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Raman Spectroscopy

Pharmaceutical compounds distribution and cosmetic products analyzed by confocal Raman spectroscopy

Application Note

Pharmaceutical & Cosmetic RA78

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Abstract: In the final step of the formulation process, pharmaceutical and cosmetic industries have to control their products to check if the compounds' distribution in the final product, or in its application form, i.e. dispersed on a skin for an intracutaneous product, are homogenous and stable in order to guarantee the product's efficacy. In this paper, we present why confocal Raman microscopy is an excellent tool for product characterization after formulation.

Keywords: Compounds distribution, Pharmaceutical, Cosmetic, Synthetic skin.

Introduction

During pharmaceutical and cosmetic formulation process, an important step is in the control of the distribution of the compounds once the product is designed in its final state. For example, in a pharmaceutical tablet, the size and distribution controls over a large area of the tablet are important for drug release control. That can be also applied on liquid products, like a nasal spray or oral suspensions. This specific subject is more detailed in Application Note (REF AN nasal spray). It also concerns the emulsions and creams commonly proposed by cosmetic companies. In that case, the point of interest is in the analysis of the distribution of the compounds after the application of the cream. In order to simulate skin, cosmetic manufacturers commonly use some rough PMMA slides.

This step in the control process is required so a technique is able to chemically characterize the product as they are, in a non-invasive and non-destructive manner. Thus, vibrational spectroscopies are well designed for such characterization. Moreover, confocal Raman microscopy is the perfect tool for this. Indeed, the micron resolution of this optical microscopy is required for a perfect characterization of small particles. The main interest of Raman microscopy also comes from the capability of this technique to be applied on any sample, with no need for preparation. Based on its very well resolved spectral bands, confocal Raman microscopy is also able to distinguish between a large amount of chemical products. In this paper, we demonstrate how confocal Raman microscopy is perfectly suitable for pharmaceutical and cosmetic characterization on final products. Thus we apply this technique on tablet characterization and cream on skin model distribution.

