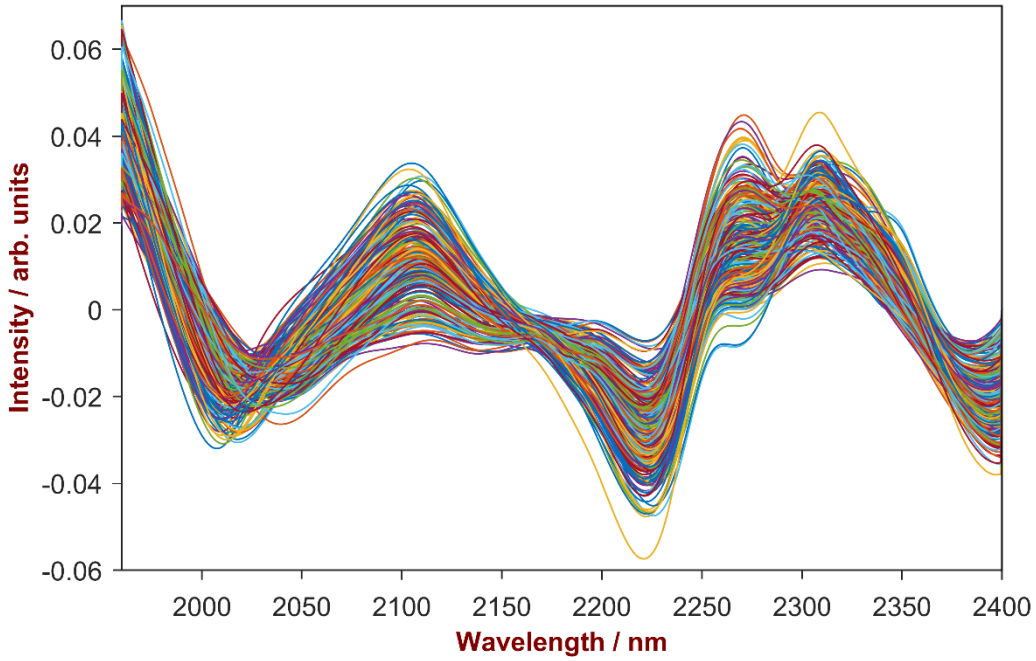
Near-Infrared Spectroscopy Application Note NIR–42

Determination of USP Heparin Units using near-infrared spectroscopy (NIRS)



The product strength of Heparin sodium can be determined using near-infrared spectroscopy with excellent figures of merit.

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Method description

Introduction

Heparin is a glycosaminoglycan used as an anticoagulant for therapeutic uses. It can either be used directly for humans given by injection or used as a lock flush solution to maintain the patency of intravenous injection devices (IID). The U.S. Pharmacopeial Convention (USP) regulates the product strength of Heparin Sodium doses as well as the Heparin Lock Flush Solution. The product strength of Heparin sodium has to be determined accurately and precise to guarantee the desired physiological effect on patients as well as an effective maintenance of intravenous injection devices. This determination is run using UV-Vis spectroscopy needing multiple reagents and takes up a great deal of time. A reduction of time expense and reagents should be strived for. This can be accomplished using near-infrared spectroscopy.

Configuration

The spectral measurement of the Heparin sodium precipitates was performed using the Metrohm NIRS DS2500 Analyzer in combination with the Mini Sample Cup. The software package Vision Air 2.0 Pharma Complete was used for data acquisition, data management and development of the quantification method (Tab. 1).

Tab. 1: Used equipment and software for this application.

Equipment	Metrohm order code
NIRS DS2500 Analyzer	29220010
NIRS Mini Sample Cup Holder for DS2500	67430040
NIRS mini sample cups	67402030
Vision Air 2.0 Complete Pharma	66272209

Fig. 1: The NIRS DS2500 Analyzer collects spectral data from 400 nm to 2500. Therefore, determination of the product strength of Heparin via primary method such as routine measurement can be carried out on the same analyzer.

Experimental

The product strength of Heparin sodium precipitate was determined of provided samples by the customer. The samples showed a product strength of 50 – 140 USP U/mg. The used Vis-NIR instrument in the study was Metrohm NIRS DS2500 Analyzer, which was operated in stationary diffuse reflectance mode with the Mini Sample Cup (Fig. 1). Absorbance spectra were obtained using 32 co-added scans. The quantification method was developed in Vision 4.1 Pharma (Metrohm chemometric software) using the algorithm of Partial Least Squares Regression (PLS). Although the NIRS DS2500 Analyzer allows spectral data collection from 400 nm to 2500 nm, the PLS evaluation was performed using the spectral regions 800 – 1000 nm, 1120 – 1300 nm, 1500 – 1850 nm and 1960 – 2400 nm. The data was pre-treated using Detrend function of order 2 (see title image).

The developed model yielded a Standard Error of Prediction SEP = 4.3 USP U/mg using 6 factors (Fig. 2). Because of the very low SEP, this method shows very suitable for analyzing the product strength of Heparin sodium precipitate for the use in injection solutions and Heparin Lock Flush Solution.

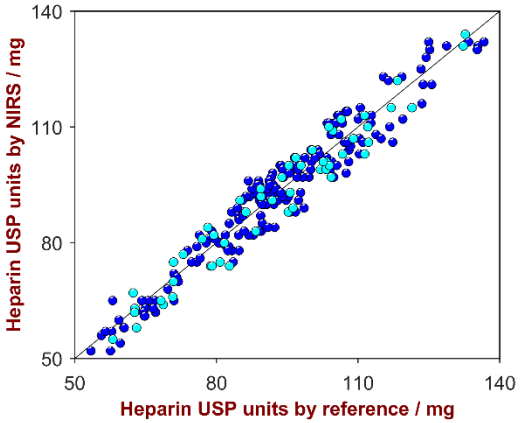

Fig. 2: Correlation plot of the predicted Heparin sodium product strength by NIRS versus the laboratory values. Displayed are the training data (blue) and validation data (turquois).

Results

This application note demonstrates the applicability of Vis-NIR spectroscopy to determine the product strength of Heparin sodium precipitate. Due to the extended spectral range of the NIRS DS2500 Analyzer, the primary method such as the routine measurements can be carried out using the same analyzer.

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Near-Infrared Spectroscopy Application Note NIR-042
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