

Characterisation and Mapping of active pharmaceutical ingredients and excipients in a tablet BY RAMAN and infrared spectroscopy on the same microspectrometer

Aim of the measurements

The objective of the measurements is to identify the unknown components and their respective dispersion within pharmaceutical tabs by Raman and FT-IR microspectrometry.

Conditions of measurements :

The LabRAM IR provides a unique functionality to collect Raman and infrared spectra on the same microscope. This strongly facilitates the operation and handling of the samples.

The Raman spectra have been acquired by using an excitation at 633nm.

The IR spectra have been acquired by using an ATR objective and the spectral resolution is 4 cm^{-1} . The spectra have been adjusted taking account of the effect of depth penetration.

Identification of the different ingredients

Several point measurements have been carried out in different areas of the sample and two typical spectra have been obtained. The main Raman bands have been pointed out and a spectral search using an electronic library enables to identify the components characterized by these two spectra (Fig.1) as being Lactose and Starch.

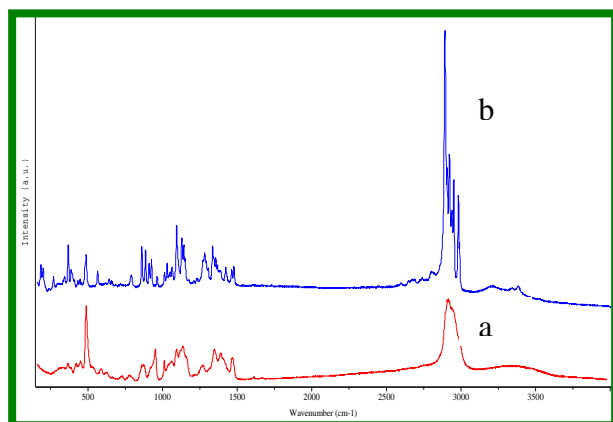


Figure 1: Spectrum recorded on the tablet and assigned to starch (a) and lactose (b). The spectra have been translated in the y axis in order to make the comparison easier.

In order to improve the chemical description of the sample, a Raman mapping has been acquired on the area presented below (Fig.2). The area is $35 \times 35\text{ }\mu\text{m}^2$ large and one spectrum has been recorded every $1\text{ }\mu\text{m}$.

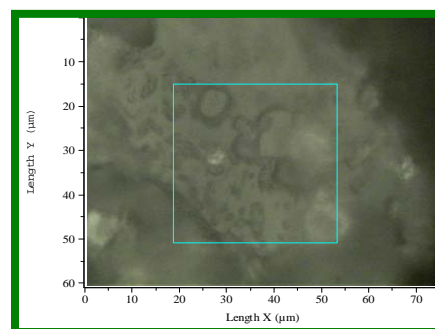


Figure 2: Video image of On each spectrum, the area of the bands characteristic of starch and lactose are calculated. Then the Raman mapping (Figure 3) shows the spatial distribution of the compounds and allows us to identify another ingredient characterized by the spectrum plotted Fig.4. For this third spectrum, the spectral library did not identify the component. However, some useful information can be extracted from this spectrum as the main Raman band pointed out at 1005 cm^{-1} characterizes a substituted aromatic group.

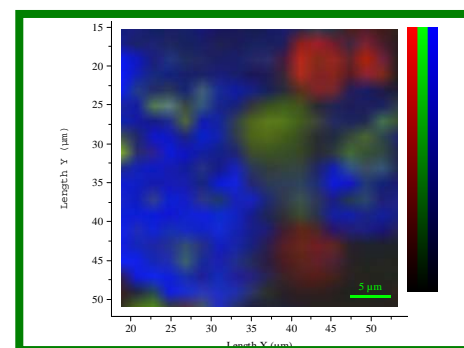


Figure 3: Map recorded on the surface defined Fig.2. The color scale displays the area of a band characteristic of starch (red), lactose (green) and a third component (blue) which spectrum is reported Fig.4.

