



Bringing Clarity and Unprecedented Speed to Drug Formulation

Agilent 8700 Laser Direct Infrared (LDIR) Chemical Imaging System



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Chemical Imaging of Solid Dosage Forms

During pharmaceutical solid dose formulation development, factors such as salt exchange, polymorphism, hydration, temperature, and pressure affect tablet dissolution, stability and even therapeutic efficacy.

Molecular spectroscopy techniques such as Raman, FTIR and NIR imaging are often used to visualize the distribution of ingredients in solid dose (tablet) formulations. The resultant images are used to troubleshoot issues that may arise in production of the tablet or to support drug formulation. Unfortunately, these traditional spectroscopy techniques often require considerable time to obtain a detailed image as well as a high level of user expertise. This means chemical imaging of tablets is typically available only to expert spectroscopists.

The Agilent 8700 Laser Direct Infrared (LDIR) Chemical Imaging System

The Agilent 8700 Laser Direct Infrared (LDIR) Chemical Imaging System is the first chemical imaging system that enables non-experts in infrared microscopy to get the data they need to support solid dosage form development and to ensure effective quality control.

The intuitive Agilent Clarity software and user interface of the 8700 LDIR simplifies and automates the numerous steps required to obtain a detailed, high resolution tablet image. The speed and resolution of the system enables tablets to be imaged far more rapidly and in greater detail than with conventional FTIR or Raman imaging. In addition, the 8700 LDIR is equally sensitive to both active pharmaceutical ingredients and excipients, without the problem of fluorescence that can hinder Raman imaging.

The 8700 LDIR provides a faster and easier way to assess the effects of physiochemical properties on drug performance and formulation development.

Advantages of the 8700 LDIR for Simplified Tablet Imaging

Agilent's innovative design uses Quantum Cascade Laser (QCL) light to create exceptional chemical images. Other chemical imaging techniques cannot offer the combination of analysis speed, flexible field of view, variable resolution and ease-of-use available with the 8700 LDIR.

The Agilent 8700 LDIR offers the following advantages over conventional FTIR or Raman imaging:

- Laser Direct Infrared (LDIR) provides a rapid and simplified path to chemical imaging. Only a few key wavelengths are measured to visualize individual components in each tablet. A full tablet scan takes just a few minutes.
- More tablets can be analyzed in greater detail, in less time, which leads to better informed and faster decisions, saving time and money.
- After an initial high-speed scan of the whole tablet, specific areas of interest can be scanned at higher resolution, all without changing objectives or refocusing.

Analysis using the 8700 LDIR is straightforward and highly automated with an intuitive user interface, ensuring reliable and meaningful images.

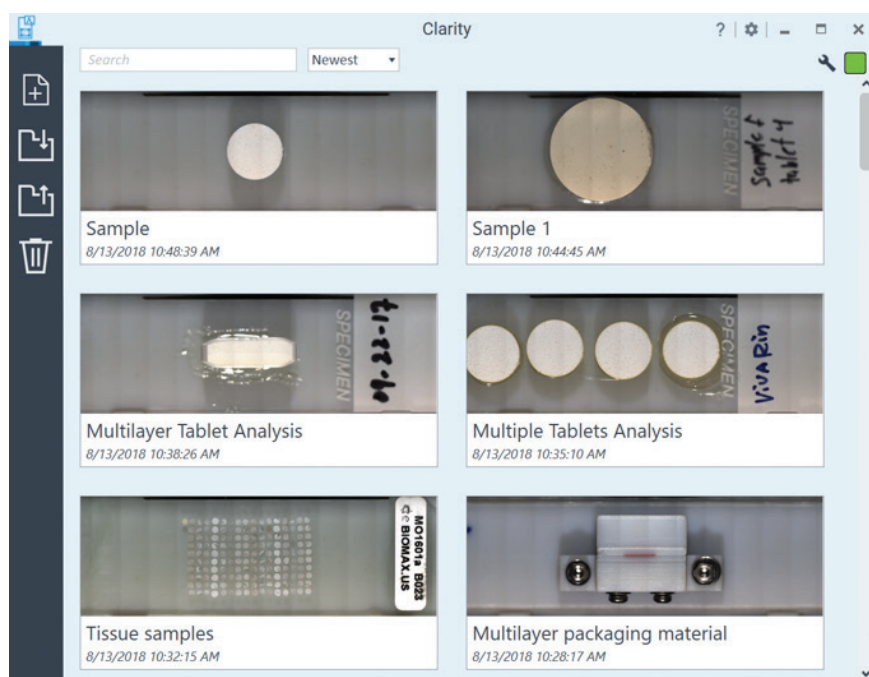



Figure 1. The Agilent Clarity LDIR software interface features intuitive software icons with tool tips to guide the user, e.g.  start a new sample analysis. To display the tool tips, hover the mouse pointer over the icons.

The green status indicator in top right means instrument and software are ready to use.

Benefits of LDIR Imaging with the 8700 LDIR

- Aids in correlating physicochemical effects with therapeutic effectiveness in product development and assessing overall stability.
- Enables a better understanding of tablets differences which may arise in a single batch or between different production batches.
- Automated Attenuated Total Reflectance (ATR) sampling ensures quick identification of contaminants and unknowns using standard library searching.

