APPLICATION NOTE

RB 3148435

Verification of 3 different Opadry whites using a handheld Raman analyzer

Pharmaceutical companies that manufacture tablets, capsules, and other solid dosage forms use film coatings on their products to differentiate appearance and to 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.

In choosing a film coating, pharmaceutical manufacturers consider the active pharmaceutical ingredients (API) and excipients' attributes (e.g. solubility, stability, particle size) and the API's intended delivery profile (e.g. immediate release, controlled release, sustained release, enteric release).

Colorcon® produces a range of Opadry® film coatings that are widely used by pharmaceutical manufacturers and available in diverse formulations suitable for various API and excipient characteristics and release profiles. A dry mix concentrate, different Opadry formulas appear identical and share a similar chemical compound structure making discrimination between them challenging. 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.

Portable Raman instruments can authenticate materials anywhere in the plant, without sample preparation and are fast substituting conventional testing methods. The Thermo

Scientific™ TruScan™ RM handheld Raman analyzer's built-in multivariate residual analysis decision engine can identify most materials, however, building advanced methods, which further enhance specificity, can benefit differentiation of highly similar, formulated materials.

Thermo Scientific TruTools™ is an embedded chemometrics package which runs on TruScan RM and expands its analytical capabilities. TruTools provides advanced preprocessing of spectra, analysis of qualitative variance, quantitative analysis of components and a platform to implement customized chemometric models including PCA, PLS, and PLSDA on board the handheld device.

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In this application 3 types of Opadry white (Opadry II White, Opadry White Ys-1-7000, and Opadry White Ys-1-7068) were analyzed using TruScan RM with TruTools.

Representative spectra of the three groups show unique and reproducible Raman features, however, the difference between spectra for the 3 Opadry formulations is still relatively small. The region between 800 cm^{-1} and 2500 cm^{-1} has been selected for analysis to remove the dominant peaks of Titanium (IV) oxide, anatase (TiO_2) used as the primary pigment, and represented by three strong peaks in the spectral region below 800 cm^{-1} (figure 1).

In this study, the raw spectra are preprocessed utilizing first-derivative filtering and mean centering, shown in figure 2, before the final classification by TruTools. These three formulations are easily established visually — the underlying rich spectral signatures are well suited for multivariate analysis.

Exploration of the data set with Principal Component Analysis (PCA) (figure 3), shows excellent separations between the three classes with greater than 88% of the data contained in the first two principle components of the analysis. This indicates an ability to automate the Opadry White spectral analysis through further multivariate-based differentiation of the three products.

