

# Chemical Imaging of Solid Dosage Forms

## Using the RamanStation 400

### Introduction

In Raman chemical imaging, the spectra are acquired in a grid pattern (or map) and processed using software to provide a two-dimensional representation of the sample composition. This map can be constructed from any number of spectral properties such as the intensities or areas of particular peaks of interest, but importantly, these spectral properties can be chosen to reflect the chemical composition. This means that the spectral maps can show variation in concentration or even properties like crystallinity across the mapped area.

The biggest restriction is usually the length of time taken to complete the data acquisition. In this example using the PerkinElmer® RamanStation™ 400, the total accumulation time was reduced by 40x over conventional Raman imaging instruments.

Typically, the Raman chemical images are displayed in false color. PerkinElmer Spectrum™ Insight software makes it straightforward to move seamlessly from raw data to the finished images which contain the chemical information that is needed.

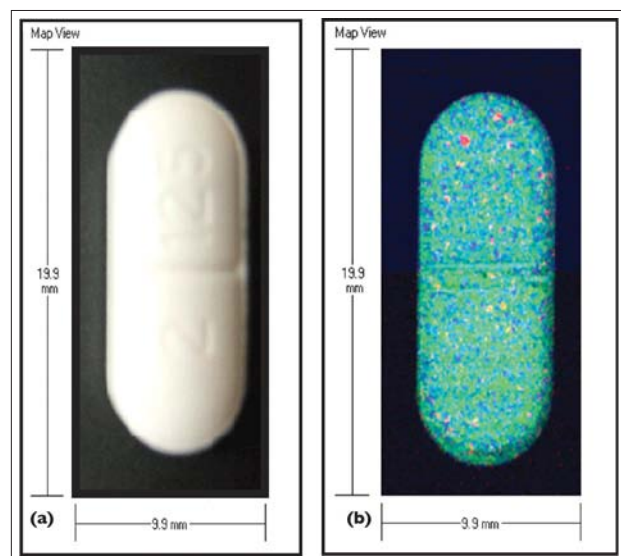


Figure 1. (a) Imodium Advanced® caplet and (b) chemical image of an Imodium Advanced® caplet.

### A Case Study

Imodium® is retailed as 18 mm x 8 mm “Advanced Caplets” (Figure 1a). For this study, a 100 x 200 array of spectra at 0.1 mm spacing was recorded with 0.4 s data acquisition per point using a RamanStation 400 equipped with a 785 nm laser. As can be seen in Figure 1b, this gave full coverage of the caplet surface. Fast data accumulation is only possible because of PerkinElmer’s unique echelle detector system which allows high resolution data for the entire useful Raman spectral range to be collected in a “single shot”. This advantage becomes very significant when the thousands of spectra needed to build up a chemical image are being recorded. A data set of equivalent signal-to-noise, range and resolution could take up to 260 hours to collect using conventional Raman instruments. Using the RamanStation 400 however, this data was mapped in less than 5 hours.

The RamanStation 400 allows chemical images to be recorded rapidly through an intuitive software interface. The echelle systems have the unique advantage that they allow full coverage maps of even large samples (as shown in Figure 4) to be recorded at high spectral resolution. The resulting 20,000 spectra were analyzed, using PerkinElmer’s Spectrum Insight software, in two different ways to illustrate two possible methodologies.

In the first method, peaks characteristic of three different components were identified from the raw data set (see Figure 2). The software was used to find the area of each of these and, with no other spectral pre-processing required, these data were then used directly to create the false color RGB image shown in Figure 1B. This image shows the distribution of the three major constituents throughout the caplet. The caplets were known to contain loperamide HCl, simethicone and CaPO<sub>4</sub>. Using this information, it was also possible to run a quantitative chemometric

analysis on the data. First, a chemometrics training set was constructed from spectra of the raw materials (shown in Figure 3). Using this training set allowed quantitative information on the concentrations of each of the constituents at each point on the caplet to be determined using standard multivariate data reduction methods: PLS-1 (Partial Least Squares), cross-validation, 1st derivative (Savitzky-Golay 25 points), spectral range:  $1497\text{ cm}^{-1}$ – $317\text{ cm}^{-1}$ .