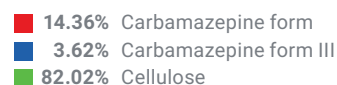
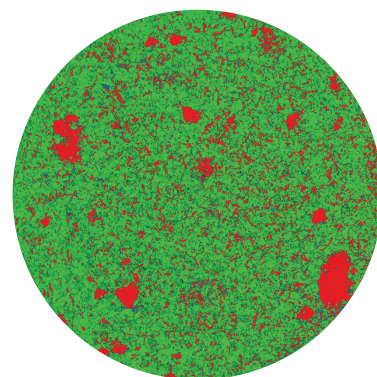


Figure 2. A chemical image showing the constituent distribution across the surface of a carbamazepine tablet.

Typical 8700 LDIR Workflow for Tablet Analysis

Step 1: Create a spectral library of tablet constituents:

1. Press a pellet of each pure constituent present in the tablet.
2. Attach up to 5 pellets on a slide and load into 8700 LDIR instrument.
3. The 8700 LDIR automatically:
 - a. Loads the slide.
 - b. Provides a visible image mosaic of the slide.
4. Double click on one of the constituents to focus the IR beam.
5. Select an area in the pellet and simply click on the spectral survey icon.

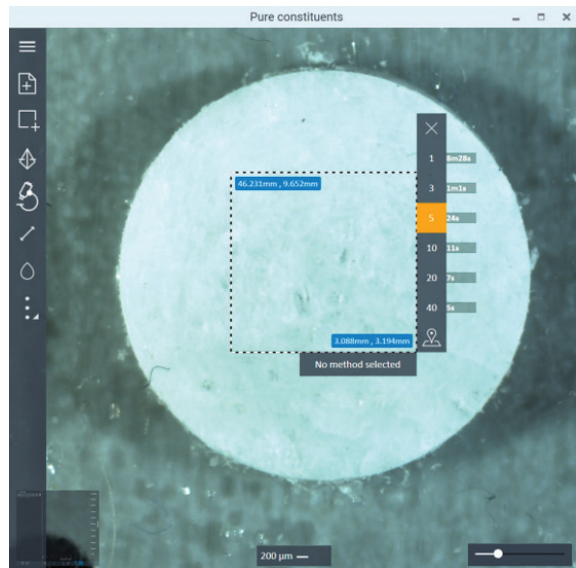


Figure 3. Click on the survey scan icon to start the library spectra collection.



Figure 4. Selection of reference spectra for pure constituents from the library.

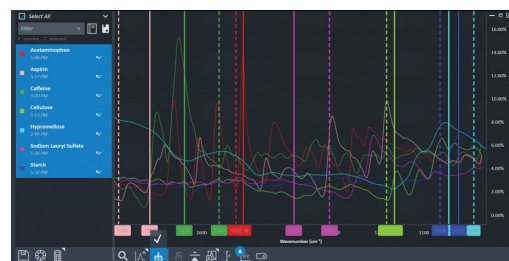


Figure 5. Automated wavenumber selection for each constituent by the software. Solid lines indicate peak points and broken line indicate baseline point selections for each constituent.

6. The Agilent Clarity software records a preconfigured number of spectra and averages them to create a spectrum.
7. After collecting survey spectra for each constituent, name the constituent spectra and add to the library. The spectra are ready to use for creating the method. Eject the pure constituents sample and load the tablet sample for analysis.

Step 2: Build a chemical imaging method to perform tablet analysis

8. Select the library spectra of the pure constituents of tablet to be imaged (see Figure 4).
9. Click on the 'classification' icon to create the method. The software automatically selects wavenumber for each constituent that maximize the image contrast between the constituents. Save the method. (See Figure 5).
10. Select the region to be imaged, either the whole tablet or small region of interest. The Agilent Clarity software will indicate the time required to map all the constituents at different pixel sizes (resolution).
11. Select the pixel resolution for imaging the tablet.
12. The Agilent Clarity software automatically acquires data and displays the spectral image of the tablet with mapping of individual constituents in different colors and calculates the surface concentration for each constituent (see Figure 6).

For the tablet with same constituents, simply load the saved method and start the analysis. The process is similar for new tablet analysis with different constituents.

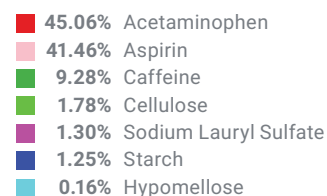
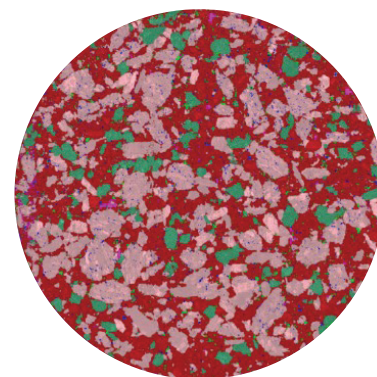


Figure 6. A high spatial resolution chemical image of a generic headache tablet consisting of three APIs (acetaminophen, aspirin and caffeine) and four excipients. All seven components were imaged across the entire tablet (11 mm diameter) with 10 micron pixel size in only 1 hour.

Agilent Sample Planer

The Agilent Sample Planer is used to prepare samples for analysis using the Agilent 8700 LDIR Chemical Imaging System. Preparing a flat surface has never been easier.

- Prepares flat sample surfaces.
- Simple manual adjustment to control sample thickness.
- Requires no power supply enabling portability.
- Maintenance free.



For more information, visit:

www.agilent.com/chem/8700-lidir

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