

alpha500 - Large Area Scans on Tablets

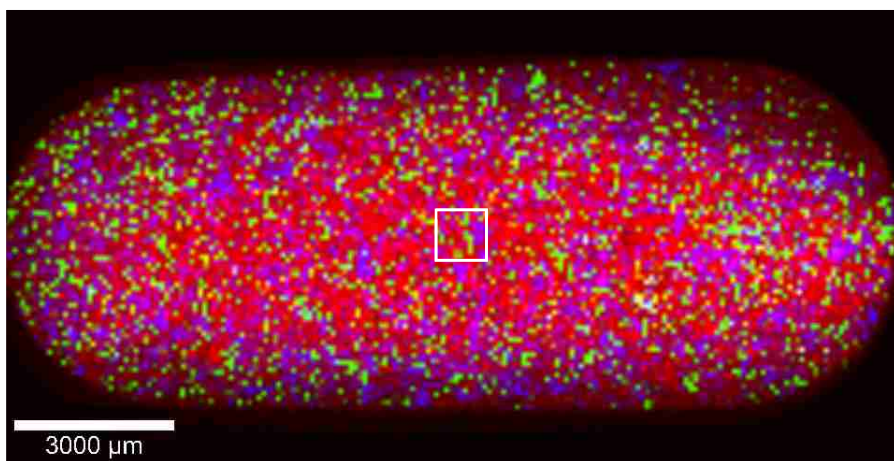
Knowledge of chemical components and their distribution in a tablet or any other solid medical product is of immense importance for R&D as well as quality control in the pharmaceutical industry. Confocal Raman Microscopy provides the ability to non-invasively map the chemical properties of samples such as these with highest resolution. Large area scans performed using the alpha500 or alpha700 Confocal Raman Imaging systems allow large samples to be imaged in order to produce an overview of the distribution of the chemicals across an entire tablet.

Acetylsalicylic acid (ASA, Aspirin) Tablet

The experiments presented here examined two tablets of Acetylsalicylic acid, commonly known as ASA or Aspirin. Using an alpha500 system, spectra were recorded with true confocal (diffraction limited) resolution at every image pixel. In order to optimize the signal to noise ratio, fit procedures can be performed by the integrated software tools. From a small region of interest, a basis spectrum is generated by averaging all spectra within this area. The basis spectrum can be fitted to the measured spectra, resulting in an optimized image.

Three images, obtained by the fit procedure for each scan were combined into the colored images shown in Figs. 1 and 2.

Tablet A was imaged with 200 x 100 pixels and the total scan range was 18 x 9 mm. In Fig. 1 the ASA component is shown in red, while the excipient is color-coded in green. The blue part may be an ASA in a different configuration. The corresponding spectra are shown in Fig. 1d. Figs. 1b and 1c show zoomed in images of the marked areas. In Fig. 1b the scan range was 1 x 1mm, in Fig. 1c it was 80 x 80 µm, at 150 x 150 pixels.



1a

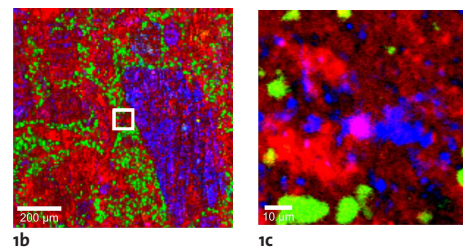


Fig. 1a: Large area Raman scan of a ASA tablet. Scan range: 19 x 9 mm, 200 x 100 pixels; **1b:** Zoom-in of the marked area in Fig 1a, 1x1 mm, 150 x 150 pixels; **1c:** Zoom in of the marked area in Fig 1b, 80 x 80 µm, 150 x 150 pixels.

