

## Powder Moisture Analysis Using FT-NIR

Controlling the production process and using quick and reliable methods of quality control can help to improve product quality.

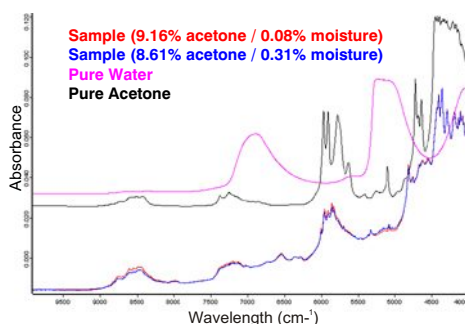


Manufacturing a pure product can be critically important to the next steps in the manufacture of a drug product. As a result the removal of residual moisture and solvents from the crystallization, filtration and drying steps can be crucial to producing a stable product. A quick and reliable method of analyzing samples for moisture and residual solvent compared with the traditional time-consuming moisture analysis method (Karl-Fischer titration method or loss on drying) and solvent analysis method (headspace GC analysis) would therefore be preferable. Near-infrared spectroscopy can be used as a substitute for these methods because it has high sensitivity, especially to moisture, is fast and non-destructive and has a high degree of automation, enabling analytical departments to save considerable time and resources.

The spectrometer used in this study was the new *MPA*<sup>TM</sup> (Multi Purpose Analyzer) FT-NIR spectrometer, which is designed to bring flexibility into analytical laboratories. Its versatile and modular concept combines up to four different measurement techniques. The user can decide for each measurement whether to use the classical sample compartment, a fiber optic probe, an integrating sphere or the transmission unit with an automated sample changer – all fully software controlled. The *MPA*<sup>TM</sup> combines the highest performance and outstanding flexibility on a small footprint with an intuitive and easy to operate interface, making it an ideal tool for daily laboratory work, as well as for more detailed method development.

### Experimental

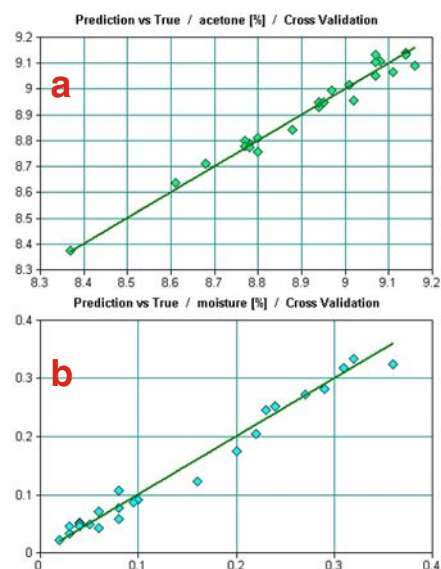
The objective of this study was to demonstrate that FT-NIR can be used to determine the moisture and acetone content in an active pharmaceutical ingredient. An *MPA*<sup>TM</sup> laboratory FT-NIR spectrometer with the integrating sphere module and a 30-position autosampler was used to measure 25 powder samples, with known reference values stored in individual 22mm glass vials.



**Figure 1** FT-NIR absorption spectra (10000-4000  $\text{cm}^{-1}$ ) of two powder samples with different moisture and acetone contents. The spectrum of pure acetone and water are shown offset. The spectral differences at around 8500 and 5100  $\text{cm}^{-1}$  can be directly correlated to the different moisture/acetone contents of the two samples.

The integrating sphere is an excellent accessory for measuring diffuse reflectance spectra of heterogeneous powders due to the large measurement area (2.25 $\text{cm}^2$ ). Samples with moisture and acetone in the range 0.02-0.36% and 8.37-9.16%, respectively were analyzed. In this example the vials were placed on the autosampler and 64 scans (~50s) were collected at a resolution of 4  $\text{cm}^{-1}$ . Spectra of two of the powder samples are shown in Figure 1 along with spectra of pure acetone and water. The spectral

differences at around 8500  $\text{cm}^{-1}$  and 5100  $\text{cm}^{-1}$  can be directly correlated to the different moisture/acetone contents within the two samples. The PLS calibration model results are shown in Figure 2 where a prediction accuracy of 0.017% is achieved for moisture and 0.032% for acetone.



