



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 |

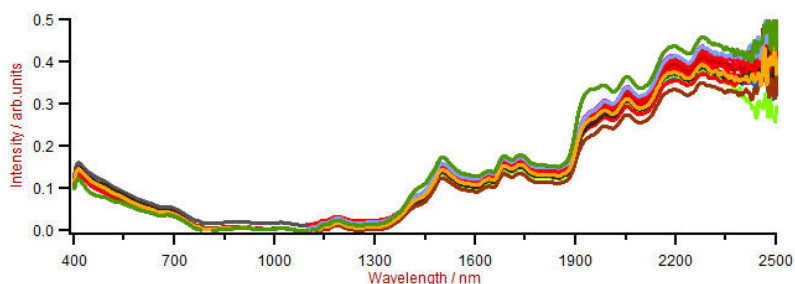


Figure 2. Protein samples measured with varying water content.

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 | R^2 | SEC | SEV |
|-----------|-------|--------|--------|
| 2 | 0.99 | 0.054% | 0.061% |

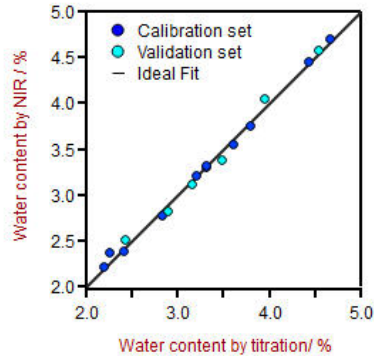


Figure 3. Correlation graph for moisture predicted by NIRS vs titration.

CONTACT

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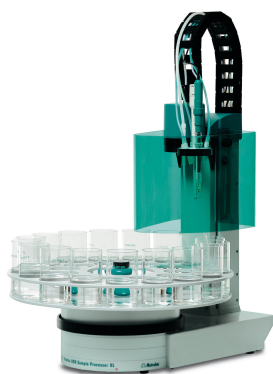
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CONFIGURATION



NIRS XDS Interactance OptiProbe Analyzer
Robust measurement system for the monitoring of reactions in technical centers and in pilot plants.

The NIRS XDS Interactance OptiProbe Analyzer enables the simple and reliable monitoring of chemical reactions in technical centers and pilot plants. The method development and the scale-up of production processes are areas of application in which the NIRS XDS Interactance OptiProbe Analyzer supplies precise results regarding the identity and quality of a wide variety of samples. Whereas solids, strongly scattering liquids and slurries are measured with the reflection probe, the immersion probe is used to analyze aqueous products, clear liquids and solvents. The probe is connected to the analyzer through an optical fiber to enable secure measurements even under rough and/or dangerous conditions in the processing environment.



815 Robotic USB Sample Processor XL (1T/1P)

Robotic USB Sample Processor XL with one workstation and one built-in membrane pump for the automatic processing of routine samples in series with large quantities and for complex sample preparation or parallel runs. In addition to the built-in pump, an additional one (membrane or peristaltic) and up to three dosing devices for Liquid Handling tasks can be connected.

Because of the multitude of application variants, rack, stirrer, titration head, robotic arm, Swing Head and sample vessels must be tailored to the application and ordered separately.

The control is "stand alone" using Touch Control. The following software products can be selected for the PC control: tiamo™ titration software, MagIC Net chromatography software, viva voltammetry software, or OMNIS.



Vision Air 2.0 Complete

Vision Air - Universal spectroscopy software.

Vision Air Complete is a modern and simple-to-operate software solution for use in a regulated environment.

Overview of the advantages of Vision Air:

- Individual software applications with adapted user interfaces ensure intuitive and simple operation
- Simple creation and maintenance of operating procedures
- SQL database for secure and simple data management

The Vision Air Complete version (66072208) includes all applications for quality assurance using Vis-NIR spectroscopy:

- Application for instrument and data management
- Application for method development
- Application for routine analysis

Additional Vision Air Complete solutions:

- 66072207 (Vision Air Network Complete)
- 66072209 (Vision Air Pharma Complete)
- 66072210 (Vision Air Pharma Network Complete)



tiamo™ 3.0 light USB: 1 license

tiamo™ 3.0 light computer program for controlling a titration system.

Up to two Metrohm instruments (Titrino, Titrand, etc.) can be connected; balances and other generic (i.e. non-Metrohm) instruments can be included without limitation

Graphical method editor with numerous templates

Layout manager for individual monitor interface

Professional database with reevaluation

High-performance report generator

Data export as PDF file, CSV, SLK

No parallel titration

No data export in XML format for LIMS

Dialog languages: German, English, French, Italian, Spanish, Czech, Portuguese, Polish, Russian, Slovakian, Japanese, Chinese, Traditional Chinese