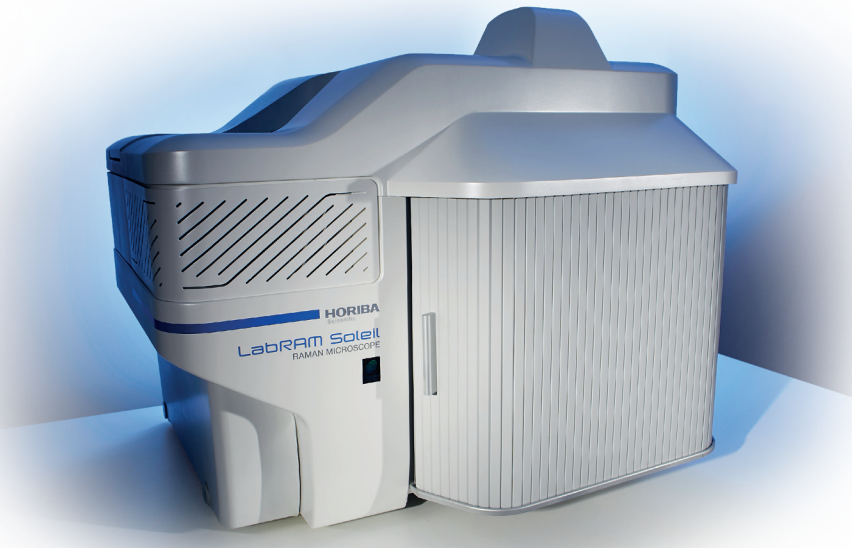

*Figure 1: HORIBA **LabRAM Soleil™** Raman microscope*

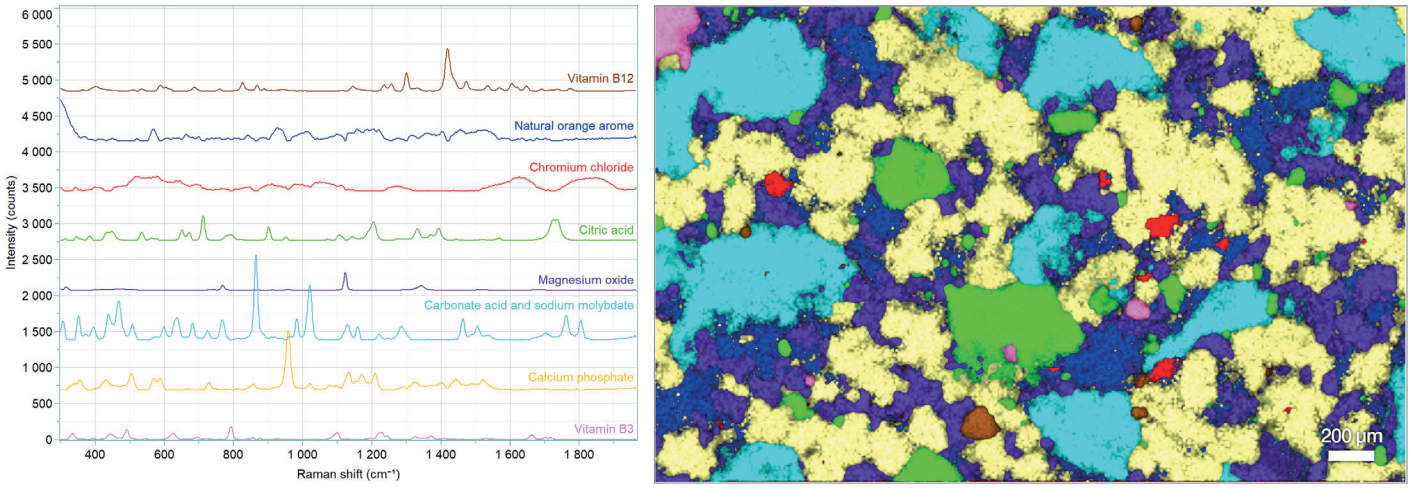

Figure 2: 8-vitamins tablet Raman mapping. Left: MCR spectra identified by the database. Right: Chemical distribution based on MCR decomposition. Scale bar: 200 µm.

Instruments and methods

Our HORIBA **LabRAM Soleil™** is a confocal Raman microscope offering the highest throughput in the market with no compromise on resolution. This is a consequence of the unique optical design of this microscope basedon dielectric mirrors, with very low signal loss, coupled with high quality gratings, our main expertise. These outstanding characteristics are required to obtain the best quality spectra needed for compounds analysis in final pharmaceutical and cosmetic products.

In order to differentiate the compounds presence in the product, the integrated *MVAPlus* multivariate tool is the solution. Including multiple algorithms, *MVAPlus* is able to analyze up to 4,000,000 of spectra to find the major compounds of a sample and display their distribution. Additionally, *ViewSharp* from *EasyNav* package is also used to analyzed rough samples as the skin model. With this tool based on the video image contrast, the focus on the sample is automatically adjusted on the surface of the sample.

All of these hardware and software features leads to the high quality information that we can take from a tablet or cream samples.

Two samples were analyzed. The first one is a commercial 8-vitamin pharmaceutical tablet. The second is a cosmetic cream spread on a rough PMMA slide used to simulate the roughness of skin.

Results

Controlling the compounds distribution is important in pharmaceutical and cosmetic products. Confocal Raman microscopy is the most appropriate technique to characterize such products in their final forms. First we analyzed an 8-vitamin pharmaceutical tablet in order to control the chemical grain sizes and distribution. A Raman map of a part of the tablet was so acquired. Applying the Multivariate Curve Resolution (MCR) algorithm from the *MVAPlus* tool, the reference spectra are obtained. They are then used to decompose each spectrum of the map and obtain the distribution of the compounds over the sample as shown in Figure 2. The compounds are automatically identified thanks to the direct link with the spectral database software *KnowItAll* from Biorad Laboratories. Based on these analyzes, a complete characterization of the compounds distribution characteristics is provided directly, and provides information about the quality of the distribution of the grains in the tablet.

