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Discriminant Analysis of Cellulose Esters Using FT-NIR

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Key Words

- FT-NIR Spectroscopy
- Antaris
- Cellulose
- Drug Delivery
- Ester

Introduction

Cellulose derivatives are widely found in foods and pharmaceuticals where they are used as emulsifiers, dispersing agents, and thickeners. While cellulose itself is not readily soluble in water, various derivative esters have increased solubility, even if these esters are hydrophobic in nature. This seemingly contradictory behavior is due to the ester groups disrupting the cellulose crystalline structure. In addition to solubility, different esters have different glass transition temperatures, tensile strengths and water vapor transmission rates. The amount and type of esterification present in cellulose material therefore becomes exceedingly important when considering its use in food products or pharmaceuticals.

Cellulose acetate esters are heavily exploited in pharmaceuticals where they are typically used for controlled drug delivery. Their controlled porosity and solubility make them good excipients and coatings for solid dosage forms. Each sugar residue in cellulose has three hydroxyl groups that are amenable to esterification. Quantitative measurement of the amount of ester present will either be reported by percent or by degree of substitution (DS). The DS of a particular material indicates the average number of ester groups found on each residue and will fall between 0 and 3. To provide for greater complexity, cellulose acetate materials are further derivatized with proprionate or butyrate groups to various degrees. As a result, a given cellulose material may primarily be a cellulose acetate with additional proprionate or butyrate ester groups. Figure 1 indicates the possible choices of groups on each residue. The sheer variety of esters available allows a great deal of control over how a drug performs after ingestion. Figure 2 demonstrates typical dissolution profiles for solid dosage pharmaceuticals combined with various cellulose acetate ester types.

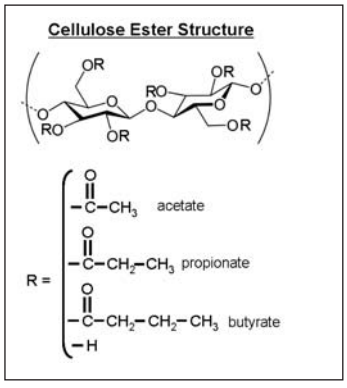

Figure 1: Cellulose esters

Unfortunately, the nature of these esters is such that they physically look similar to each other. Furthermore, since they all have similar chemical structures, time-consuming analytical techniques may be required to distinguish between them. Commonly, mass spectroscopy is required to resolve the type and degree of substitution present in a given sample.

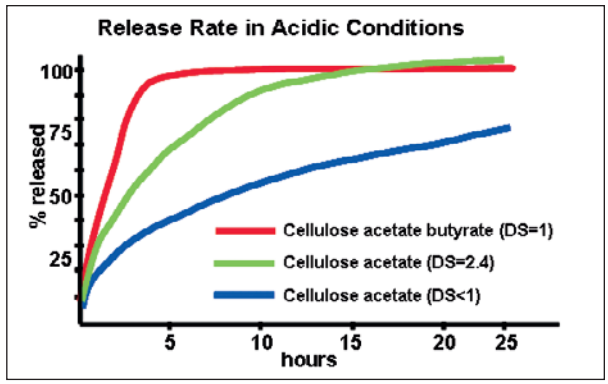

Figure 2: Typical dissolution profile for drug compounded with various cellulose acetate esters

The Thermo Scientific Antaris™ II FT-NIR analyzer (Figure 3) has proven to be a superior tool for identifying and classifying different materials and was explored for use with this particular application. Fourier transform near-infrared (FT-NIR) spectroscopy can be used to confirm the identity of cellulose esters with great speed and accuracy. FT-NIR uses the part of the electromagnetic spectrum between the UV-Visible and the mid-infrared regions to detect overtone and combination vibrations present in nearly all organic molecules. The unique structure of specific organic molecules allows them to generate characteristic spectral patterns when irradiated with near-infrared light. As a spectroscopic technique, FT-NIR can generate results in seconds without sample preparation or sample destruction, which is clearly advantageous over other spectroscopic methods. Because of the utility of the Antaris II FT-NIR analyzer in discriminating between similar raw materials, it was chosen for this study to analyze different cellulose acetate esters.

Figure 3: The Antaris II FT-NIR analyzer, showing how samples were analyzed with the integrating sphere

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Experimental

Nine cellulosic materials were obtained from Eastman Chemical Company (Kingsport, Tennessee) or Acros Organics (Fair Lawn, New Jersey). The materials represented a range of type and degree of esterification. Microcrystalline cellulose had no ester groups present, while the others were acetate esters with various amounts of additional proprionyl or butyryl moieties. Table 1 summarizes the various relevant characteristics of the cellulosic materials studied.

ID	%	DS	ester	MW (kDa)
B 17	17	0.7	butyryl	65
B 38	38	1.8	butyryl	40
B 46	46	2.0	butyryl	20
B 52	52	2.5	butyryl	30
P 45	45	2.3	propionyl	25
P 47	47	2.5	propionyl	75
P 48	48	2.6	propionyl	25
A 40	40	2.4	acetyl	30
microcrystalline cellulose	0	0	——	

Table 1: Identity and characteristics of cellulose materials used

Three samples of each material were taken and placed in glass vials. The samples were analyzed three or four times using the integrating sphere module (total of ten scans for each material). Between scans the contents in the vials were shaken then compacted by gently rapping the vial on a solid surface. This ensured consistency in the density of the material, while simultaneously ensuring variety in sampled material. The samples were scanned between 10,000 and 4000 cm^{-1} at a resolution of 8 cm^{-1} with 16 scans per analysis. No attenuator screen was in place and a 1X gain was used. Baseline offsets were minimized by analyzing the data as first-derivative spectra. Figure 4 shows the variation between the different cellulose materials in the first derivative spectra as well as the regions used in the chemometric analysis.

