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COMMUNICATION

Application of Near-Infrared Spectroscopy in the Pharmaceutical Solid Dosage Form

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ABSTRACT

Near-infrared (NIR) spectroscopy, one of the most rapidly growing methodologies in pharmaceutical analysis, has been used to analyze the pharmaceutical solid dosage form. The objective of this study was to examine the information that can be gathered from NIR spectroscopy and demonstrate the potential utility of the technique as an alternative to current methods of tablet performance testing. The tablet formulation included active drug (acetaminophen or theophylline), binder (hydroxyethylcellulose), filler (lactose, calcium sulfate, dibasic calcium phosphate dihydrate, or microcrystalline cellulose), and lubricant (magnesium stearate). The compression forces were varied from 5 to 25 kN. A Foss/NIRSystems scanning near-infrared spectrometer was used to measure the diffuse reflectance from the tablet surface. Each tablet was scanned on opposite sides to reduce the effects of positioning. First derivative and multiplicative scatter correction data treatments were explored. A calibration for compression force, independent of the filler, was developed. In addition, the spectra were able to distinguish among the fillers used. A comparison of these spectra with data collected earlier suggests that the technique could differentiate among drugs as well. Near-infrared diffuse reflection spectroscopy, when properly calibrated, can determine the compression force used to prepare a tablet. This measurement may be independent of the different active drugs or fillers used in the tablet formulations.

Key Words: *Hydroxyethylcellulose; Near infrared.*

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INTRODUCTION

Near-infrared (NIR) spectroscopy is one of the most rapidly growing analytical techniques in pharmaceutical analyses because it offers rapid, nondestructive analyses of pharmaceutical dosage forms. It has been used to measure such properties as sample composition and identification, moisture content, content uniformity, homogeneity of mixing, degradation products, and particle size measurements (1–7).

This study investigated the use of NIR spectroscopy in measuring the compression force used to prepare a series of tablets with varying active drugs, binders, fillers, and lubricants. In addition, the investigators were interested in knowing if the technique could distinguish among different fillers used to prepare the tablet series. NIR spectroscopy can obtain this information rapidly and without destruction of the tablet.

EXPERIMENTAL

The materials used were hydroxyethylcellulose (Natrosol® 250L, 250M, and 250HHX, Pharm, Hercules Inc., Aqualon Division, Wilmington, DE); acetaminophen powder USP (Rhone-Poulenc Inc., Specialty Chemicals, Cranbury, NJ); theophylline anhydrous powder USP (Knoll, AG, Ludwigshafen/Rhein, Germany); magnesium stearate NF (Witco Corp., Organics Division, Chicago, IL); microcrystalline cellulose (Avicel, NF, FMC Corp., Food and Pharmaceutical Division, Newark, DE); lactose, regular grind, NF (Wisconsin Dairies, Formost Ingredient Group, Baraboo, WI); calcium sulfate, hydrous, NF (U.S. Gypsum Co., Industrial Gypsum Division, Chicago, IL); and calcium sulfate dibasic USP (DiTab, Rodia, Cranbury, NJ).

All formulations were made using similar low-shear wet granulation techniques. The blended materials were granulated to a suitable end point using purified water; the granules were oven dried until the moisture content was less than 2%. Final tablets were tested for hardness, thickness, weight, and friability. Strength tests were performed using a Vanderkamp Friabilator (Van-Kel Industries, Inc., Chatham, NJ) and Vector Schleuniger Hardness Tester (Vector Corp., Marion, IA). In each group, the compression force varied from about 5 kN to about 25 kN, and the fillers lactose, DiTab, Avicel, and calcium sulfate were used to prepare each set. Each tablet contained 50% acetaminophen or 50% theophylline, 30% hydroxyethylcellulose, 19% filler, and 1% magnesium stearate.

Each tablet was measured by a diffuse reflection technique in a Foss/NIRSystems scanning NIR spectrometer over the wavelength range 1100–2500 nm. In this wavelength region, various molecular bonds exhibit first-, second-, and third-order overtones of the fundamental vibrations observed in the infrared region. These various absorbance characteristics arise from the nature of the chemical bond and are, therefore, characteristics of the material being studied. The nature of diffuse reflectance measurements is that they are influenced not only by the chemical properties of the sample, but also by the scattering properties. In the NIR spectral region, these properties can be used to classify materials as being similar or dissimilar to each other, as well as to relate the apparent particle spacing to the compression force.

To reduce the effects of surface phenomena (blemishes, etc.) in individual tablets, as well as to eliminate the effects of tablet position in the sample beam, a special

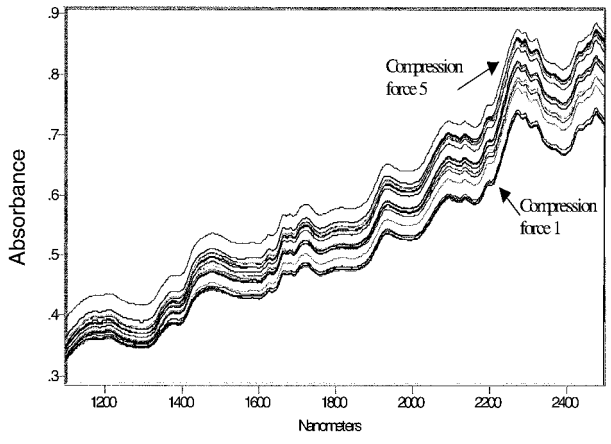

Figure 1. Spectra data of absorbance for tablets made at different compression forces.