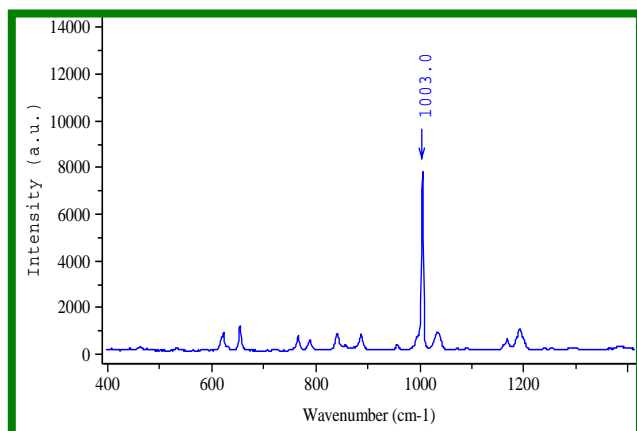


Figure 4: Spectrum recorded during the Raman mapping and characterising a third component in the tablet.

Some complementary measurements have been made by FTIR:

Complementary FT-IR measurements

Spectra have been measured in different areas of the sample and the two spectra displayed below could be obtained.

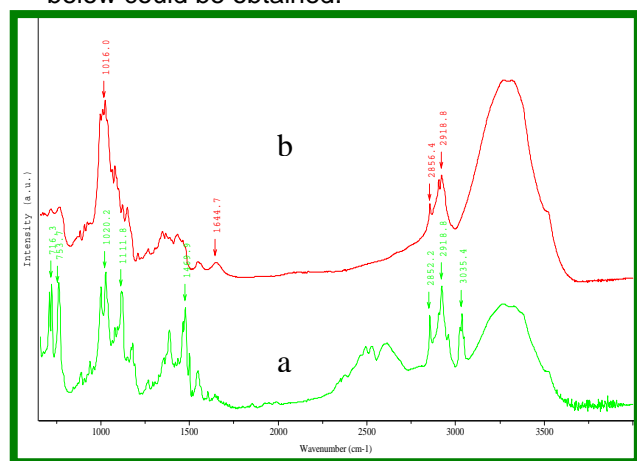


Figure 5: Two characteristic FTIR spectra obtained on different points of analyse on the tablet.

FTIR spectrum (b) can be correlated to our reference spectrum of lactose.

This FTIR measurement confirms the results obtained by the Raman mapping technique showing that the lactose is present.

On spectrum (a), some additional bands can be noticed. In particular, the infrared bands around 3030 cm^{-1} are due to the stretching vibration of C-H bonds in alkenes or aromatic compounds.

A subtraction has been made between the two spectra to extract the IR spectrum of the unidentified third entity (Fig. 6). That allows us to make a spectral search and identify the spectrum as characteristic of diphenhydramine.

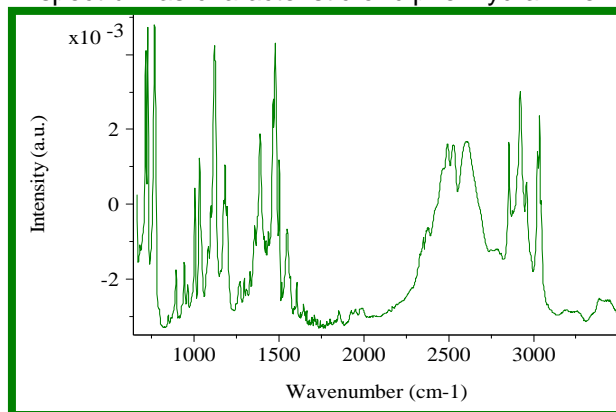


Figure 6: Subtraction of spectra (a)-(b) of Fig. 5.

Conclusion

The different components of this pharmaceutical sample can be characterized easily by Raman spectroscopy and the comparison with spectra from our libraries allowed us to identify some of these molecules. A good spectral discrimination could be obtained as the characteristic spectral fingerprints have exclusive features. The Raman imaging technique is a very powerful tool as shown here, as it also enables to characterize the spatial distribution of the components with a high spatial resolution.

The complementary results obtained by FTIR spectroscopy on the sample confirm the presence of lactose and allows the identification of the third component also observed by Raman spectroscopy.

The combination of FTIR and Raman analysis on the same spectrometer represents a powerful analytical tool to readily record both IR and Raman vibrational information from a same sample position.