Application note | AN51668

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Transmission FT-NIR spectroscopy for analysis of polymers and pharmaceutical formulations

Author
William J. McCarthy, Thermo Fisher Scientific, Madison, WI, USA

Industry/application
Materials science; polymer and pharmaceutical analysis

Products used
- Thermo Scientific Antaris™ FT-NIR analyzer
- Transmission module and sample accessories

Goals
Enable reliable transmission measurements of solid and semi-solid samples (like polymers or pharmaceuticals) that are traditionally difficult to analyze. Demonstrate quantitative analysis without extensive sample preparation and optimize measurement conditions, such as temperature, for challenging samples. Replace reflectance-based methods with a simpler, more direct transmission approach.

Key terms
- FT-NIR
- Transmission spectroscopy
- Diffuse reflectance vs. transmission

Key benefits
- Minimal or no sample preparation
- Improved analysis of challenging samples through temperature control
- Flexible sampling of solids, liquids, and low-melting materials
- High precision and reproducibility with automated background collection and controlled measurement conditions

Abstract
Near-infrared spectroscopy has significant fundamental advantages that allow the use of transmission for solid samples such as polymers and pharmaceutical formulations in the near-infrared.

Introduction
Near-infrared radiation (identified in 1800 by Sir William Hershel) was the second region of electromagnetic spectrum discovered after the visible, yet little analytical work was performed in the near infrared until the 1950's when Karl Norris at the United States Department of Agriculture (USDA) began investigating agricultural products. Finding transmission difficult, he worked primarily with diffuse reflectance. When transmission is used in NIR, it is more commonly transflectance, in which the beam is reflected from a mirror-like substrate. Yet, the major advantages of Fourier transform near-infrared (FT-NIR) spectroscopy readily lend themselves to true transmission spectroscopy. The intensity of near-infrared bands is approximately an order of magnitude weaker than the fundamental midinfrared features allowing for relatively long pathlengths. Glass does not absorb strongly in the near-infrared, allowing the use of inexpensive culture tubes and glass vials as sample containers. Cross contamination in the analysis is eliminated since the tubes can be thrown away after use. Glass sampling also makes it possible to easily obtain high quality spectra by heating samples with low melting points so that the spectrum can be obtained in liquid state. Thick samples, particularly packaging materials (typically from thickness of ~0.125 to 3 mm), do not have to be pressed or dissolved and cast as films but can be run as processed.

Experimental

All spectra were acquired on a Thermo Scientific™ Antaris™ FT-NIR Analyzer (the updated Antaris II model is now available) with a 20-second measurement time at a resolution of 8 cm^{-1}. The background spectra were obtained automatically as part of the collect using the internal background position. The three-position (non-heated) cardholder (Figure 1) was used for the polymer film studies. The polymer film was a commercially purchased protective sheet holder approximately 0.120 mm thick. The cast films (0.190-0.225 mm thick) were polymer alloys of polystyrene and polyethylene. A quantitative model for the cast films was built using Classical Least Squares (CLS) model in Thermo Scientific™ TQ Analyst™ software. To study the effect of temperature, a proprietary waxy pharmaceutical formulation was examined in transmission. The waxy formulation was broken into small (< 1 mm^3) pieces and placed in a 6 mm-diameter disposable glass vial.

The tube was placed in the sample position of the heated cuvette/culture tube holder in the Antaris analyzer (Figure 2). The temperature was raised from 28 °C to 60 °C at 2-degree increments. (Figure 3) Prior to collecting the spectrum of the sample, the temperature was allowed to equilibrate and then a background was collected using the computer controlled sample shuttle.

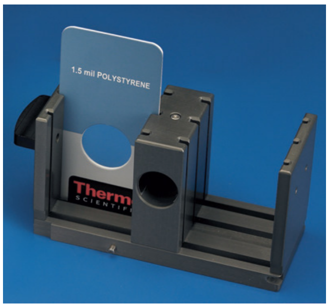

Figure 1. Three-position cardholder.

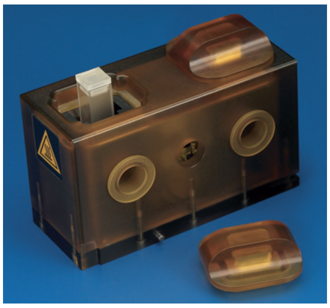

Figure 2. Heated three-position cuvette/culture tube holder.

