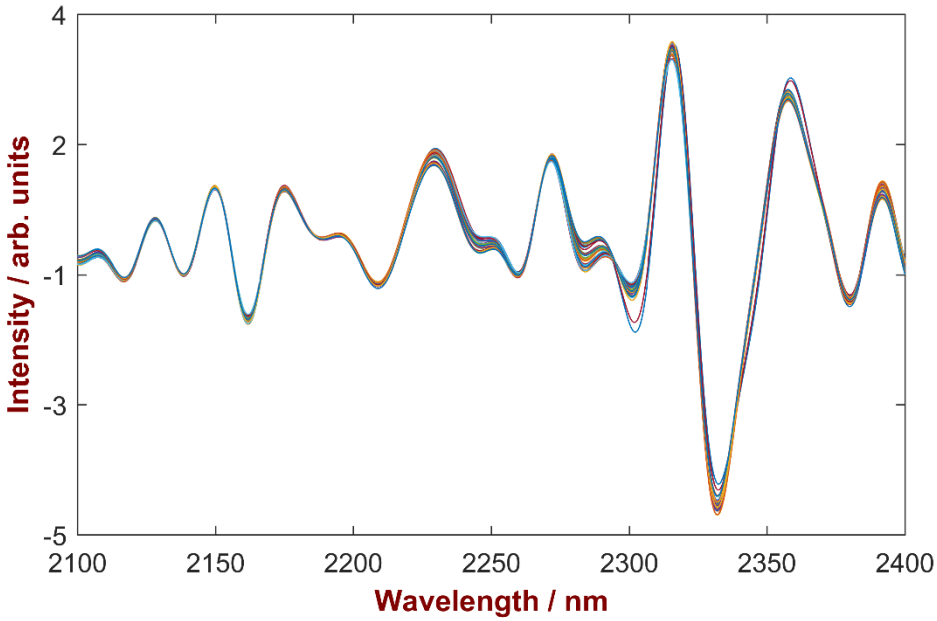
NIR Application Note NIR–066

Content uniformity of pharmaceutical solid dosage forms using Vis-NIR spectroscopy exemplified on Cefixime tablets.



This Application Note describes content uniformity testing of Cefixime tablets using Vis-NIR spectroscopy. The standard error of 2.3% was found to be in the same range as the standard error of the reference method of 1.5%. Without any sample preparation, this technique is faster and easier to handle than the traditional (HPLC) method.

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Method description

Introduction

Content uniformity testing is a fundamental part of quality control in the pharmaceutical industry. It is defined as the degree of uniformity in the amount of active pharmaceutical ingredient (API) among dosage units. The manufacturer needs to demonstrate that each batch has a content within a narrow range around the target concentration. In pharmaceutical analysis, the main objective is to reduce analysis time without loss in efficiency. Usually, high performance liquid chromatography (HPLC) is used as a quantification method. However, the drawbacks of this method are sample destruction and a long analysis time, due to extensive dissolution and extraction procedures. HPLC requires a solvent or usually a mixture of multiple solvents, as a mobile phase. Depending upon the type and the amount of solvents consumed, the analysis can be very cost intensive. In addition, this technique carries the risk of operator error, if the user isn`t trained accordingly. Alternatively, the manufacturer can utilize visible-near-infrared spectroscopy (Vis-NIR). With this technology, a tablet can be analyzed as-is without any sample preparation. As a consequence it involves no sample destruction, which enables further testing if necessary.

In the present Application Note Cefixime tablets were used for the development of a Vis-NIR method for the determination of the API in tablets.

Experimental

31 tablet samples provided by a customer were analyzed in the present feasibility study. The error of the reference method was estimated to be 1.5%. The spectra were collected in reflection mode on a NIRS RapidContent Analyzer over the full wavelength range (400–2500 nm). Samples were positioned using NIRS XDS iris. The software package Vision Air 2.0 Pharma Complete was used for analysis and development of the quantification method. Tab. 1/Fig. 1 lists the used equipment.

Tab. 1: Used equipment and software.

Equipment	Metrohm number
NIRS XDS RapidContent Analyzer	2.921.1110
NIRS XDS iris	6.7425.000
Vision Air 2.0 Pharma Complete	6.6072.209

Fig. 1: The NIRS XDS RapidContent Analyzer was used for spectral data acquisition over the full range from 400 to 2500 nm.

Results

Fig. 2 shows Vis-NIR spectra of Cefixime tablets. Redundant spectral information was excluded from the method development by the selection of analyte specific wavelength ranges combined with dedicated spectral pre-treatments. An example of this procedure is shown in Fig. 3, which demonstrates spectra pretreated with a 2nd derivative and Standard Normal Variate (SNV) over the full wavelength range.

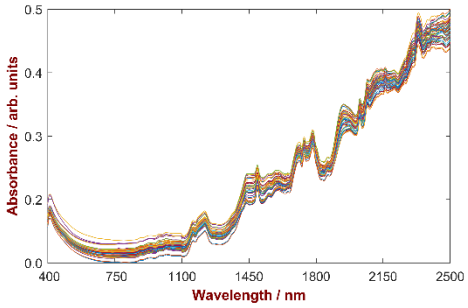

Fig. 2: Vis-NIR spectra of Cefixime tablets over the full wavelength range.

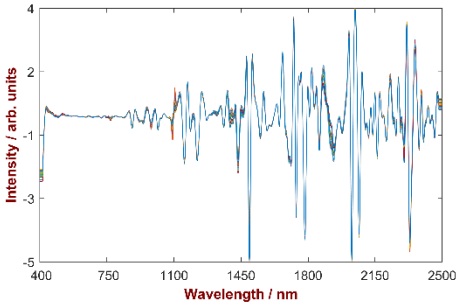

Fig. 3: Spectra pretreated with 2nd derivative and SNV over the full wavelength range.

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The correlation coefficient for this model is 0.968, which shows strong correlation between the HPLC measurements and Vis-NIR predictions. In addition, a Standard Error of Calibration (SEC) of 1.6% and a Standard Error of Cross-validation (SECV) of 2.3% confirm the suitability of this technique for content uniformity (**Tab. 2**).

Tab. 2: Results of the quantitative method development for Cefixime content.

Regression model	PLS, 4 factors
Pre-treatment	2nd derivative + SNV
Wavelength ranges	1120–2300 nm 2280–2346 nm
R^2	0.968
SEC	1.6%
SECV	2.3%

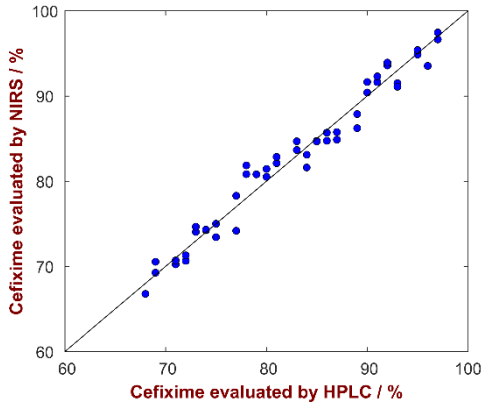

Fig. 4: Correlation plot of the Cefixime content predicted by NIRS versus the reference values.

Summary

This Application Note shows that the NIRS XDS RapidContent Analyzer is the ideal instrument for quality control of pharmaceutical products. Due to short analysis time, Vis-NIR spectroscopy allows the API content to be controlled at different production steps. The standard error was found to be in the same range as the error of the reference method. Additionally, it should be pointed out, that for further pharmaceutical products such as liquid dosage forms, similar NIR methods can be developed.

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