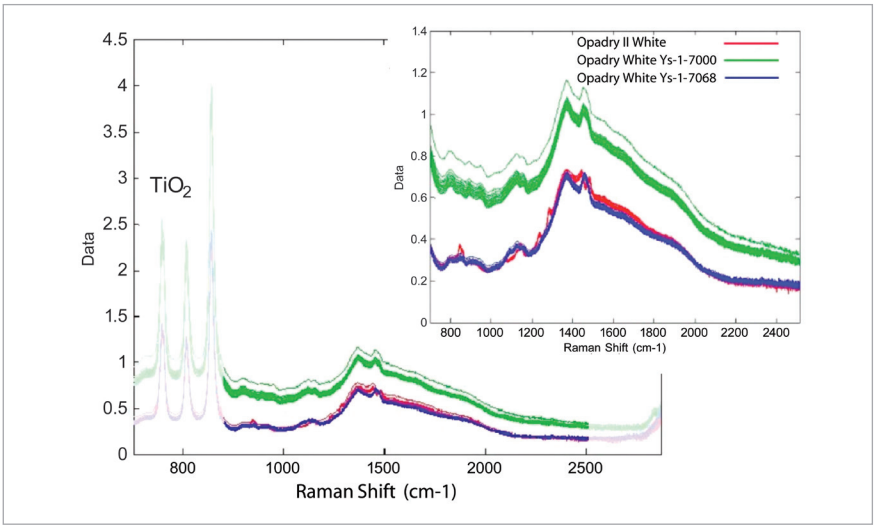

Figure 1. Raman spectra collected from TruScan RM and region of analysis

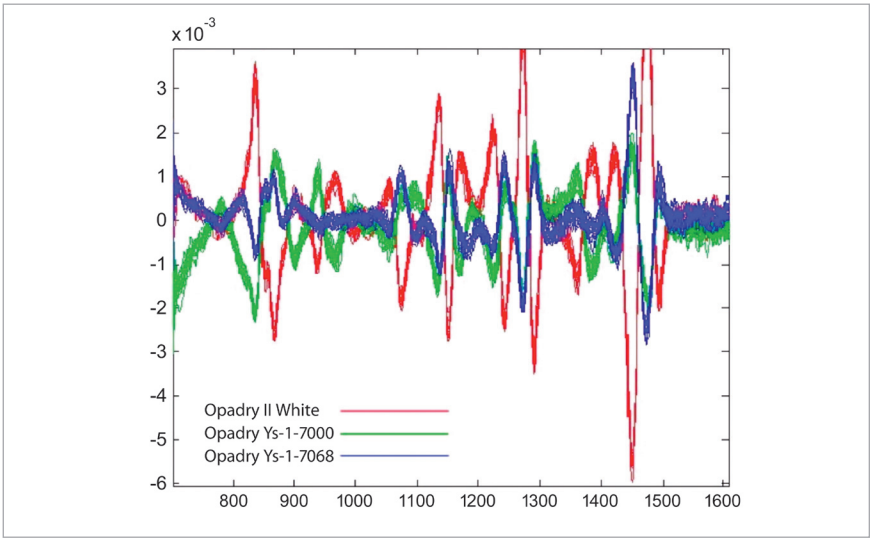

Figure 2. Preprocessed raw spectra utilizing first derivative filtering and mean centering

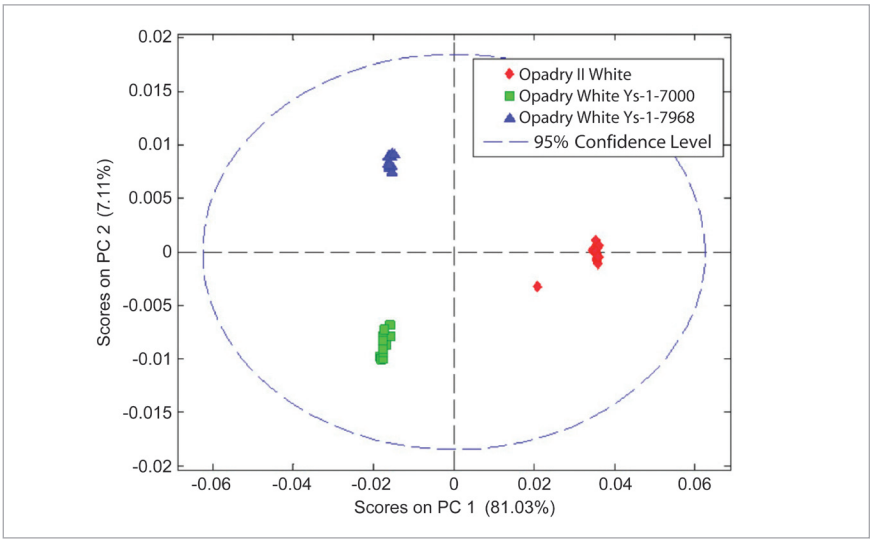

Figure 3. PCA analysis shows good separation of the 3 classes

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As a further extension of our PCA results, a PLSDA model is developed to take advantage of the known identity of each of the three products and performs well, identifying each Opadry White as a distinct class. Figure 4 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 the probability equal to 100%.

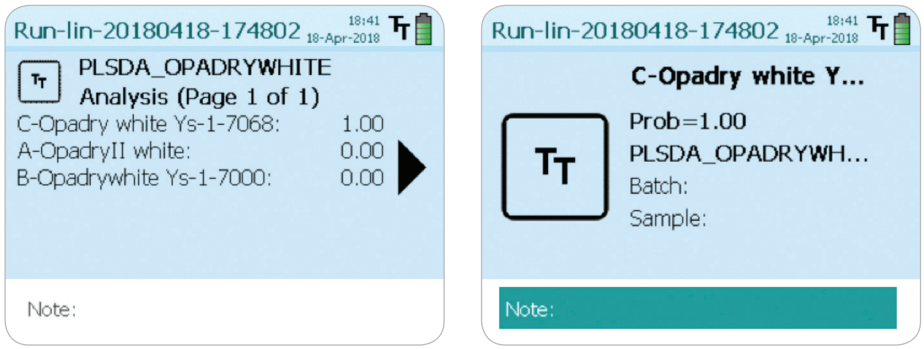

Figure 4. TruTools PLSDA model run on a TruScan RM shows definitive results.

Conclusions

Raman spectroscopy provides many advantages for pharmaceutical material analysis including robust, non-contact and non-destructive scanning, and spectral specificity all of which afford the ability to identify a wide range of common compounds. For many years, hand-held 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 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 based identification, thus requiring additional chemometric flexibility for analysis. This feasibility test shows TruScan RM with TruTools data preprocessing and PCA and PLSDA models provides qualitative results capable of identifying three types of Opadry White correctly and efficiently. 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.

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