RamanFest November 09-10 2023 Paris FRANCE

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Low Frequency Raman microscopy for API polymorphisms analysis

Since the physical state can affect the pharmaceutical behavior of drug substances, it is important to know what controls crystallization, solid state reactions, phase stability, and solubility. There are numerous methods that have been used to measure the solid state composition of pharmaceuticals; these include X-ray diffraction, optical microscopy, thermal analysis, dissolution testing, particle size analysis, NMR, and infrared (IR) spectroscopy. Raman spectroscopy is a now a validated technique in this industry as a very powerful characterization technique.

Indeed, Raman spectroscopy can provide qualitative and quantitative information of the polymorphy, with 1 µm spatial resolution when necessary. The new generation in Raman technology provides many advantages over the other techniques. Thus, it is a non-destructive analysis, samples can even be examined in transparent glass or plastic containers. Microscopic samples as small as 1µm can be easily characterized, and finally little or no sample preparation is required. Moreover, polymorphic and pseudo-polymorphic phases in microscopic samples can be mapped. This last point is important as the pelletizing can create pressure-induced polymorphic transformation.

By definition, the differences between two polymorphic phases is in the crystal modes, which can be characterize on the low Raman frequencies region. That increases the difficulty for the discrimination of the phases. Thanks to the standard Super Low Frequency standard module available on LabRAM SoleilTM, it becomes easy to reach 30 cm-1 frequency, and so to characterize polymorphisms without additional options. This provides so low frequency spectra with no intensity compromise.

In this presentation, we present an example of polymorphisms characterization by Raman microscopy using the Super Low Frequency module.

Figures

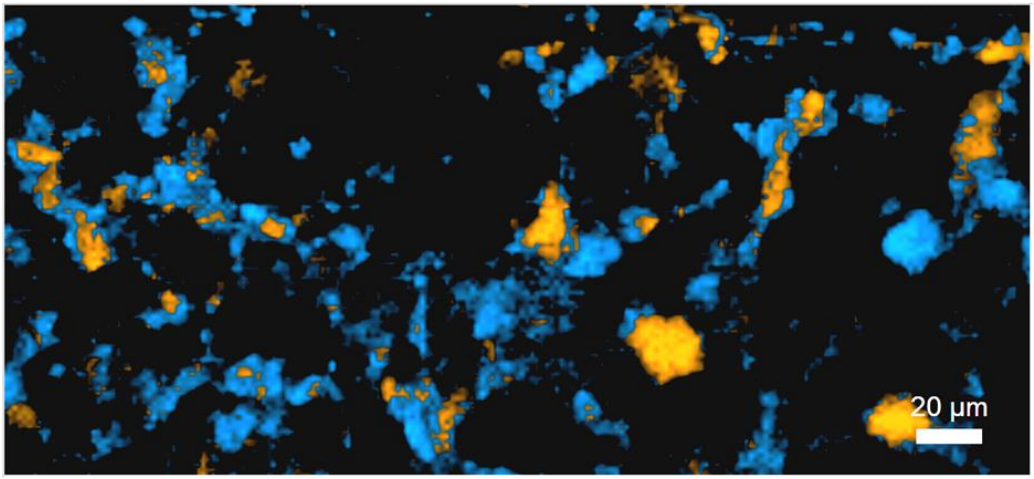

Figure 1: Carbamazepine distribution in tablet (blue: Form I, orange: Form III, black: excipients)