



Application Note AN-NIR-078

Automated moisture analysis in pharmaceutical peptides

Non-destructive quality control

The quantification of residual moisture in lyophilized pharmaceutical peptides is an important measure for quality control in the pharmaceutical industry. Analyses are routinely performed for process control and to ensure that production lots meet required specifications. For development purposes, such measurements are necessary during stability studies and to optimize the freeze-drying process (lyophilization).

Currently, Karl Fischer titration is widely used for moisture determination in routine analysis. However, measuring the water content by this method is time consuming and the sample is destroyed during analysis. This Application Note shows that near-infrared spectroscopy (NIRS) is a fast, reagentless, non-destructive method to determine moisture content in lyophilized pharmaceutical products.

EXPERIMENTAL CONDITIONS

17 spectra of samples with varying moisture content were collected using a Metrohm NIRS XDS OptiProbe Analyzer in combination with the 815 Robotic Sample Processor. With the attached large sample rack, it was possible to automate measurements of up to 62 samples in series. The reference values were obtained by KF-titration. The data set consisting of spectra and lab values was split into a calibration set (11 samples) and validation set (6 samples). Outlier detection was performed on pre-treated spectra (2nd derivative) using a maximum distance in wavelength space algorithm.



Figure 1. The NIRS XDS OptiProbe Analyzer and the 815 Robotic Sample Processor.

Pre-processing	Algorithm	Validation type
2 _{nd} derivative	PLS	Independent validation set

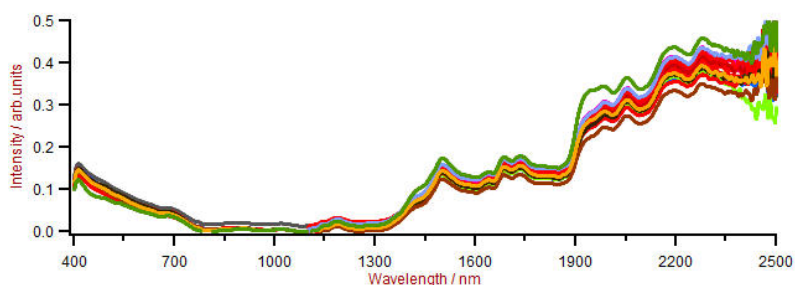


Figure 2. Protein samples measured with varying water content.

RESULT & CONCLUSION

The obtained correlation graph displays a very high correlation ($R^2 = 0.99$) between moisture predicted by NIRS and the KF-titration primary method. SEC and

SEV values are in the range of 0.060%, which proves that NIRS is a sensitive and suitable technique for moisture determination.

# Factors	R2	SEC	SEV
2	0.99	0.054%	0.061%

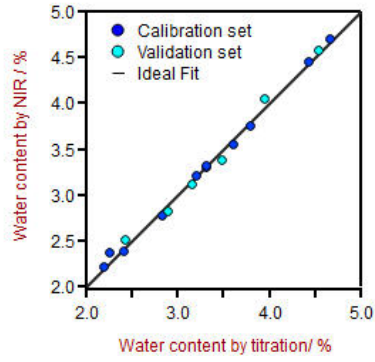


Figure 3. Correlation graph for moisture predicted by NIRS vs titration.

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