eurofins | EAG Laboratories

APPLICATION NOTE

3D Confocal Raman Imaging of Pharmaceutical Creams and Tablets

Confocal Raman microscopy is a very powerful technique to analyse complex mixtures containing a range of different components. The focused laser used during Raman analysis enables the acquisition of images with a resolution (or pixel size) of 1µm. Furthermore, the confocal properties of the microscope allow the non-destructive acquisition of spectra from beneath the surface of the sample.

A very good use of Raman microscopy is for the analysis of pharmaceutical products to determine the spatial distribution of components of interest. This is possible on both solid materials such as tablets or on ointments, gels or creams that contain multiple components. The pharmaceutical industry is very concerned with determining both the spatial distribution of the active pharmaceutical ingredients (APIs) in their products and also the size of API particles or agglomerations in solid and liquid products. A good understanding of the distribution of the API (and any changes in distribution during storage/stability studies or during the lifetime of the product with the consumer) is essential since variations may affect the effectiveness of the product substantially. Such potential changes in products are also of extreme interest to regulatory agencies.

In this study, confocal Raman spectroscopy using a Horiba HR LabRam Evolution instrument, was used to investigate the distribution of two APIs in a semi-transparent cream.

An optical photo of the cream is shown in Figure 1. A 532 nm green excitation laser was used for the analysis, The cream has two different API's: A and B which can successfully be distinguished using Raman spectroscopy (Figure 2 top and bottom) since they have substantially different unique peaks. This allows us to produce 2D maps/images showing their distribution. The 2D Raman map reveals the particle distribution of each API, their shapes and the size of the API particles or agglomerations (Figure 2 centre).

Maps of both APIs can also be non-destructively acquired using confocal Raman spectroscopy at different depths within the sample: Examples of maps at 40 µm and 70 µm depth are shown in Figures 3 and 4. The distribution of the APIs vary with depth (as seen in a comparison of Figures 3 and 4) and is comprehensively presented in a 3D reconstruction of multiple confocal images (Figure 5).

As detailed above, it can be seen that Raman microscopy is a near-essential tool to successfully non-destructively investigate the distribution of APIs in pharmaceutical products.