Then, we analyzed a cream spread on a rough PMMA slide simulating skin roughness. Adjusting the focus automatically based on the topographical profile provided by the *ViewSharp* module, a Raman map was acquired on a large area to control the compounds spread over this area. The compounds distribution based on the multivariate analysis of the spectra is obtained easily, correlated with the topographical profile provided by the *ViewSharp* tool (Figure 3). Based on this map, it appears that the cream is homogeneously spread quite well on the surface as we observe a good mixture of the different compounds on the surface, and no specific area with only one compound. As for the pharmaceutical tablet, the compounds can be identified by comparing with the spectral databases.

Conclusion

Confocal Raman microscopy is an excellent technique to characterize the compounds distribution in solid products like a pharmaceutical tablet, where compounds are in grain form. In this case, Raman spectroscopy offers a complete chemical identification based on spectra, correlated with spatial and size distributions. In the same way, confocal Raman microscopy is an excellent tool to characterize compounds distribution of a cream spread on a rough surface, as skin typically is.

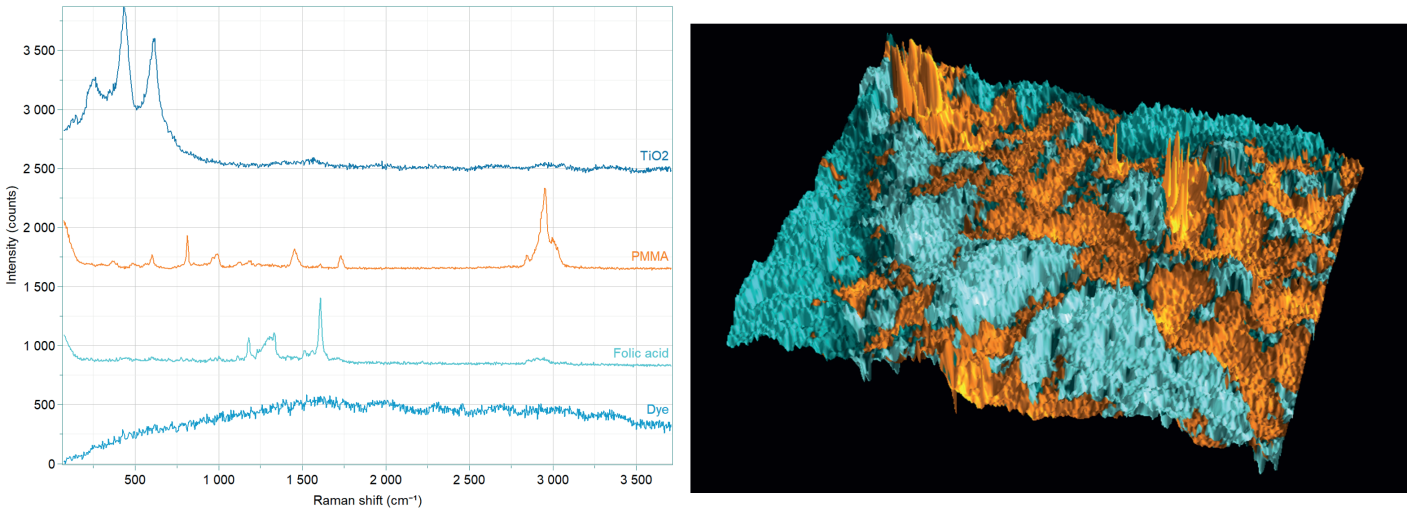

Figure 3: : Cosmetic cream spread on a synthetic skin Raman map. Left: Reference spectra. Right: Chemical compounds distribution based on CLS decomposition overlayed on the topographical image resulting from ViewSharp.

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