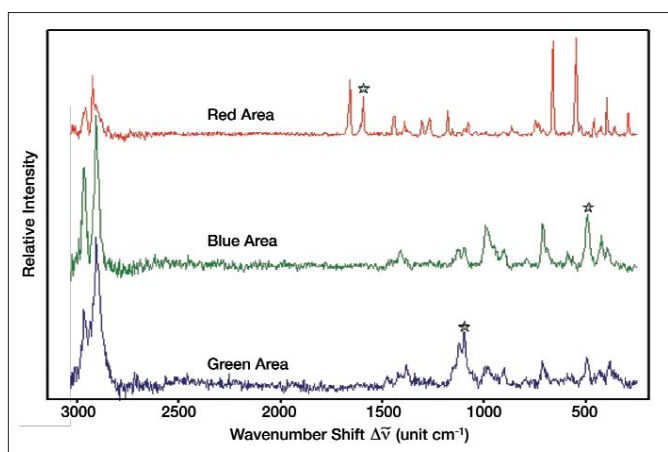


Figure 2. Representative spectra from the Imodium Advanced® caplet chemical image, peaks marked were used to construct the image.

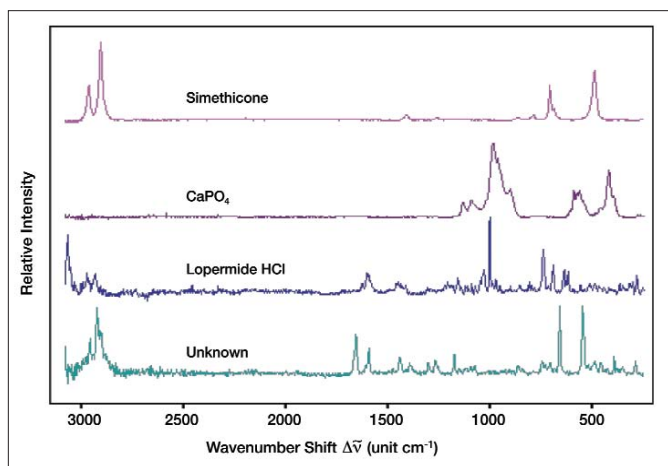


Figure 3. Representative spectra of the components used in the calibration training set.

This set of numerical concentration data is also displayed as a false color image in Figure 4. The image shows the variation in the concentrations of simethicone and  $\text{CaPO}_4$  across the caplet.

## Conclusions

Chemical imaging is an extremely powerful technique for characterization of solid dosage forms. The RamanStation 400 spectrometer allows large areas (tens of millimeters) to be mapped. The entire area is mapped with full coverage – rather than discrete, widely-spaced sample points. This data can be obtained rapidly with no compromise in spectral and spatial resolution while the Insight software allows quick and easy analysis of data using either univariate or multivariate (chemometrics) models.

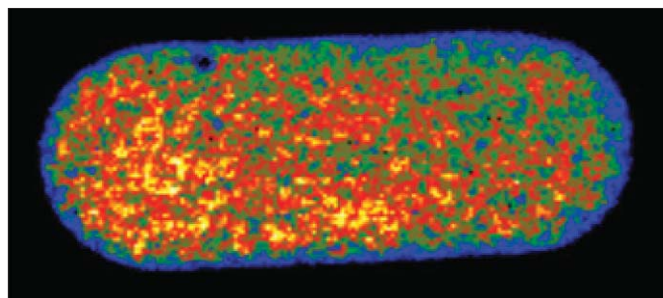


Figure 4. False color image of API in Imodium Advanced® caplet.

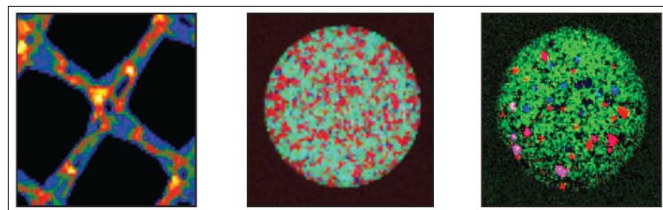


Figure 5. Selection of other chemical images.