Application Brief

Pharmaceuticals

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Agilent 8700 Laser Direct Infrared (LDIR) Chemical Imaging System for Identifying and Detecting Salt Exchange in Pharmaceutical Tablets

Introduction

Active pharmaceutical ingredients (APIs) in tablets need to maintain their chemical state (acid, base or salt form) and structure to achieve their expected therapeutic effects. APIs often transform from the acid or base form to a salt or vice versa due to imperfect packaging and/or environmental conditions. This unwanted conversion can significantly affect tablet dissolution, stability, and bioavailability.

The Agilent 8700 LDIR Chemical Imaging System can detect and identify salt exchange in tablets and is a fast and effective tool for troubleshooting and formulation development studies.

Key Benefits of Agilent 8700 LDIR Chemical Imaging System

- The 8700 LDIR provides fast molecular imaging, using only a few diagnostically important wavelengths to effectively image each tablet constituent. A comprehensive chemical image of an entire tablet takes only minutes. This allows more tablets to be analyzed in greater detail, in less time.
- An image can be acquired at any spatial resolution without the need to change objectives or refocus the instrument. This is critical, as it permits a rapid whole tablet scan to find regions where salt exchange has occurred and then rapidly perform additional high resolution imaging of the local chemistry in those selected areas.
- Infrared spectra are easy to interpret and extensive libraries enable spectral identification.
- The 8700 LDIR is equally sensitive to both APIs and excipients and is unaffected by fluorescence effects, allowing comprehensive imaging of all constituents in a sample.
- Integrated Attenuated Total Reflection (ATR) sampling is fully automated for unknown component identification and imaging down to 0.1 micron pixel size.

- The speed of analysis minimizes unwanted exposure of tablets to humidity, producing more reliable and reproducible results.
- As the 8700 LDIR is highly automated and easy to use, it is an excellent “walk-up” imaging system for users with a range of expertise who are involved in drug formulation development, stability determination and troubleshooting.
- Reduced running costs and maintenance with no need for liquid nitrogen.

Analysis Example: Salt Exchange in Over-the-Counter Indigestion Tablets

When an indigestion relief tablet is exposed to humidity or moisture, the citric acid converts to sodium citrate salt in the presence of sodium bicarbonate, producing water and carbon dioxide as by-products. These by-products may cause tablets to crumble and discolor over time as well as lose their therapeutic effect. By focusing on automatically selected wavelengths that best discriminate between these constituents, LDIR can rapidly produce an image showing their distribution, as shown in Figure 1.

LDIR imaging was used to identify and monitor salt exchange (sodium citrate formation) in a tablet exposed to room humidity. The interface where salt formation occurs and grows is evident in the image of the tablet taken after exposure to ambient humidity for a few hours (Figure 2, top) and after a full day (Figure 2, bottom). The formation is clearly indicated by the increase in domain size of sodium citrate (aqua color) around citric acid (yellow color).

To identify a salt, any pixel of interest may be selected and a fingerprint region spectrum can be obtained in one second before matching with library spectra. Using the automated classification analysis, the distribution of constituents on the surface of tablet can be visualized. This provides a rapid way to observe the changes in the constituents in a tablet exposed to humidity.

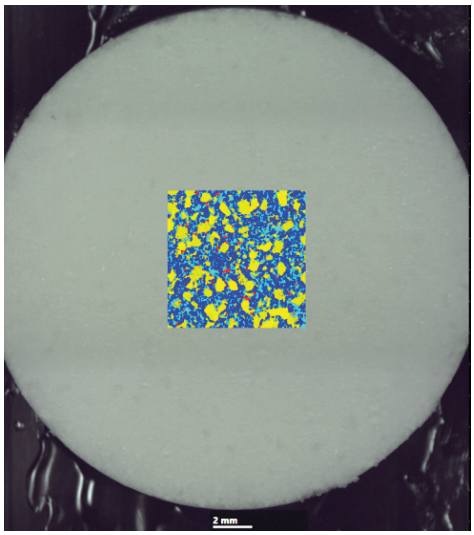

Figure 1. Excipients and APIs present in a pharmaceutical tablet cannot be distinguished in a visible light image. Laser direct infrared imaging reveals the distribution of each chemical in minutes, as shown here in the 7 mm × 7 mm center of the tablet.

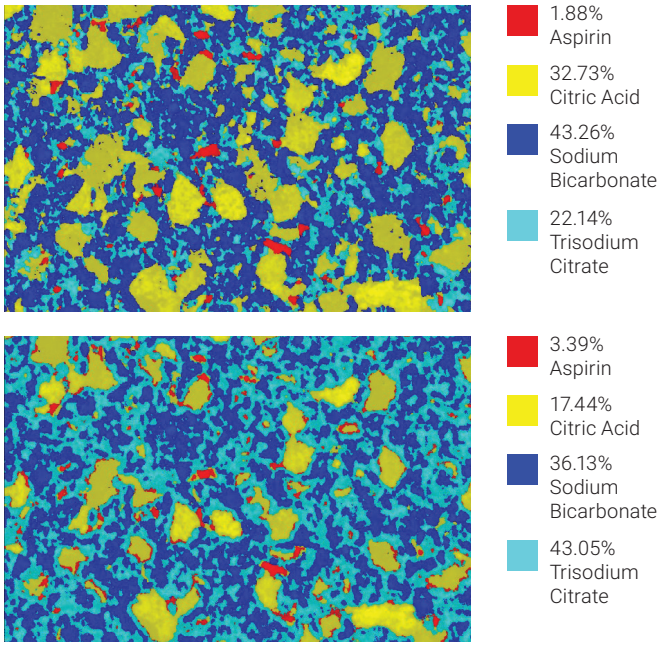

Figure 2. Top: LDIR chemical image of the central region of the tablet after it was microtomed and exposed to ambient humidity for two hours. Bottom: The same area after 24 hours of exposure. Each image is 7 × 7 mm and shows four constituents. Each image was acquired in only 11 minutes at 10 µm pixel size.

www.agilent.com/chem/8700-ldir

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