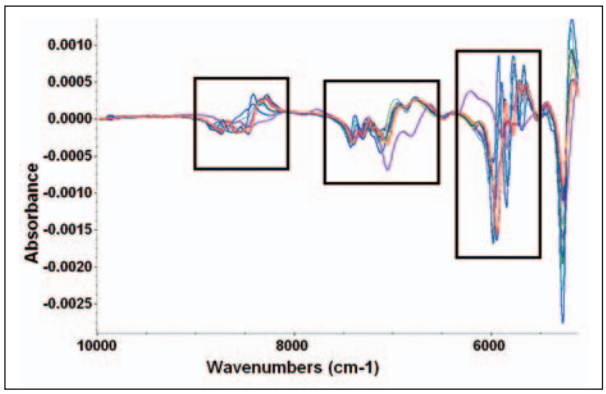

Figure 4: First derivative spectra of representative cellulose materials. Spectral regions used in the analysis are indicated by the rectangles.

Discriminant analysis was performed using the Thermo Scientific TQ Analyst™ software. The multiplicative signal correction option was chosen for the pathlength, and Norris smoothing (segment length = 5; gap = 5) was performed. Additionally, unique distributions were calculated for each class in a technique commonly referred to as SIMCA. A principal component scores plot shows exceptionally clear discrimination between the various cellulose ester types. The cellulose acetate butyrate esters are widely separated from each other and the other cellulose derivatives as shown in Figure 5. The cellulose acetate proprionate esters required a different region to discriminate.

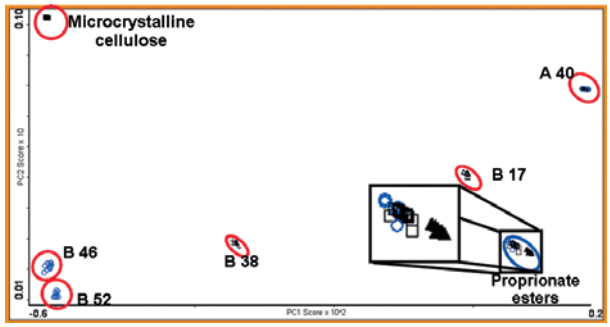

Figure 5: Principal component plot of the cellulose materials. All classes are well separated indicating successful discrimination. Proprionate esters (inset) are resolved in Figure 6b.

Figure 6a shows the spectral differences between these materials from 5050 to 4800 cm^{-1}. A second chemometric analysis on this region using similar parameters as before allowed discrimination between these proprionate esters (Figure 6b).

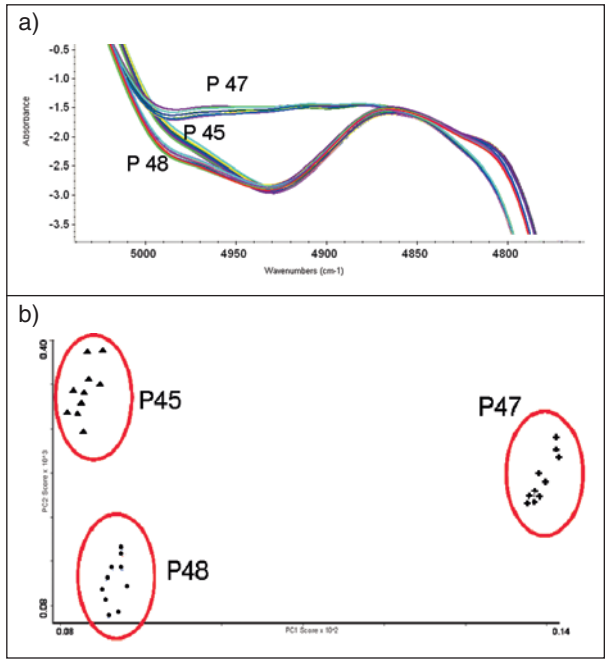

Figure 6: Panel A shows spectral variation between 5050 and 4800 cm^{-1} for the cellulose acetate proprionate esters. Panel B shows a principal component scores plot indicating good discrimination between these materials.

To validate the effectiveness of this analysis, new samples of the cellulose materials were obtained and scanned. These materials were then classified according to the chemometric analysis described above. Table 2 shows the results of this analysis. All of the test samples were correctly identified and placed into their proper class. This data indicates the method is suitable for identifying new samples of the cellulose materials.

Validating Samples	Identified As
B17	B17
B38	B38
B46	B46
B52	B52
P45	P45
P47	P47
P48	P48
A40	A40
Micro Cel	Micro Cel

Table 2: Validation samples were analyzed using the parameters determined from the calibration materials. All of the validation samples were correctly identified.

Conclusion

A series of cellulose materials including various cellulose acetate esters were obtained and analyzed with the Antaris II FT-NIR analyzer. Chemometric analysis showed there were sufficient spectral differences between the different materials, even when the chemical differences were subtle. These spectral differences were used to build a chemometric model and correctly identify new samples. This study demonstrates the validity of using FT-NIR for proper classification of various cellulose and cellulose ester materials.

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