys-1-7068) were also analyzed using TruScan RM with TruTools. These three Opadry whites all contain Hypromellose, Titanium Dioxide, and Macrogol as predominant components, where Opadry II white has an additional component, Lactose Monohydrate; Opadry White Ys-1-7068 has Hydroxypropyl Cellulose as the additional component in the formulation. Raw Raman spectra collected from the device are shown in Figure 5. Such small differences has made the discrimination between them even harder by the conventional methods. Here using TruScan RM with TruTools, identification of these extremely similar materials is realized in less than one minute without any further sample preparation, even measuring though the primary packaging container.

Figure 4: Pass or Fail Screen Display of PCA model for verification of raw materials. Detailed chemometric results are also shown on the screen.

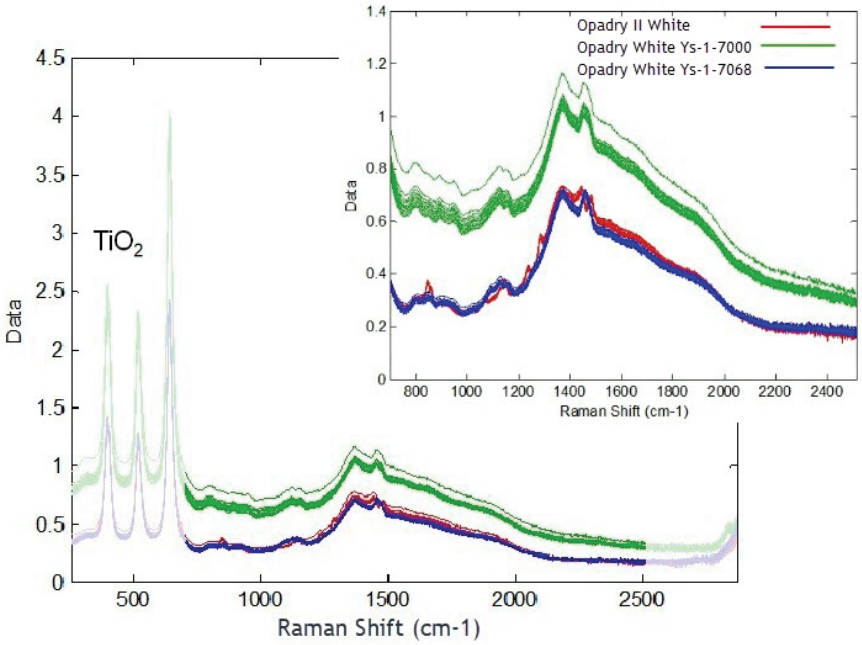

Figure 5. Raman spectra collected from TruScan RM and region of analysis

Partial Least Square Discrimination Analysis (PLSDA), a supervised classification model, has been deployed for the discrimination. The region between 800 cm-1 and 2500cm-1 has been selected for analysis to remove the dominant peaks of Titanium(IV) oxide to focus on the difference between the other components. The raw spectra are pre-processed utilizing first-derivative filtering and mean centering, before final classification by TruTools. These three formulations are easily established visually – the underlying rich spectral signatures are well suited for multivariate analysis. PLSDA analysis of three Opadry White Classes shows excellent separations between classes with greater than 88% of the data contained in the first two principle components of the analysis.

Figure 6 shows the onboard display of the TruScan RM with TruTools for the positive identification of Opadry White Ys-1-7068; the material identity is clear with 100% probability.

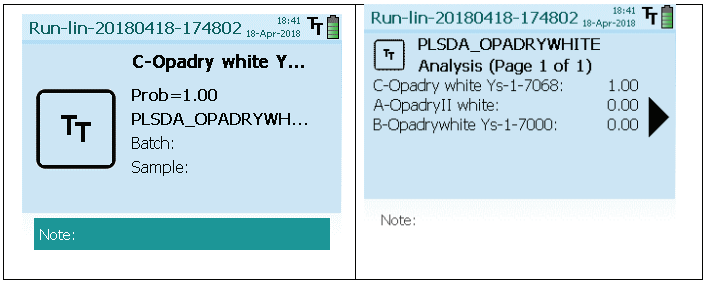

Figure 6. TruTools PLSDA model run on a TruScan RM shows definitive identification results

Summary and prospects.

Raman spectroscopy provides many advantages for pharmaceutical material analysis including non-contact and non-destructive scanning, and spectral specificity which afford the ability to identify a wide range of standard/common compounds. For many years, handheld Raman spectrometers have been successfully employed for pharmaceutical raw material identity verification. TruScan RM uses a native multivariate residual analysis decision engine to identify most raw materials in an easy and rapid manner.

In some instances, sample complexity – highly similar chemicals, materials with different physical properties, and mixtures with similar components – yields complex and highly overlapping spectra which may prevent standard TruScan RM identification, thus requiring additional chemometric flexibility and power for analysis. This feasibility test shows via PCA and PLSDA chemometrics, TruScan RM with TruTools provides qualitative results capable of identifying and verifying similar Opadry materials. Additional studies with different batches of these same materials would be required to validate the robustness of the models to correctly predict the identity of the materials under evaluation.

There is potential that other Opadry materials such as Opadry Red, Opadry green and Opadry Orange may also be identified correctly and efficiently. For dark coloured Opadry (for example, Opadry Brown), the use of lower power laser should be considered to avoid sample degradation. TruTools allows users to adjust acquisition parameters to optimize the quality of spectra (SNR) for further analysis without compromising samples.

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