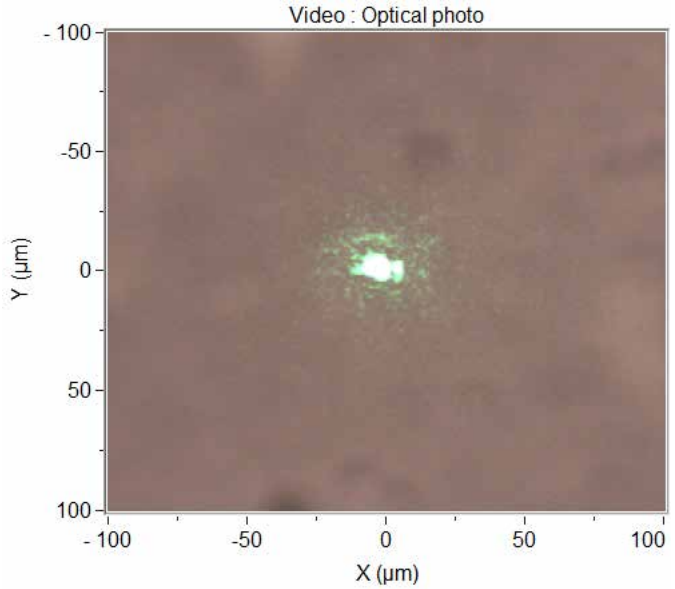

Figure 1: An optical photo of the cream

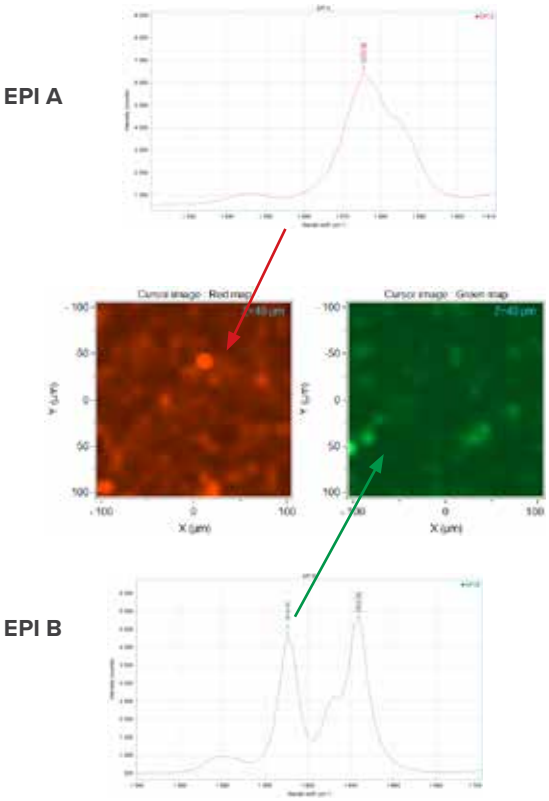

Figure 2: Raman spectra of APIs used for the 2D cream mapping

3D Confocal Raman Imaging of Creams and Tablets

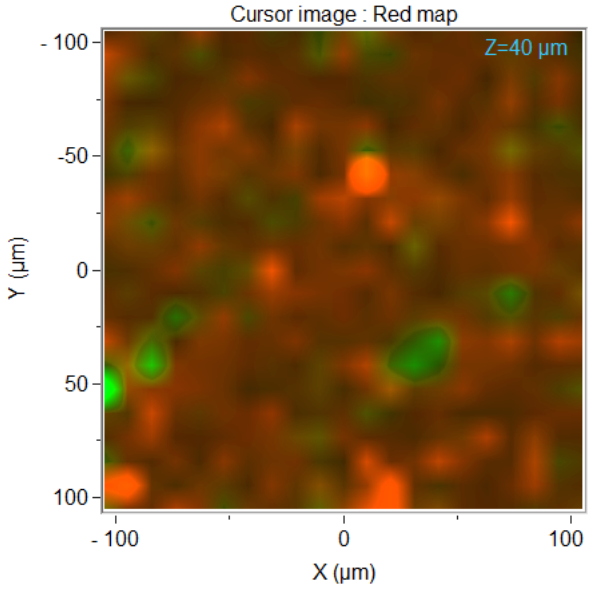

Figure 3: 2D mapping at 40 µm deep

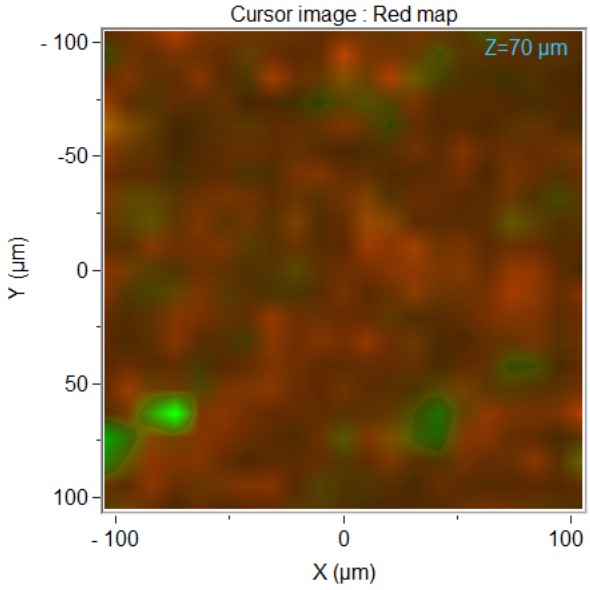

Figure 4: 2D mapping at 70 µm deep

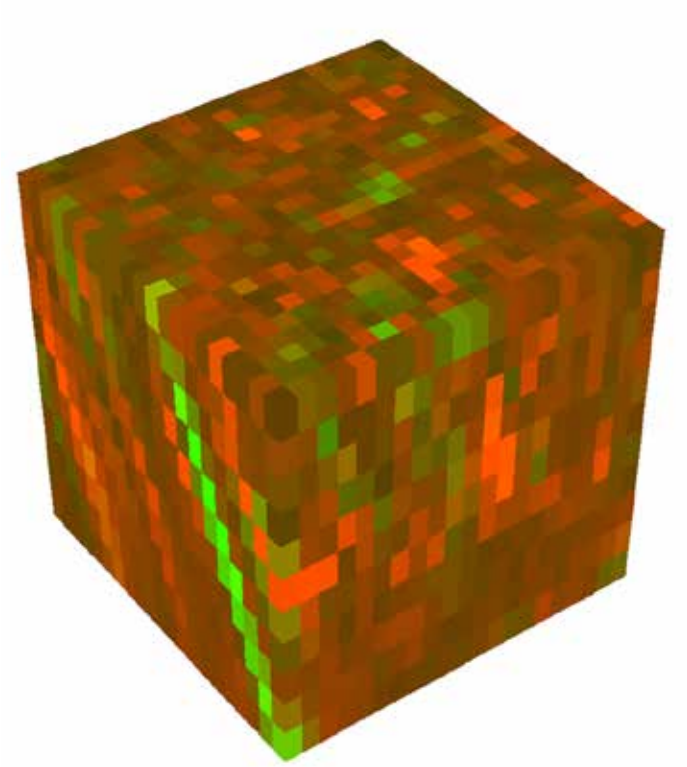

Figure 5: 3D mapping of the cream within a cube with 100 µm side. High-resolution 2D images can be obtained at any of the vertical steps into the sample.