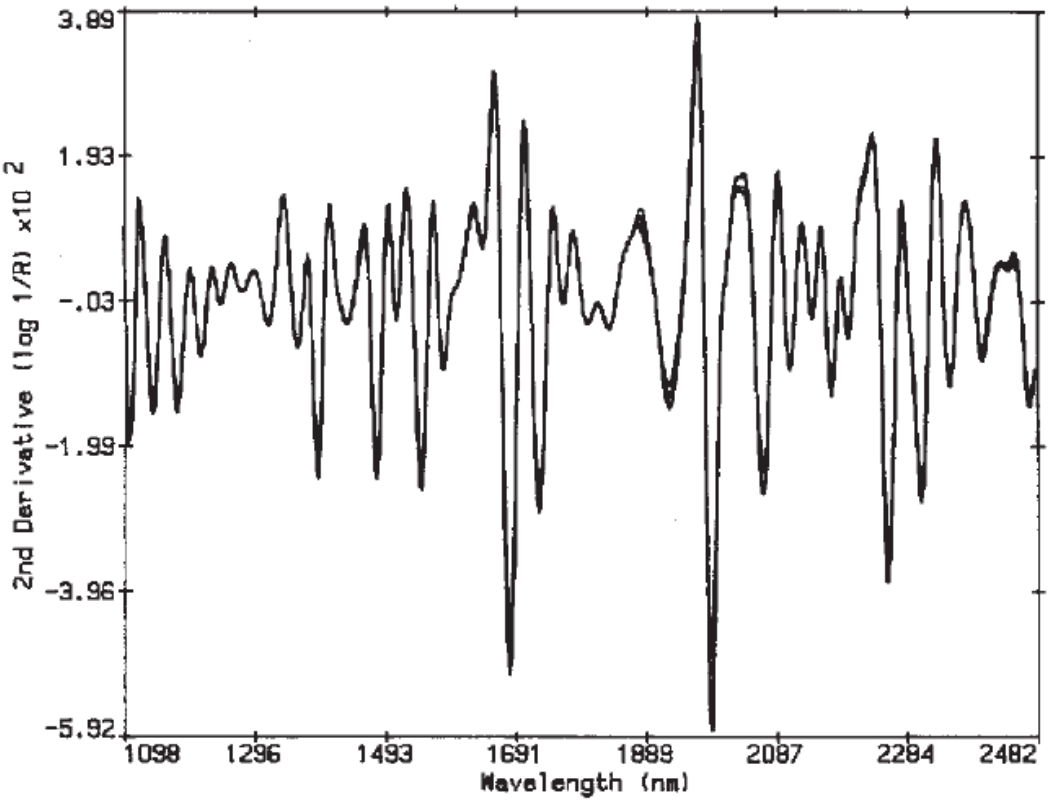
Near-Infrared Spectroscopy Application Note NIR–2

Nondestructive, single tablet analysis using the NIRS XDS RapidContent Analyzer



This Application Note shows the potential of NIRS as a rapid (< 30 s) and nondestructive screening tool for solid dosage forms (e.g., tablets). NIRS requires neither sample preparation nor solvent use. Interferences that derive from scattering are minimized by converting to second derivative spectra.

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Method description

Introduction

The most commonly used method for dosage form analysis is high-performance liquid chromatography (HPLC). Routinely, an operator and a degreed pharmacist check the identities and weights of all ingredients for commercial lots of solid dosage forms. The components are then blended by a validated procedure, and tableted in a manner dictated by standard operating procedures (SOPs) for that product.

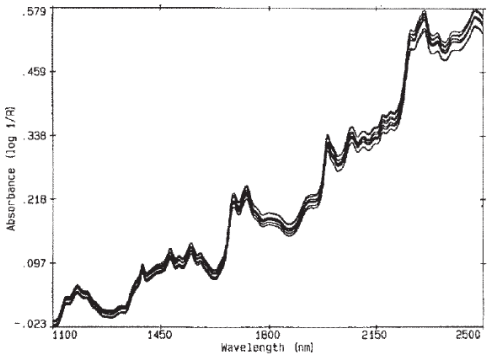
While the methodology permits good results, HPLC has the disadvantages of intensive sample preparation to extract the active materials from the matrix and a time-consuming separation analysis step. Both parts of the analysis use solvents and thus must be used in a well-vented laboratory. The average time for an assay is often hours when the preparation step is included. In addition, the equipment takes up a fair amount of bench space while the solvents, vials, filters, syringes, columns, and other disposables amount to a considerable ongoing expense.

It may not be strictly necessary to separate the just-blended materials to assay for uniformity of the actives if an alternate, nondestructive method can be applied. Near-infrared spectroscopy (NIRS) is a nonintrusive, nondestructive method which uses chemometrics (the use of computer programs to relate spectral, physical, or chemical values) to make sense of the combined spectra of a dosage form. NIRS is a rapid technique requiring little or no sample preparation and no solvents.