**Figure 2** Cross validation results of PLS based models for the prediction of moisture (a) and acetone (b) show excellent correlations. Moisture ( $R^2 = 97.6$ , RMSECV = 0.017%), Acetone ( $R^2 = 97.2$ , RMSECV = 0.032%).

### Quantitative analysis

Near-infrared spectra result from combination and overtone bands of C-H, N-H, O-H.. vibrations. Since most solvents and moisture contain at least one of these bonds, they are ideal for near-infrared analysis.

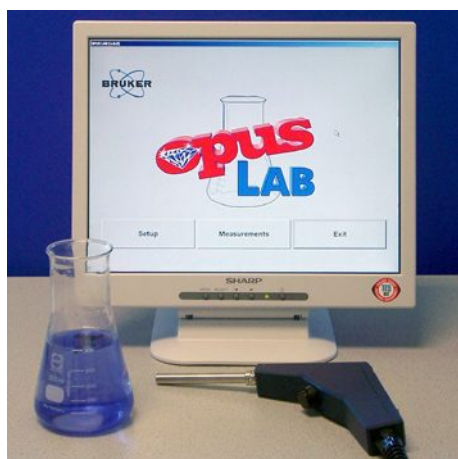


Figure 3 OPUS/LAB, easy set-up for routine measurements and subsequent evaluation

The OPUS/QUANT quantitative analysis software package uses partial least squares (PLS) to develop quantitative models. Calibration model development requires measuring the FT-NIR spectra of multiple samples containing a range of concentrations of the components of interest. The unique Quant self-optimisation routine is then applied to develop the calibration model. The results of this study (shown in Figure 2) clearly demonstrate the capability of FT-NIR for this application with cross validation accuracies (RMSECV) of 170ppm for moisture and 320ppm for acetone.

**Measurement options**

Bruker Optics offers a wide variety of laboratory and process instrumentation to meet your specific needs.



Figure 4 Placing a sample cup onto integrating sphere of the MPA™ FT-NIR analyzer.

Multi purpose FT-NIR analyzer MPA™ offers a simple transmission option (heatable if required) for liquid materials that uses disposable glass vials. Alternatively, a liquid transmission fiber optic probe can be used. For solids we offer several different solutions. Powders can be sampled with either a diffuse reflectance powder probe or with an integrating sphere and a 22 mm vial autosampler. For inhomogeneous materials an integrating sphere with a 50 mm or 97 mm rotating cup assembly would be recommended. Tablets can be measured using the tablet transmission option.



Figure 5 Vial autosampler for the MPA™ FT-NIR spectrometer.

**Implementation**

In a QC laboratory environment the MPA™ can be used along with our user-friendly OPUS/Lab software, which not only performs the measurement but also automatically performs the analysis of unknown samples. In addition, this software allows an identity test to be combined with a quantitative analysis such as moisture content, purity etc.

**Laboratory Preferred Configuration**

- MPA™ FT-NIR Spectrometer
- Fiber optic probes
- Sample compartment
- Tablet Transmission
- Integrating Sphere
- Autosampler



Figure 6 MPA™ FT-NIR Spectrometer

**Advantages of MPA™ FT-NIR Spectrometer**

- Easy to use
- 30 position autosampler
- Fast, reliable, precise and accurate results
- Low operating costs
- Modular design
- Easy maintenance
- Pre-aligned optical components
- 21CFR11, GMP, GLP Software compliance

For more information contact us:



**USA**  
 Bruker Optics Inc  
 + 1 978 439-9899  
 www.brukeroptics.com  
 pat@brukeroptics.com

**Europe**  
 Bruker Optik GmbH  
 + 49 7243 504-600  
 www.brukeroptics.de  
 info@brukeroptics.de

**Asia**  
 Bruker Optics Asia Pacific Ltd.  
 + 852 2796-6100  
 asiapacific@brukeroptics.com.hk