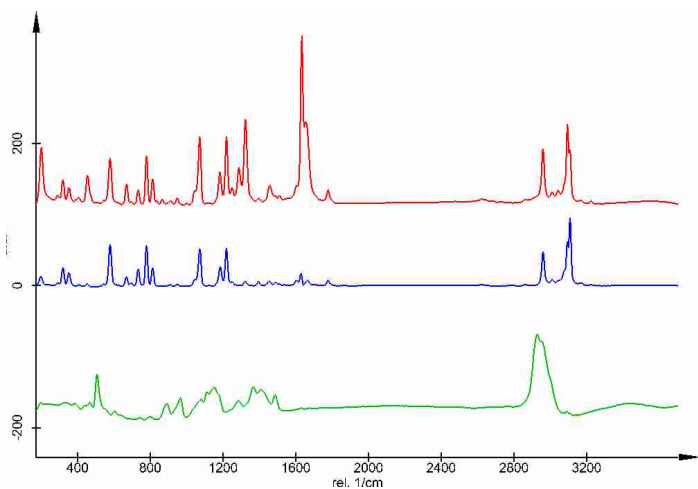


Fig.1d: Corresponding Raman spectra.

Tablet B was imaged with 200 x 200 pixels and the total scan range was 12.5 x 12.5 mm (Fig 2a). The ASA is again shown in red while the two excipients are shown in green and blue. Fig. 2b shows the corresponding spectra.

It is interesting to note that the two Aspirin tablets from two different manufacturers show such dramatic differences. First, tablet A seems to show a much higher

concentration of ASA relative to the excipients when compared to tablet B. Second, Tablet A seems to show two configurations of ASA, while tablet B shows only one form.

Large samples, such as the tablets imaged, are virtually always tilted relative to the scanning plane. This could in general cause one side of the image to be out of focus. In order to compensate for this, the WITec Control software allows the user to define

the scan plane before the scan by focusing on three points. The tilt of the focal plane is then calculated and automatically compensated for during the scan.

After acquiring the large area overview scans the alpha500 additionally allows to define an arbitrary number of sample positions on the tablet for automatically image these positions at the highest resolution (as seen for example in Fig. 1c).

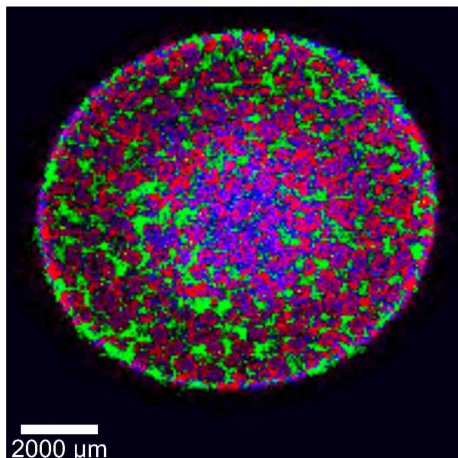


Fig. 2a: Large Area Raman image of ASA tablet (tablet B), scan range: 12.5 mm x 12.5 mm, 200x200 pixels (=40,000 spectra).

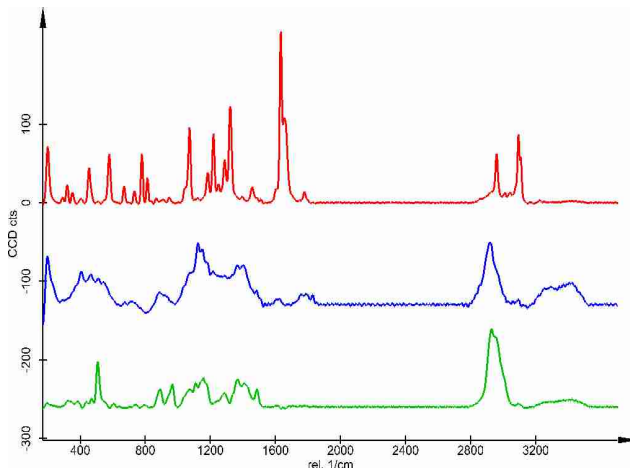


Fig. 2b: Corresponding spectra of the compounds contained within the tablet.