Experimental

A NIRS XDS RapidContent Analyzer was used for sample analysis. The instrument includes a centering iris used to position the samples. The samples were collected in reflectance mode in the 1100–2500 nm region. Several commercial lots of procainamide HCl tablets, both 500 and 750 mg, were obtained for this study. One hundred individual tablets were scanned from each lot, and 10–20 individual tablets with the largest apparent spectral differences were further analyzed by the reference HPLC method. The HPLC results were appended to the NIR spectra and, based on the regions where the active absorbed, a calibration model was developed.

Figure 1
750mg Tablets; Absorbance spec.



Results and discussion

Absorbance spectra of the procainamide HCl tablets are shown in Figure 1. Many of the apparent spectral differences are due to scattering, both multiplicative and surface. Converting to the second derivative spectra eliminates many of these surface effects. The resultant spectra (see Figure 2) were used for calibration. The numerous regions where spectral differences occur between the active and placebo tablets are shown in Figure 3.

Figure 4 displays the second derivative enlargement of the active, matrix, and tablet. In this spectral region, the active contributes most of the absorbance to the overall tablet spectrum, while the matrix contribution is minimal. This spectral region is suitable for calibration development.

Using one lot of 750 mg tablets, a calibration model was developed at 1368 nm. A correlation of -0.84 and a standard error of calibration (SEC) of 1.7 mg were obtained. The largest relative residual error between NIRS and HPLC was 0.53%. A second lot of 750 mg tablets was chosen for validation. The standard error of prediction (SEP) was 1.4 mg, with the largest relative residual error of 0.43%. The comparable SEC and SEP prove that the calibration model is valid.

To test the versatility of the technique further, a 500 mg lot of tablets was analyzed. Results were quite satisfactory. In general, the equation used for tablet analysis becomes more «robust» as tablets with assay values farther from the mean are added to the sample set.

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Method description

Figure 2
2nd Derivative Spectra of Tablets

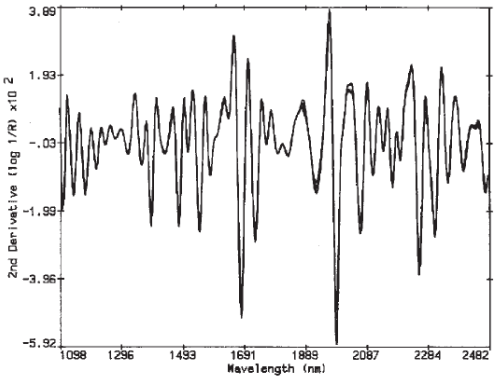
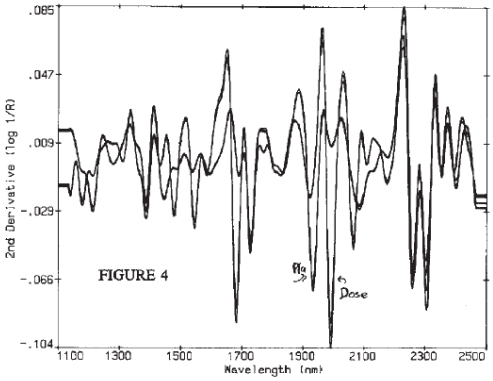


Figure 3
Placebo vs Active Tablet

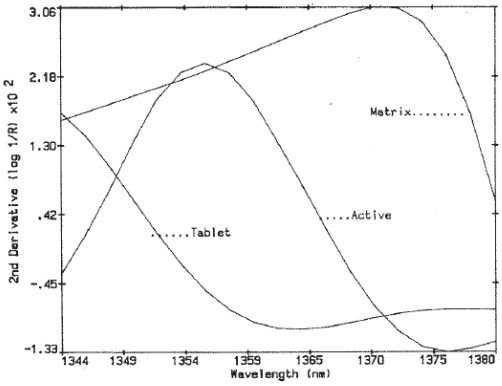


Since a normal, commercial tableting process is usually well within control, outliers are seldom encountered. As they are found, however, they are added to the sample set to increase its range. The equation used for finished product release will continue to improve as more diverse values are added to the calibration set over time.

Conclusions

Near-infrared spectroscopy may be used as a nondestructive, rapid assay for solid dosage forms. The analysis takes approximately 30 seconds to perform, requires no sample preparation and is location insensitive. The assay may be performed in a conventional quality control setting, i.e., a laboratory, or may be done on-site in production. In the second case, the time consuming procedure of labeling, transporting, separating, then assaying the product can be eliminated.

Figure 4
Matrix, Active, Tablet



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