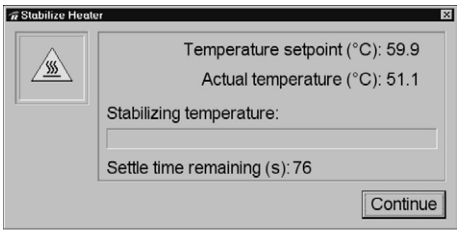

Figure 3. Temperature control in Thermo Scientific RESULT™ software.

Results and discussion

Transmission of polymers

The near-infrared transmission of the polymer sheet demonstrates that excellent spectra can be obtained from commercial samples run as received. All of the absorbance peaks are in the linear range (absorbances are directly proportional to concentration) and can be readily observed and quantified (Figure 4). The absorbance peaks in the mid-infrared spectra of the same sheet are either in the non-linear range, which would make quantitation difficult or are completely absorbing (Figure 5).

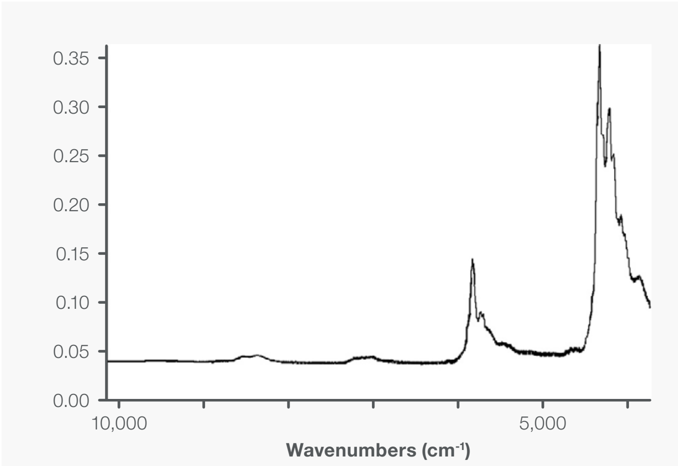

Figure 4. FT-NIR spectrum of plastic sheet.

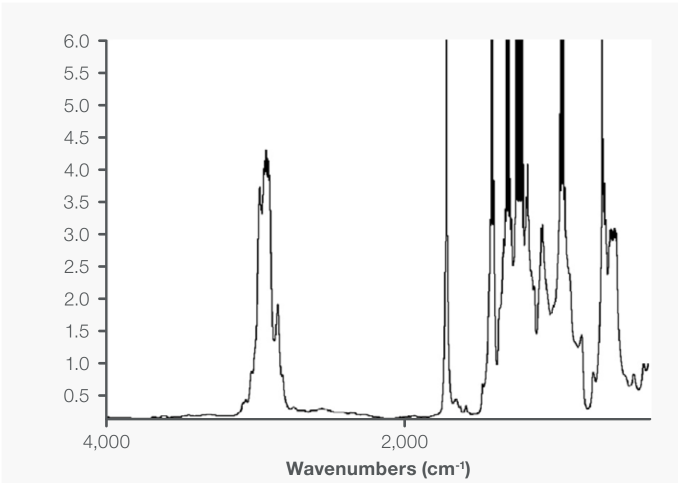

Figure 5. Mid-infrared plastic sheet.

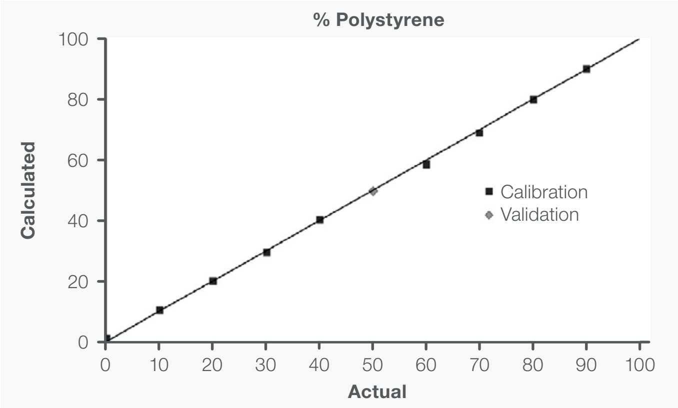

Figure 6. Calibration plot for polystyrene.