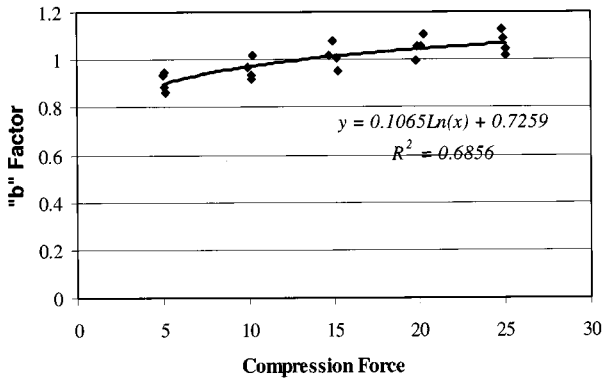

Figure 2. The ''b'' factors versus compression forces.

Table 1

Relationships Between Compression Force and Filler Concentration

Property	Wavelength Selected (nm)	Correlation Coefficient	Standard Error of Prediction
Compression force (kN)	1370	.9802	1.47
Lactose (%)	1706	−.9600	2.43
Di-Tab (%)	1748	.9633	2.33
Avicel (%)	1216	.9519	2.66
$CaSO_4$ (%)	1990	−.9939	0.96

holder was constructed that enabled sampling of each side of a tablet while it was spinning in the sample beam. A total of 30 scans were averaged for each side of a tablet. Both sides of every tablet were scanned, and scans were averaged for each group of tablets. All tablets were handled using forceps to avoid contamination.

RESULTS AND DISCUSSION

Spectra data were obtained as shown in Fig. 1. These spectra were used to determine the relationship between wavelength and compression force, as well as to classify the type of filler used.

Compression Force

When derivative spectra were analyzed for relationships between compression force and filler concentration (nominal 19%) to the spectra, the data in Table 1 were obtained. As the table shows, there is reasonable correlation between compression force and the energy reflected at 1370 nm in the tablet set examined. It is possible that the wavelength selected would change with different for-

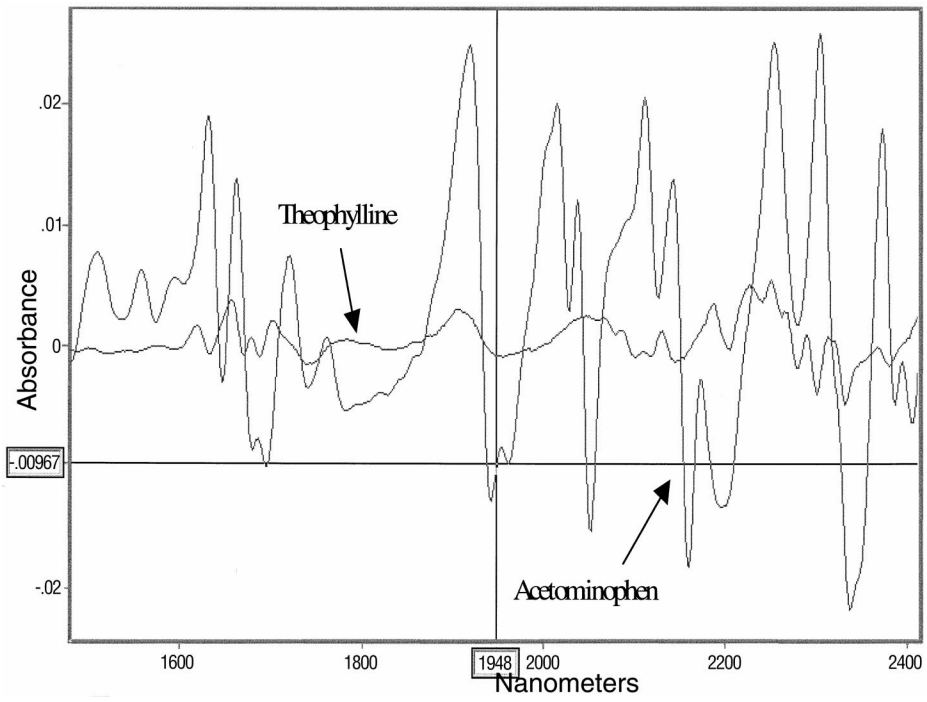

Figure 3. Spectra data of absorbance for theophylline and acetaminophen tablets.

mulations; this was not been explored in this work. Although not established definitively, it is presumed that increasing the compression force changes the spacing between the particles in a tablet. With a change in spacing, the path length over which NIR radiation is transmitted changes, resulting in changes in observed intensity at specific wavelengths. When multiplicative scatter correction (MSC) techniques are used, there appears to be a log relationship between compression force and the ''b'' factor relating to path length (Fig. 2).

Filler Classification

The data show that differentiation between the four fillers used in this study is possible. Due to the limited nature of the sample set (only two concentrations, 0% or 19%, of each filler type were represented), development of a quantitative calibration for the amount of filler present was not possible. Within the sample set, however, there is a strong differentiation between the presence/absence of any of the specific fillers used.

Drug Classification

Earlier, spectra were collected from a similar set of tablets prepared using the same filler, binder, and lubricant as some of the tablets in this set, but with a different drug (theophylline). Comparisons of these spectra (Fig. 3) show significant differences among them. Since only the drug is different and since the drug concentration is about 50% of the tablet, it appears that this technique could be used to distinguish among these formulations as well.

CONCLUSIONS

Near-infrared reflection spectroscopy offers a fast, convenient, nondestructive means of measuring the compression force used to prepare a tablet independently of the filler used. Sampling techniques are straightforward and require little expertise. The technique may also be able to distinguish among different fillers. These capabilities could be useful, not only in analysis of finished tablets, but also could be used to identify raw materials prior to tablet preparation. It is conceivable that, with advance preparation of a spectral library containing various formulations of tablets, NIR spectroscopy could be used to classify a suspect tablet as belonging to a specific group.

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