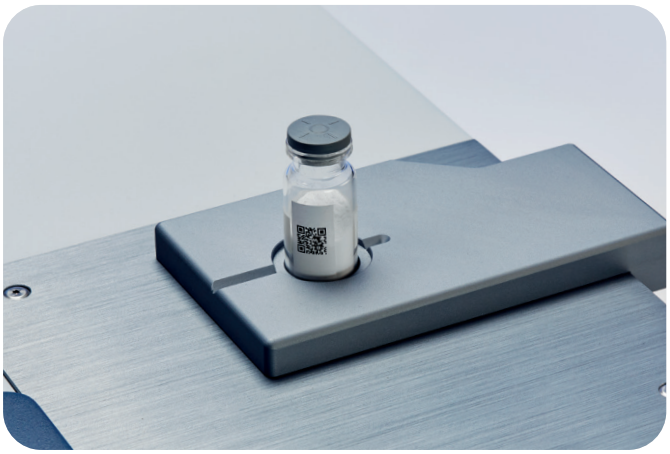


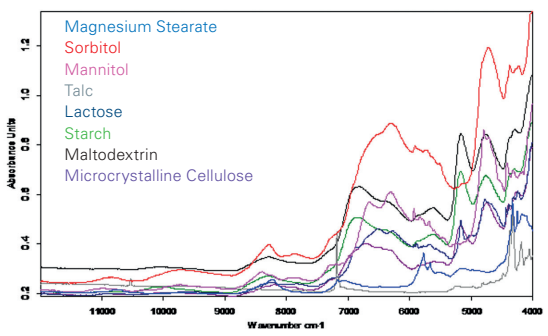
Application Note AN N510

Pharmaceutical Raw Material Identification

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

Increased efficiency reduces the cost of manufacturing the drug products derived from the raw materials, thereby making these products available to end users at a lower cost. Pharmaceutical companies often deal with a large number of raw materials and, without careful monitoring, confusion between similar / mislabeled substances can easily occur. In addition, before they can be used in the production process incoming raw materials may also have to be tested to see that they meet certain specifications, such as moisture content, purity etc. Therefore the manufacture of high quality pharmaceutical products requires two steps of initial quality analysis: identification of the incoming raw materials and quantitative analysis of the raw materials. For both of these steps, near-infrared (NIR) spectroscopy has proven to be an easy-to-use and powerful tool.

Figure 1



FT-NIR absorption spectra (12,000-4,000 cm-1) of eight common pharmaceutical excipients measured through glass vials.

Near-infrared spectra can be collected directly from both solids and liquids with no sample preparation. The measurements can often be made non-invasively and non-destructively through disposable glass vials. High quality spectra can be collected in a few seconds and the NIR analysis is generally more accurate than wet chemical methods. Moreover, in contrast to the time-consuming wet chemical analysis, the NIR method produces no waste, requires no chemical reagents, and is therefore quick, simple and cost-effective. In addition, a variety of sampling accessories are available, such as liquid and solid fiber optic probes, integrating sphere, disposable liquid vials and autosamplers. All of these factors make NIR spectroscopy a quick, reliable and inexpensive analytical method for QA/QC work in the pharmaceutical industry.

Experimental

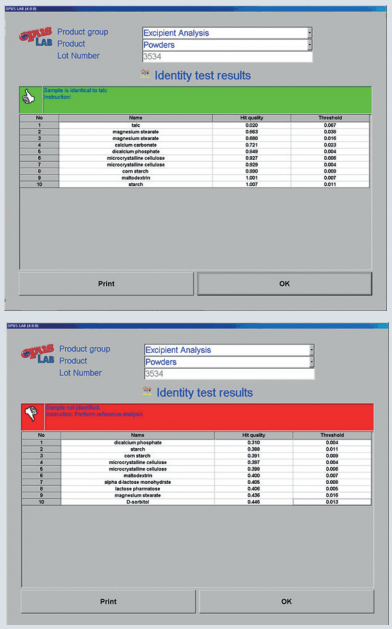
Eight powdered pharmaceutical excipients from different batches and vendors were collected and placed in 22mm glass vials. Bruker Optics' MPA II FT-NIR spectrometer with an integrating sphere and autosampler along with a fibre

optic powder probe was used for these measurements. The MPA II was chosen because it is an excellent method development system with up to 5 different sampling accessories. Bruker Optics also offers process-hardened systems such as the MATRIX-I or the MATRIX-F that can be used in a GMP receiving area or dispensary.

The samples were measured using both the powder probe (by placing the probe directly in contact with the powder) and the integrating sphere. In the latter case, the vials were placed into the autosampler and measured in sequence. Spectra were collected through the bottom of the glass vial and 10 scans (~7s) were collected at a resolution of 8 cm^{-1} (see Figure 1).

A qualitative analysis model based on a Euclidean distance algorithm was developed and unknowns were analyzed using the OPUS/LAB software. OPUS/LAB has a very simple user interface that provides clear identity test reports, as shown in Figure 2.

Figure 2



Qualitative analysis for the identification of raw materials and other samples is made easy with OPUS/LAB. The result page clearly shows the pass/fail of an analysis together with the hit list.

Qualitative Analysis

Near-infrared spectra result from combination and overtone bands of C-H, N-H, O-H… vibrations. Since most pharmaceutical excipients and actives are organic compounds, they are ideal for near-infrared analysis. Their unique near-infrared spectra enable them to be easily identified. The OPUS/IDENT qualitative analysis software package uses either a Euclidean distance algorithm or Factor Analysis to develop a library and identify the materials. Typically the development of a library requires sampling batches of each substance from different accepted lots and suppliers that contain all the expected sample/supplier variation.

Measurement Options

The MPA (multi purpose analyzer) offers a unique combination of sample accessories. For liquid raw materials we offer a simple transmission option (heatable if required) 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 either with 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.

Implementation

In a QC laboratory environment a system such as the MPA II can be used along with the user-friendly OPUS/LAB software, which not only performs the measurement but also automatically performs the analysis of unknown samples (see Figure 2). In addition, this software allows the identity test to be combined with a quantitative analysis such as moisture content, purity etc.

In a dispensary a different approach is necessary due to the possibility of an explosion hazardous area. In this case the instrument will be located in a safe area some distance away from the sampling area. Custom fiber optic probes (for liquid and solid samples), an explosion proof workstation and bar code reader along with a simple graphical user interface at each workstation are used.

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