capsules

A simple test to differentiate gelatin from hypromellose capsules

Enrique Requejo Gabás and Fernando Díez Menendez
Qualicaps
Luis Polo Díez and Nour Kayali
Complutense University of Madrid

This article describes how to use FT-IR spectroscopy to differentiate gelatin from hypromellose capsules, enabling quick verification of incoming capsule samples.

Gelatin has been the main polymer for making hard capsules since they were first manufactured on a large scale in the USA in the 1870s [1]. The first alternative polymer, methylcellulose, was introduced by Eli Lilly in the 1950s and, for the first time, it was necessary to develop a test to distinguish between them.

Thus, US Federal Standard 285A [2], which federal agencies consulted when purchasing capsules, published instructions for conducting a simple test called "S6.2.14" or "Water resistance." It entailed immersing the capsules (n = 25) in purified water at 25°C ±1°C for 15 minutes and, unless otherwise specified, the capsules were to show no sign of disintegration.

Although not stated in its title, the test's purpose was to distinguish between a gelatin and a methylcellulose capsule: Only the latter would dissolve at that temperature. In fact, the test simply showed that gelatin capsules would fail, but it offered a means of distinguishing between the only two types of capsules available at the time. It did not identify the polymer.

Since that time, beginning in the late 1990s, capsules made from hypromellose (hydroxypropyl methylcellulose, or HPMC) became widely available [3]. Hypromellose capsules are soluble at less than 25°C and thus

would dissolve in the "Water resistance" test, too. To find a test that could specifically identify the sample as either gelatin or hypromellose, we investigated infrared (IR) spectroscopy, a well-known laboratory technique that requires only small samples.

Materials and methods

Materials. Gelatin and hypromellose capsules, size 3, were supplied by Qualicaps Europe (Table 1). One set of capsules contained no colorants and the other contained titanium dioxide, a pigment that serves as an opacifying agent.

Methods. All the spectra were measured using a Fourier transform (FT) IR spectrophotometer (Nicolet Magna 750 from Thermo Scientific, Waltham, MA) at a wave range of 7,400 to 350 reciprocal centimeters (cm-1) and with a resolution of 0.5 cm^{-1}. A spectral library (database) was also employed. The spectrophotometer used an attenuated total reflectance (ATR) accessory that operates by measuring the changes that occur in a totally internally reflected IR beam when the beam contacts a sample.

The ATR crystal area was cleaned and capsule pieces measuring a few square millimeters were placed onto the small crystal area. A pressure arm was placed over the pieces to hold the sample in place.

TABLE 1

Details of capsules used in the study

Capsule type	Color	TiO_2 (% w/w)	Lot number
Gelatin	Clear	0	E1105594
Hypromellose*	Clear	0	E1203155
Gelatin	White (opaque)	2.0	E1102130
Hypromellose*	White (opaque)	2.7	E1209687

* Quali-V from Qualicaps

Results

FT-IR spectroscopy measures the wavelength and intensity of the sample's absorption of IR radiation. The IR spectral data of high-molecular-weight polymers are usually interpreted in terms of the vibration of structural repeat units [4, 5].

Gelatin is a protein, and the most prominent vibrational bands are in the range of 1,650 to 1,500 cm^{-1}. Other sensitive spectral regions are due to the protein's secondary structural components. The Amide I band (1,630 cm^{-1}) is due almost entirely to the carbonyl stretch vibrations of the peptide linkages, and the Amide II band (1,530cm^{-1}) is mainly from in-plane N-H bending and from the -N stretching vibration. The latter shows much less protein conformational sensitivity than its Amide I counterpart.

Hypromellose is derived from cellulose and the IR spectra are completely different and the number of bands much lower. The most important band is at 1,060 cm^{-1} and corresponds to a stretching of the C-O-C group.

See Figures 1, 2, 3, and 4, which show the IR spectra for gelatin and hypromellose capsules. Table 2 lists the details of the most important bands.

