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Determination of water content in lactose by near-infrared spectroscopy

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Many of the conventional methods available for the determination of water content (e.g. Karl Fischer, mass-loss-on-drying, gas chromatography etc.) are labour intensive, time consuming and destructive. Near-infrared (NIR) spectroscopy, however, does not suffer from such disadvantages. NIR has been used in the food industry for several years for the determination of water content (Fearn et al 1986) but has yet to be widely exploited for use in pharmaceutical applications. The NIR region of the electromagnetic spectrum is rich in both chemical and physical information and for a quantitative determination requires calibration with samples of a known water content. Generally, mathematical treatment of the spectral data is necessary to aid selectivity of the calibration model to analyte parameters or constituents (e.g. moisture content, particle size etc). This use of powerful chemometric software to perform such manipulations generates a "black-box" mentality and dissuades some non-NIR users. In this study several calibration models were obtained using a broad range of data-pretreatment methods (e.g. spectral derivatisation, normalising etc.) and regression methods (e.g. single or multiple wavelength, principal components etc.).

Lactose monohydrate (stoichiometric water content 5.0%) was stored at two conditions; 100% relative humidity, and in an oven at 105 ^{0}C, to obtain a collection of samples with a range of water content between approximately 2 and 7% w/w . The reference water content for each sample was determined in triplicate using a Metrohm 703 KF Titrino (Metrohm UK Ltd, Buckingham, UK). NIR reflectance spectra were recorded using a Bran+Luebbe InfraProver II, (Bran+Luebbe, Nordestedt, Germany) fitted with an optical fibre probe. Each sample spectrum (4500-9600 cm^{-1}) was calculated from the mean of nine scans. Spectral manipulation and generation of calibration models were performed using NIR chemometric package, NIRCAL, (Version 2, Buhler Anatec Ltd.) and also Microsoft Excel.

An example of one of the more simple approaches to mathematical treatment of the NIR data is given in Figure 1, and shows the effect of taking a ratio of NIR absorbance values (peak heights). The quotient of the value at 5172 cm^{-1} (high correlation to water content attributed to the O-H combination band in NIR region) by the value at 6276 cm^{-1} (lower correlation to water - compensating for spectral baseline offset) plotted against reference water content. The best fit line was also plotted. After 5% w/w (stoichiometric water content for lactose monohydrate) a change in slope was observed which was compensated for by using two methods. Firstly a curve fitting procedure produced a correlation coefficient, r = 0.997, and secondly two linear regressions separated at 5% w/w, r = 0.999.

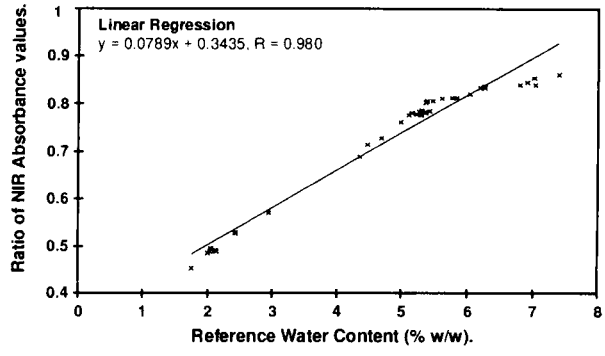

Figure 1 - Calibration equation generated using a ratio of NIR absorbance values (5172/6276 cm^{-1}) versus reference water content.

NIR has been shown to be a useful method for the determination of water in lactose samples. Very acceptable calibration models were produced using a variety of simple data treatments and giving correlations equal to the more complex methods such as principal component regression. Specificity to the total water content or information about the interaction between water and lactose molecules was observed in some models. NIR offers clear advantages for accurate water content determination since sample exposure to the environment is minimal.

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