Abstract
Qualitative evaluation of blend homogeneity using near infrared spectroscopy

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Introduction

In the preparation of pharmaceutical mixes optimisation of blending conditions is crucial to achieve homogeneity of the added formulations. Factors to be optimised include, for example, the type of blenders, the mixing time, and other parameters involved with blending operations. A rapid and easy-to-use analytical tool for evaluating homogeneity of a blend is highly desired to speed up the optimisation process. In this respect near-infrared (NIR) spectroscopy provides an ideal analytical solution. Blend homogeneity can be evaluated in either a quantitative or a qualitative way. Quantitative evaluation requires a calibration model for each component to obtain its amount. However, preparing calibration samples and submitting them for reference analysis is rather labour-intensive and not practical. Qualitative evaluation, on the other hand, does not require calibration models. A highly homogeneous blend is expected to show small spectral variation, whereas an inhomogeneous blend will show a relatively large variation. Therefore, blend homogeneity can be evaluated through any parameter reflecting spectral variation.

In this study, homogeneity of magnesium stearate in a simulated matrix consisting of lactose and acetaminophen is evaluated. As a parameter reflecting homogeneity, a standard deviation of the scores derived from the first principal component of spectra is employed. For comparison purposes, homogeneity is also evaluated through a standard deviation of the projections of spectra on a net analyte signal vector for magnesium stearate. Homogeneity of magnesium stearate prepared with various conditions, and comparison with quantitative evaluations will both be discussed.

Materials and methods

A simulated matrix consisting of 90% of lactose and 10% of acetaminophen was prepared. To this base matrix, 1% of magnesium stearate was added in a container of a high-speed blending mixer. A probe head was inserted into the sample matrix to monitor changes in spectra during the course of a five-minute mixing step. To evaluate blend homogeneity prepared with different types

of blenders, samples were gathered in a plastic bag first and then probes were inserted into the samples to conduct repeated measurements. NIR reflectance spectra over the wavenumber range of 4000 cm^{-1} to 10000 cm^{-1} were measured with a NIRFlex N-500 Fourier transform spectrometer (Buchi Labortechnik AG, Flawil, Switzerland), equipped with a fibre-optics probe. All measurements were conducted at room temperature. An average of eight co-added spectra was collected for each measurement. The resolution and point-spacing of the acquired spectra were 8 cm^{-1} and 4 cm^{-1}, respectively. For quantitative evaluations with PLS calibration models, samples containing six levels of magnesium stearate within the range of 0% to 2.96% were prepared with the same matrix, consisting of lactose and acetaminophen. Spectral processing and principal component analysis were performed with NIRCal software (Buchi Labortachnik AG, Flawil, Switzerland). The software was also used for building PLS calibration models. Calculations involved with a net analyte signal were performed with public domain statistical software, R (version 2.8.0).

Results and discussion

A two-factor PLS model with a standard error of calibration of 0.03% was obtained and used for quantitative evaluations of homogeneity of magnesium stearate. It was confirmed that the homogeneity evaluated quantitatively and qualitatively showed no significant difference. Details will be discussed in the poster presentation.