Figure 1

Spectra for gelatin clear capsules, batch E1105594

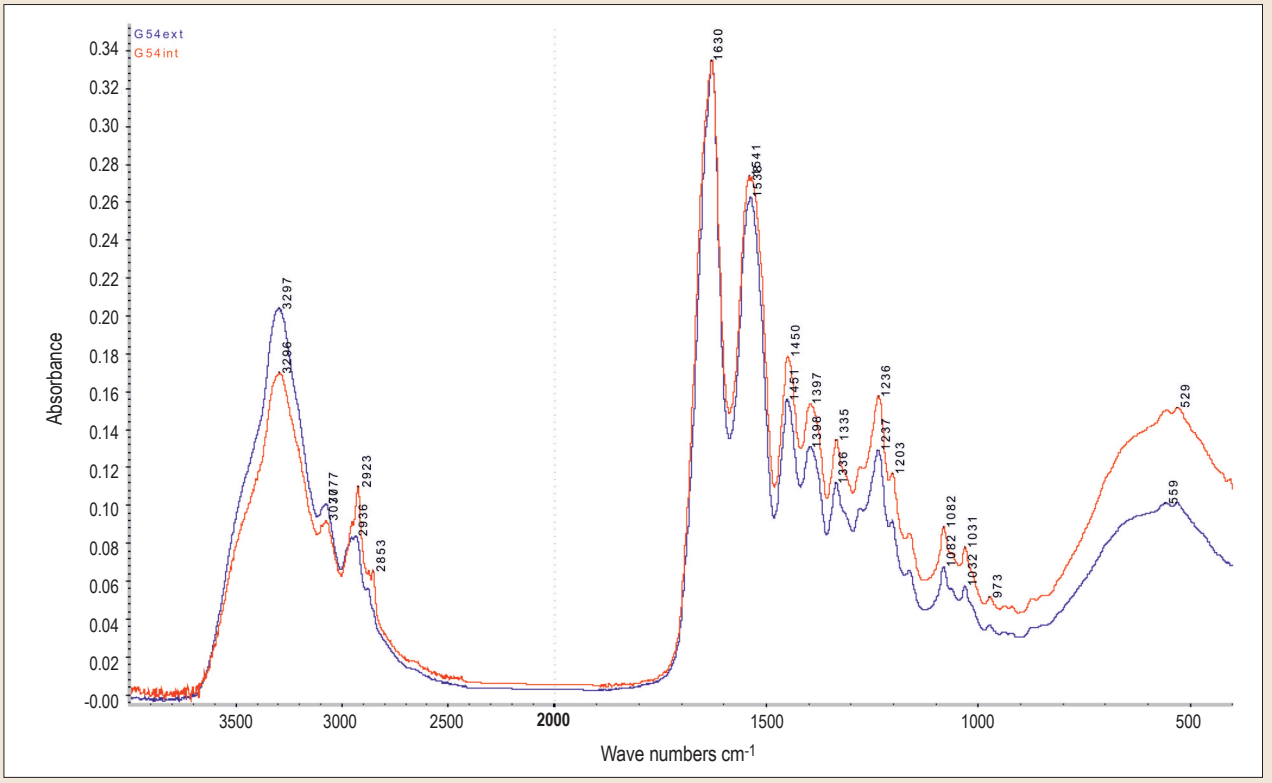

Figure 2

Spectra for hypromellose clear capsules, batch E1203155

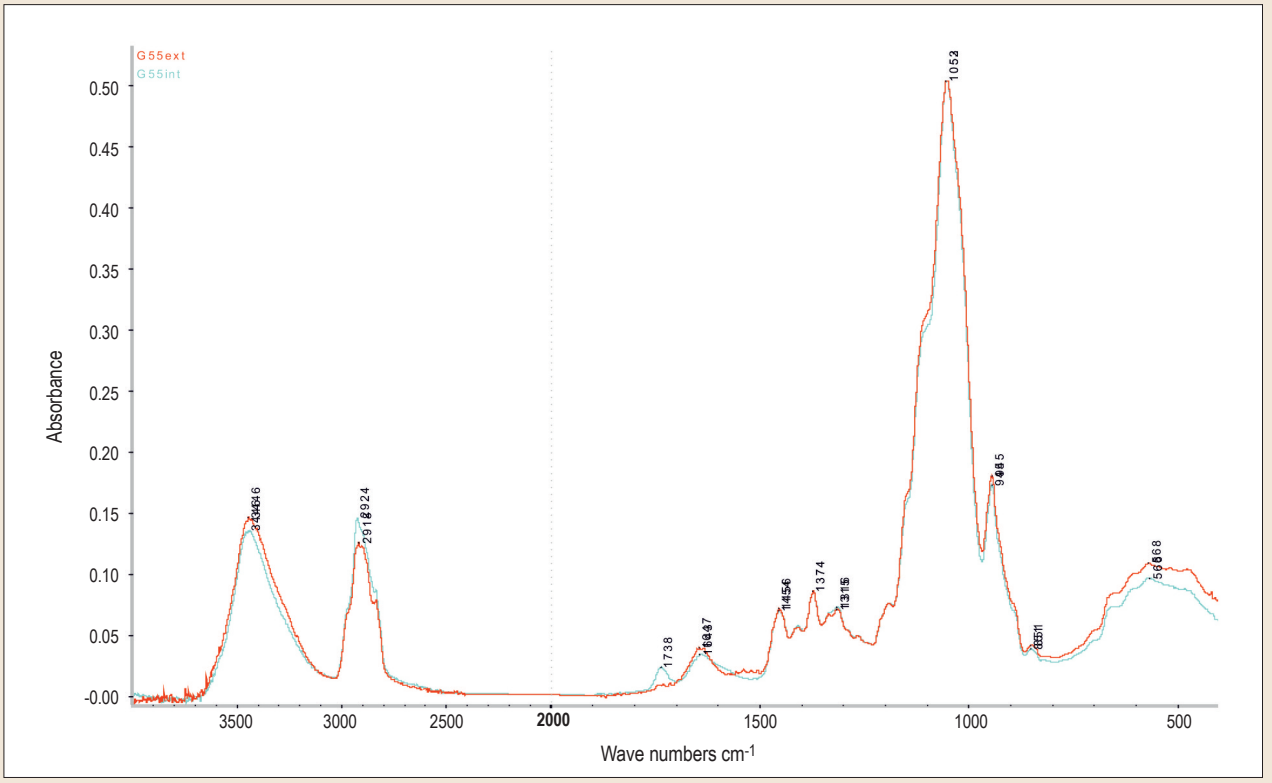

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Figure 3

Spectra for gelatin white capsules, batch E1102130

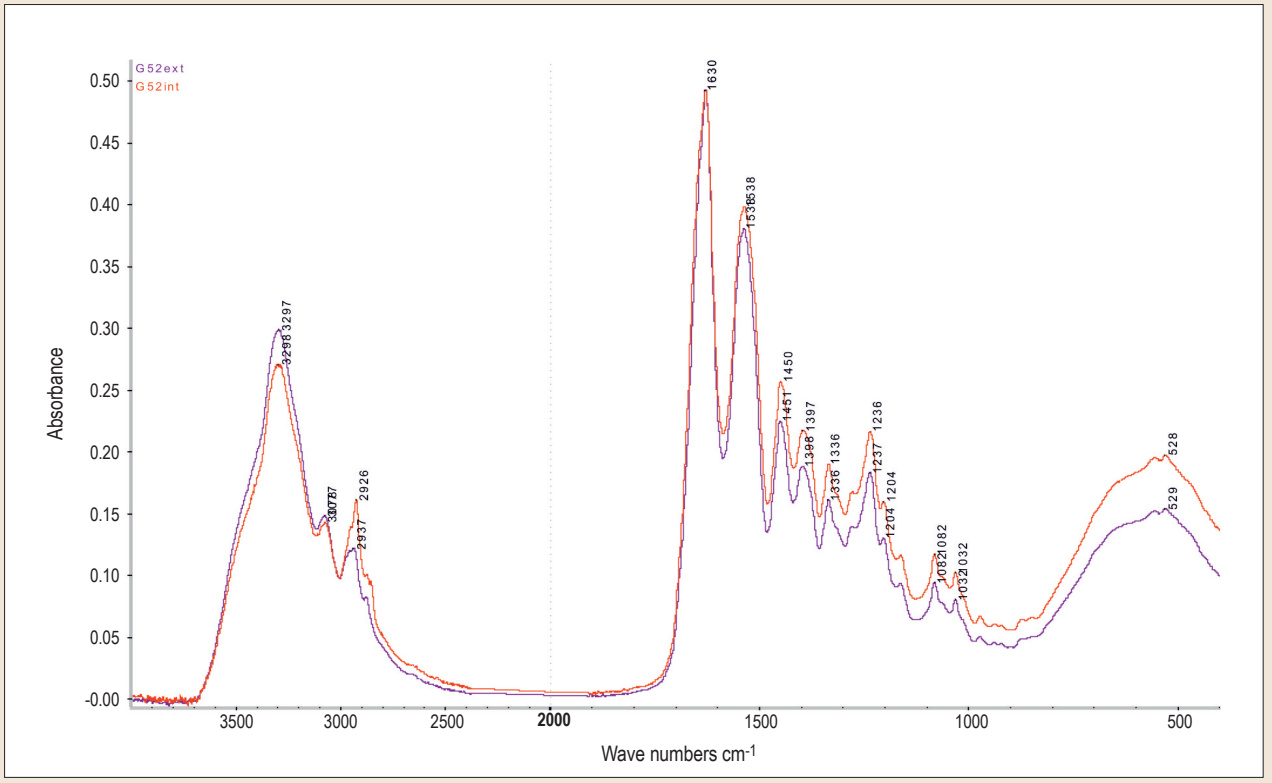

Figure 4

Spectra for hypromellose white capsules, batch E1209687

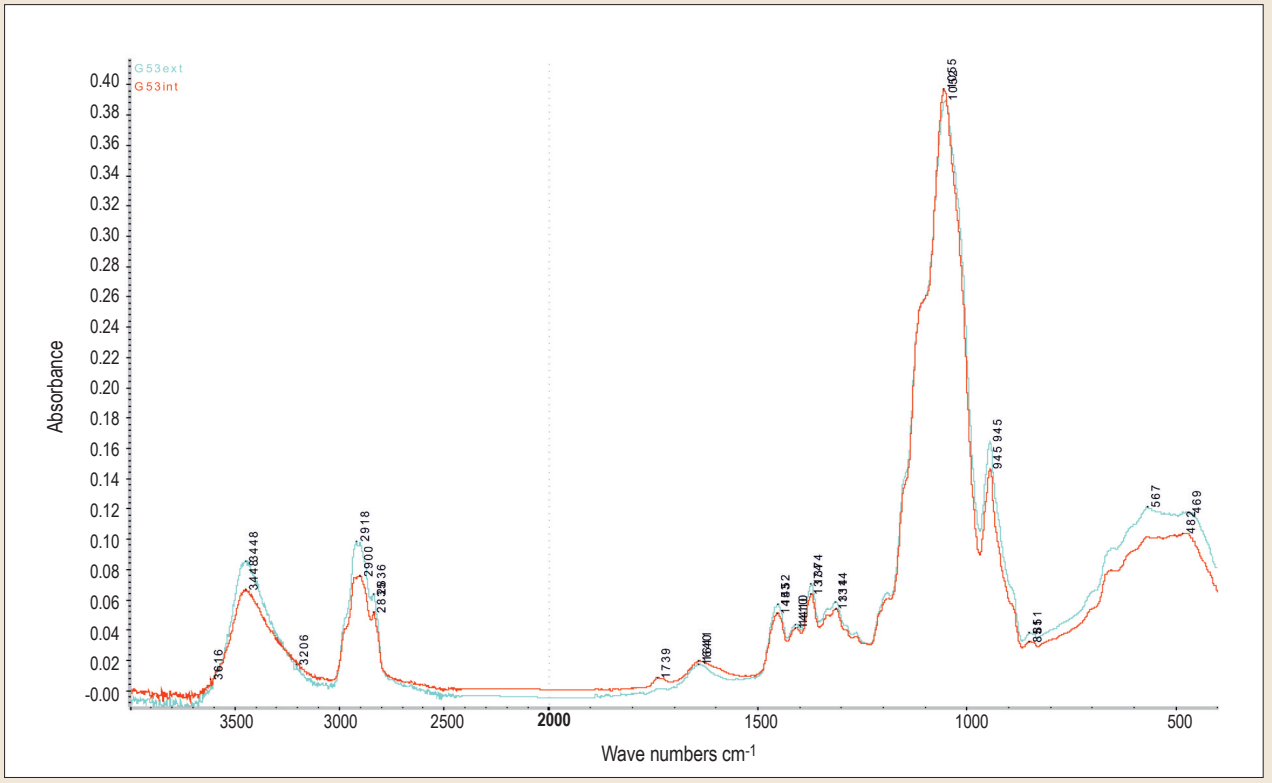

Table 2

The most important vibrational bands for gelatin and hypromellose capsules

Capsule type	Approximate frequency (cm^{-1})	Description	Intensity
Gelatin	3,286	N-H stretching	Medium
Gelatin	1,630	CO stretching	Strong
