Application Note: 50777

Dedicated Analytical Solutions for Tablets and Softgels: Transmission Analysis of Solid Dosage Pharmaceuticals

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Key Words

- Nicolet Antaris
- Diffuse Reflectance
- FT-NIR
- Pharmaceutical
- Tablets
- Transmission
- Softgels

Abstract

The majority of commercially available pharmaceutical formulations are tablets and capsules designed to be taken orally. Fourier transform near-infrared (FT-NIR) analysis is a powerful technique for measuring these materials. The advantages of using both the Softgel and Standard Tablet detectors on the Nicolet™ Antaris™ FT-NIR Analyzer will be discussed in this application note. Diffuse reflectance and transmission spectra of tablets and softgel capsules will also be shown.

Introduction

The analysis of pharmaceutical solid dosage forms is normally done by liquid chromatography, which requires tedious sample preparation and solvents that need to be recycled. Pharmaceutical companies are interested in easier techniques that would increase the number of samples per batch (more difficult with time-consuming, labor-intensive HPLC assay methods) to allow representative trending studies. For these reasons, FT-NIR analysis is an appealing alternative.

Although tablets have been successfully analyzed by diffuse reflectance, increased concerns about content uniformity have led to the desire to examine other non-destructive methods like transmission that can sample a more representative bulk of the tablet.

Formulations such as oily and semi-liquids, granule powders, semi-solid matrices, and natural herbal ingredients are difficult to compress into tablets. For these formulations, softgel capsules are a safe, cost-effective dosage form. Softgel capsules are also becoming increasingly popular because of flexibility, ease of swallowing, and the ability to tailor bioavailability. In fact, the use of capsules had its beginning in the early 1800's as a patient-friendly way to deliver bitter-tasting drugs. So, it is not surprising that many experts expect the number of encapsulated pharmaceuticals to increase.

Diffuse reflectance does not give usable information for these types of formulations; therefore, FT-NIR transmission may provide the ideal answer for fast, nondestructive analysis of non-tablet pharmaceuticals.

Experimental

All spectra were acquired with a 30-second measurement time at a resolution of 16 cm^{-1} on a Nicolet Antaris FT-NIR Tablet Analyzer (Figure 1) using the universal tablet holder. The Softgel and Standard Tablet detectors were used for the transmission study. The diffuse reflectance spectra were measured with the integrating sphere using the internal gold flag as the background. A fiber optic dip probe with a pathlength of 1 mm was used to measure the vitamin E oil.

Figure 1: Nicolet Antaris FT-Near Infrared Analyzer with Softgel detector

Results and Discussion

Two types of solid dosage detectors have been developed for the Nicolet Antaris FT-NIR Analyzer: Softgel and Standard Tablet. Both types use InGaAs detectors but with characteristics optimized for different samples (Figure 2).

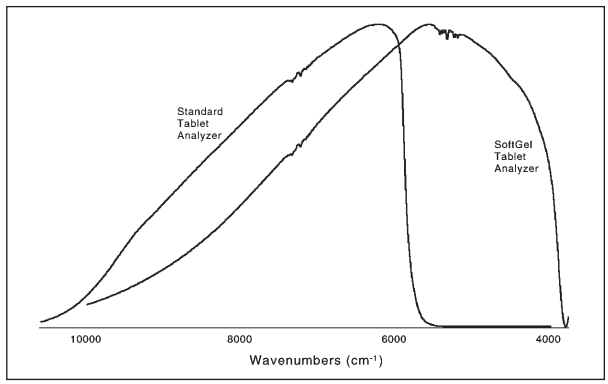

Figure 2: Comparing Softgel and Standard Tablet detector single beams (common scale)

The Standard Tablet detector high sensitivity and narrow range (12000-5880 cm^{-1}) is with wide amplification choices for low-energy, opaque samples (1x, 10x, 100x and 1000x). This detector is used for tablets, which transmit minimal signal over the entire near-infrared region due to scattering effects and thickness of the tablet (typically ~1-4 mm). Studies have shown that no measurable signal is transmitted below ~6500 cm^{-1} for typical tablets. This is due to a combination of thickness and the stronger absorptivity

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at lower wavenumbers. Although the spectral range covered with the standard tablet analyzer is less than can be covered with diffuse reflectance, a more representative amount of the bulk is interrogated. Although the spectral information is limited, this technique has been used effectively for classification studies of clinical tablets with different formulations. For these studies, the error of prediction for the transmission experiment was less than the error of prediction for the diffuse reflectance experiment.

