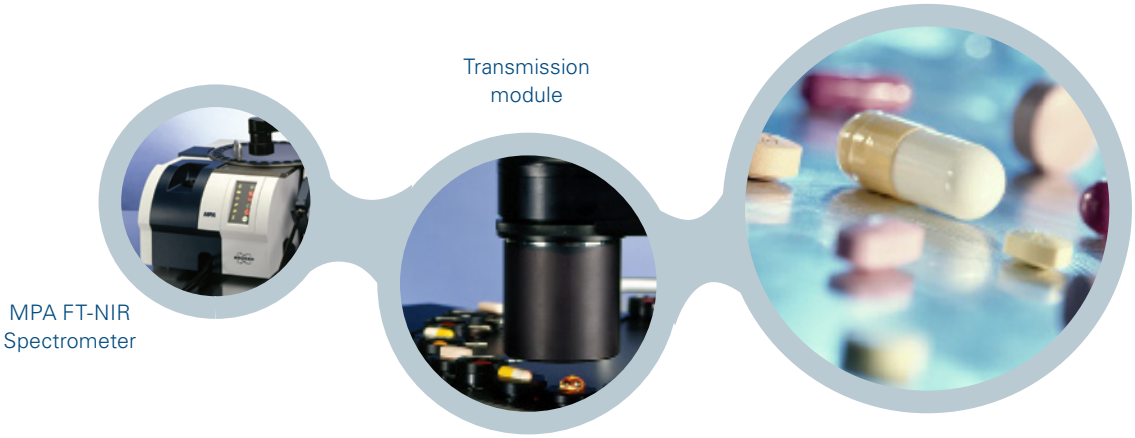
Bruker Optics



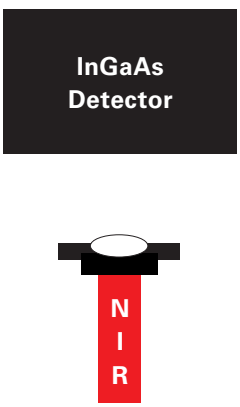
Application Note # AF 503 E

Content uniformity on tablets

New regulations make in-process testing more popular to demonstrate adequacy of mix (cGMP) and for the content uniformity of finished dosage forms.

Many regulations are in place for pharmaceutical manufacture e.g., for in-process testing to demonstrate adequacy of mix (cGMP) and for the content uniformity of finished dosage forms (USP compendial requirements). The PQRI recommendation provides a strategy to assess blend and dosage unit uniformity. Within this concept of stratified sampling, NIR spectroscopy may be used for analysis of powders and tablets.

Figure 1



Schematic of the FT-NIR tablet analyzer

NIR spectroscopy shows significant advantages for content uniformity over HPLC analysis:

- Fast, reliable and precise
- No sample preparation
- No solvents required

Bruker Optics offers customized solutions to meet the special requirements of the pharmaceutical industry. The Bruker Optics MPA FT-NIR spectrometer offers the highest flexibility in sample presentation and accessories. For example, for tablet analysis, a 30 position sample wheel with customized tablets nests presents the samples fully automatically to the external transmission head with an InGaAs detector for analysis.

Instrumentation

For tablet analysis a Bruker Optics MPA spectrometer comprising a 30 position automatic sample wheel and an external transmission module with an InGaAs detector is used. The automatic sample wheel is fitted with customized tablets nests. In this set up the light will come from underneath, shine through the tablet and is detected by the detector above the tablet. The Bruker Optics OPUS/LAB software package provides an easy to use software interface for the operators. All experiment parameters are pre-set and the operator is taken through the input of all required data. The software package is fully 21CFRpart11 compliant when

operated in a compliant environment. Software wizards are provided to make OQ/PQ testing an easy task.

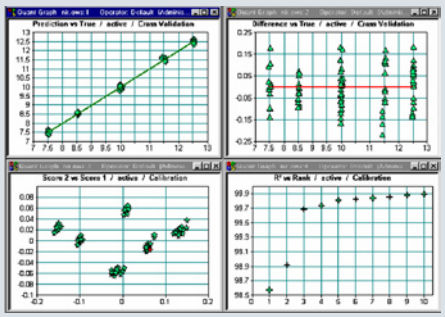
Evaluation

For all spectra subsequent analysis according to pre-defined calibration models and identity test libraries are performed automatically. The results are summarized in non-editable reports, which are printed without intervention. In addition, all measurements are recorded in an Audit Trail.

Quantitative analysis

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

Figure 2



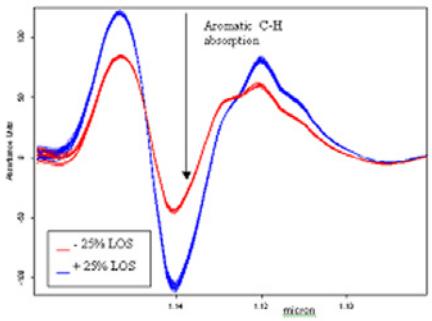
Cross validation results of PLS based models for the prediction active drug in a tablet (R^2=99.72, RMSECV=0.09mg/tablet).

Experimental

In order to monitor the potency of a batch using FT-NIR spectroscopy, spectra are taken in transmission in the spectral range from 12000 – 7500 cm^{-1} (833 – 1330 nm).

The co addition of 16 scans per spectra at a resolution of 8 cm^{-1} allows a fast data acquisition of less than 10 seconds per spectrum. The increase of active drug concentration is shown in the spectra allowing the development of a calibration model with an excellent Standard Error of Cross Validation (RMSECV) of 0.09 mg/Tab and a correlation coefficient R^2 of 99.72%. The unique self-optimise function in the OPUS software was used to develop the model. The calibration range covered a concentration of 7.5 to 13.5% of the active drug.

Figure 3



FT-NIR derivative spectra spectra (1.18 - 1.09 micron) of two tablet samples with +/- 25% deviation from the target concentration.

Measurement options

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

With the new MPA Bruker Optics offer 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.

Implementation

In a QC laboratory environment a system such as 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 or purity.

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