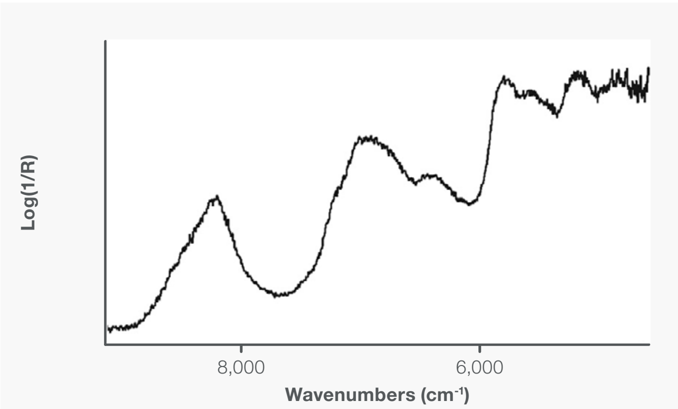

Figure 7. Reflectance spectrum of waxy formulation.

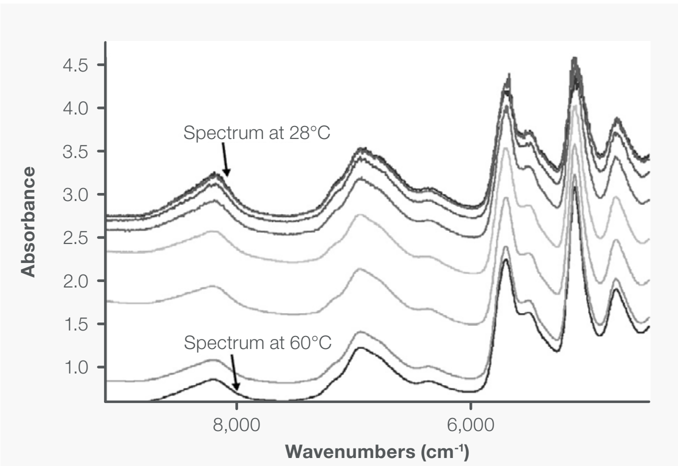

Figure 8. Spectra of waxy formulation acquired at different temperatures displayed on common scale.

Quantification of polymers

The cast films (0.190-0.225 mm thick) used for quantitative analysis were polymer alloys of polystyrene and polyethylene. Each component (polystyrene and polyethylene) was varied from 0 to 100%. Ten samples were selected as calibration standards and an additional standard was used as a validation standard. The standards were collected using the Collect Standards feature of RESULT Operation software. The CLS method was created using the Build TQ Analyst feature of RESULT Integration software. Three regions were used. As can be seen in Figure 6, the quality of the fit is excellent. For the polystyrene component, the correlation coefficient R is 0.99970 and the (root mean square) error of calibration (RMSEC) is 0.813%. For the polyethylene, R=0.99977 and RMSEC=0.712%.

Pharmaceutical formulation

Diffuse reflection is the most common method for analyzing pharmaceutical compounds. The reflectance spectrum of the waxy pharmaceutical formulation acquired with the integrating sphere (Figure 7) shows that this is not an appropriate analysis technique for this type of sample. The surface of the formulation does not provide a diffuse medium. Consequently the signal-to-noise level is low as evidenced by the noise (small, sharp peaks) throughout the spectrum. The peaks themselves are broad and ill-defined. Transmission at ambient temperature did not give acceptable results as can be seen in the top spectrum of Figure 8. At ambient temperature, the material has a diffuse, white appearance due to scattering. Because of the short wavelength in the near-infrared, small particles reflect much of the near-infrared light away from the detector. Consequently, the baseline is high (> 2.5 absorbance units) and the signal-to-noise ratio is low. As the material softens, it becomes clearer in appearance, the baseline drops, peaks sharpen and signal-to-noise rises. At 60 °C, the sample spectrum will produce good results. The spectra are presented in common scale with no baseline offset.

Conclusion

The Antaris FT-NIR analyzer transmission module provides reproducible quantifiable spectra from thick plastics, liquids and solid samples with a low melting point. While this research was conducted on the now-retired Antaris FT-NIR analyzer, the current Antaris II FT-NIR model delivers equally trustworthy analysis with the same proven NIR spectroscopy technique. The transmission module clearly demonstrates that commercially produced plastic films can be measured without sample preparation. The ability to measure thick samples in a controlled temperature environment with automatic background collection makes transmission spectroscopy with the Antaris FT-NIR analyzer a high-precision and easy-to-implement analytical technique.

Learn more at **thermofisher.com/nir**

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