Figure 3 is the spectrum of a 325-mg aspirin tablet measured using the Standard Tablet detector with a gain of 100x. Below 7000 cm^{-1}, the response is effectively zero. This can be determined by examining the single beam or noting that there is significantly more noise below 7000 cm^{-1} and absorbance peaks are absent.

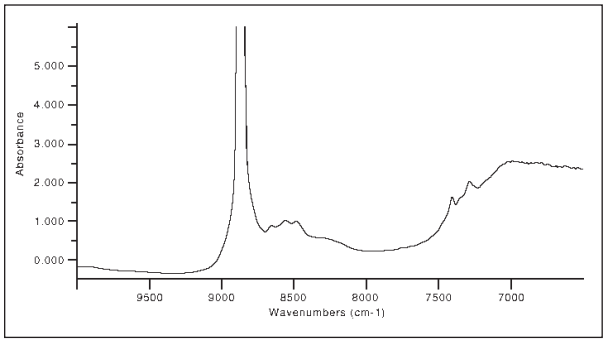

Figure 3: Spectrum of aspirin using Standard Tablet detector

The Softgel detector uses a wider spectral range (12000-3800 cm^{-1}) than the Standard Tablet detector. It also has a wider amplification range (1x, 4x, 16x, and 64x) than typical detectors. This is the detector that is used for gelatin capsules because the absorbence of the capsules is often less than tablets.

Softgel Capsule – To compare diffuse reflectance with transmission for softgel capsules, we measured a vitamin E capsule. The outer diameter was roughly 9 mm at its thickest point and the gelatin covering was several millimeters thick. The pharmaceutical formulation inside the capsule was a clear, viscous, oily liquid. Because of the thick, oily formulation and cylindrical shape, precise positioning was required to create reproducible spectra. The universal tablet holder, which allows samples to be quickly and repeatably positioned, was used to hold the capsule. The sample was kept in place for both transmission and reflectance. This was possible because when the capsule was placed on the sapphire window of the integrating sphere, it was also in the sampling position for transmission with the tablet detector module. The diffuse reflectance spectrum (top spectrum in Figure 4) measured with the integrating sphere provides very little information about the formulation because the smooth, thick gelatin encapsulation does not provide a diffuse, scattering medium. There is no evidence of spectral information related to the vitamin E. Therefore, the only viable option for this study is transmission.

The middle spectrum in Figure 4 is a transmission spectrum of the vitamin E measured with a dip probe. The oil from several vitamin E capsules was extracted and placed in a beaker in which the dip probe was inserted. This technique gives good quality spectra, but it destroys the capsule and requires sample preparation and extensive cleaning to avoid cross-contamination.

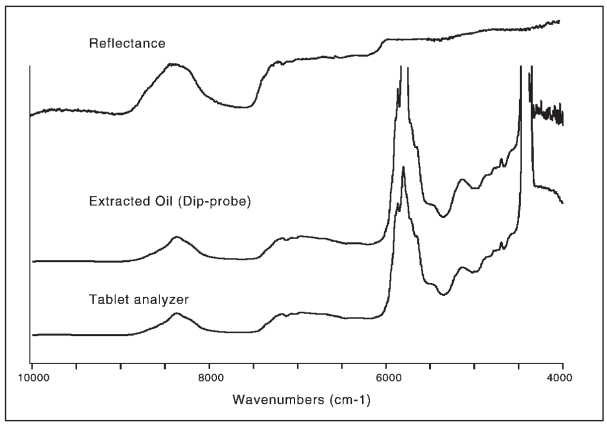

Figure 4: Analysis of vitamin E capsule

The transmission spectrum of the intact capsule measured with the Softgel detector can be seen at the bottom of Figure 4. Comparing the spectral features to those of the extracted oil demonstrates that the features from vitamin E oil dominate this spectrum. This demonstrates that the content of the capsule is being measured.

Conclusion

The Nicolet Antaris FT-NIR Analyzer provides reproducible, quantifiable spectra for solid, oral dosage forms such as tablets and softgels. The improved precision and representative interrogation of the bulk of pharmaceutical formulations using transmission should be carefully considered when choosing an analysis technique.

The unique design of the Nicolet Antaris FT-NIR Analyzer provides the ability to collect both diffuse reflectance and transmission data from a tablet without moving the sample. The reflectance and transmission data can be used to analyze the active ingredient in a tablet as well as analyzing coating characteristics.

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