Gelatin	1,530	C-N stretching N-H bending	Strong
Gelatin	1,460	Unknown	Medium
Gelatin	1,230	C-N stretching N-H bending	Medium
Gelatin	530	CO bending	Medium
Hypromellose	3,400	O-H stretching	Medium
Hypromellose	2,800	$O-CH_3$ stretching	Medium
Hypromellose	1,060	C-O-C stretching	Strong

Conclusions

FT-IR spectrophotometry is a reliable technology that is widely used by pharmaceutical companies for positive identification of incoming samples of goods and materials. It is a quick method that uses validated bench-top devices. The IR spectra for gelatin and hypromellose capsules are different. The most significant differences are found in two regions, 1,630 and 1,060 cm^{-1}. In the first region, gelatin shows a very strong band, where the hypromellose does not absorb. In the second region, the hypromellose absorbs strongly, while the gelatin does not. No differences were found in the spectra of the capsules containing titanium dioxide.

Using IR spectra to test capsules is simple and can be employed as a means of quality control for incoming products. It allows you to test and verify directly what the capsules are made of. *T&C*

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Enrique Requejo Gabás, Ph.D., MBA, is the European quality director, and Fernando Díez Menendez, MBA, is business development manager for Qualicaps Europe, Alcobendas, Spain. E-mail: fdiez@qualicaps.es. The company's US headquarters is located at 6505 Franz Warner Parkway, Whitsett, NC 27377. Tel. 336 449 3900, fax 336 449 3333. Website: www.qualicaps.com. Luis Polo Díez is a professor of analytical chemistry in the Department of Chemistry and Nour Kayali, Ph.D., is a senior mass spectrometrist at the Mass Spectrometry Center of Complutense University of Madrid, Ciudad Universitaria, 28040 Madrid, Spain. Polo teaches analytical techniques, including ATR Infrarred Spectrophotometry. He is an author of approximately 200 scientific papers. Kayali is involved in developing methods in GCMS and LCMS to identify and quantify individual organic molecules in biological and non-biological extracts.