Metrohm NIRSystems

Application Bulletin 410

Analysis of pharmaceuticals using near-infrared spectroscopy

Branch

Pharmaceuticals

Keywords

Near-infrared spectroscopy, pharmaceuticals, tablet analysis, identification, raw materials, qualitative analysis, quantitative analysis, moisture determination, active ingredient, fermentation, granulations, amino acid.

Summary

This Application Bulletin shows the examples of NIR applications and the feasibility studies using NIRSystems in the pharmaceutical industry. It includes qualitative and quantitative analysis of different kinds of samples. Each application briefly describes the measuring systems used in the studies as well as the recommended instruments and the test results.

Introduction

NIR spectroscopy has been used in the pharmaceutical industry for many years. Common pharmaceutical NIR applications include receiving inspection of excipients and active pharmaceutical ingredients (API), blend uniformity, granulation, drying and coating, and final product verification analysis. Additionally, NIR spectroscopy is an invaluable tool for the detection of counterfeit drug products and the determination of water, residual solvent and active ingredient contents. As an alternative test method, NIRS appears in the European Pharmacopoeia (2.2.40), the Japanese and the US Pharmacopeia (USP<1119>).

Contents

No. 1: Using NIR as an identification technique or raw materials and product materials

Summary

This NIR application is used to identify raw and product materials. A total of ten different compounds were analyzed for demonstration.

System

NIRS XDS RapidContent Analyzer	2.921.1110
NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The samples were analyzed in the 1100–2500 nm region. The liquid samples were analyzed in transmission mode using a cuvette with a 1 mm pathlength. All solid samples were analyzed in reflectance mode, directly through the glass vials, using the rapid-content analyzed (RCA) module. IQ2 was used for qualitative analysis.

Results

The results indicate that raw material and product identification can be performed using NIR.

No. 2: Identification of pharmaceutical raw materials

Summary

This application is showing the use of NIR to identify pharmaceutical raw materials. The most important raw materials involved adenosine monophosphate (AMP), adenosine diphosphate (ADP) and adenosine triphosphate (ATP). Besides the pure materials, six mixture samples were also provided: 90/10 AMP/ADP, 90/10 ADP/ATP, 90/10 ATP/AMP, 98/2 ADP/ATP, 98/2 AMP/ADP, 98/2 ATP/AMP.

System

Model 5000, fiber optic bundle setup module, interactance fibers and reflectance probe, transmission detector module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS SmartProbe Analyzer	2.921.1610
2m Fiber	

Sampling

The samples were analyzed in the 1100–2500 nm region in reflectance mode. The samples were analyzed using a fiber optic probe. Each sample was analyzed four separate times. A spectral library was created in the 1200–2400 nm region. It appears that NIR is sensitive to impurities in the samples.

Results

The results indicate that NIR can be used to distinguish between three types of adenosine phosphate compounds.

No. 3: Monitoring avicel, starch, and lactose in a mixture

Summary

This NIR application is used to monitor avicel, starch, and lactose in a mixture of these materials, and in the final product. Six samples were received: three containers of raw materials, and three containers of final product (which also contained triazolam).

System

Model 5000, transmission detector module, fiber optic bundle setup module, interactance fiber and reflectance probe was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS SmartProbe Analyzer 2m Fiber	2.921.1610

Sampling

The samples were analyzed in the 1100–2500 nm region using a fiber optic interactance reflectance probe. Calibration mixtures of the three raw materials were made to cover the range of 1 to 60% (w/w) of raw materials. Each sample was analyzed twice, re-mixing between scans. A calibration for lactose was performed at 2150/2022 nm (SEC of 1.0%). The second wavelength was included to correct for scattering differences in the samples. For starch, a calibration was developed at 1378/1146 nm (SEC of 1.7%). For avicel, a calibration was developed at 1348/1644 nm (SEC of 2.9%).

Results

The results indicate that NIR can be used to monitor the three constituents.

No. 4: Qualitatively distinguishing between a series of four nucleic acids bound on glass

Summary

This NIR application is used to distinguish between different nucleic acids on glass. Five samples, each containing a different nucleic acid (deoxyadenosine, deoxycytidine-modified, deoxyguanidine, and deoxythymidine) were provided for analysis.

System

Model 5000, transmission detector module, fiber optic bundle setup module, interactance fiber and immersion probe was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS SmartProbe Analyzer 2m Fiber	2.921.1610

Sampling

The samples were analyzed in the 1100–2500 nm region using a fiber optic bundle probe. A spectral library was created in the 1600–1800, 2175–2300 nm region.

Results

The results indicate that NIR can be used to qualitatively differentiate between four nucleic acids bound on a glass substrate.

No. 5: Distinguishing between samples of the nucleic acid, deoxycytidine, which differed only in linker compound

Summary

This NIR application is explaining why no difficulty existed in distinguishing between two samples of deoxycytidine (which differed only in linker compound).

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The samples were analyzed in the 1100–2500 nm region in reflectance mode. The differences of the samples of Nucleic Acid and Deoxycytidine (which differed only in linker compound) could be seen in the 1600–1750 nm region.

Results

The two spectra appear to only differ in the baseline (which indicated that the sample containing the modified linker is a larger particle size). Significant spectral differences occur between the sample with the standard linker and the sample with the modified linker. Based on these variations, it is easily understood why our qualitative software package was able to distinguish between these two compounds.

No. 6: Qualitative study of amino acids and amino acid salts through plastic bags

Summary

This NIR application is used to qualitatively study amino acids and amino acid salts through plastic bags.

System

Model 5000, reflectance detector module, horizontal setup module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The samples were measured in reflectance mode in the 1100–2500 nm region. The DCA horizontal setup was utilized for analysis. A library was developed in the 1134–1698 nm and 1840–2274 nm regions.

Results

The results indicate that NIR can be used to identify the materials through the plastic bags.

No. 7: Determining differences between catalase protein on glucose and sucrose substrates

Summary

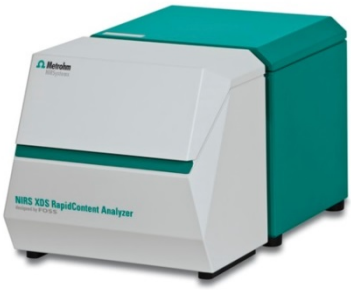
NIR spectroscopy is used to determine if any distinct spectral differences could be detected between the catalase protein on the two different substrates. Samples were catalase protein on glucose substrate, catalase protein on sucrose substrate, and a 1% mixture of catalase protein on glucose in catalase protein on sucrose.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The samples were analyzed in a micro sample cup placed in the sample transport module. All samples were analyzed five times rotating the cup between scans. Looking at the 1% solution, at approximately 1740 nm, there appears to be spectral contribution due to the catalase protein on glucose, without interference from the catalase protein on sucrose.

Results

The results indicate that NIR can be used to differentiate between catalase protein on sucrose and catalase protein on glucose. In order to be certain, a full feasibility study needs to be performed.

No. 8: Qualitative analysis of instant chocolate mixtures

Summary

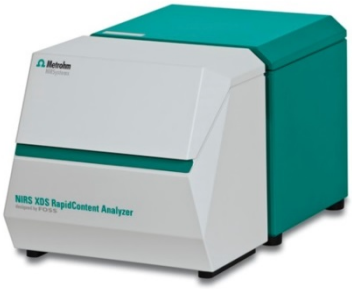
This NIR application is used to qualitatively distinguish between good and bad lots of instant chocolate mixtures.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

Four samples were provided for analysis: two samples from good lots, and two samples from bad lots. The samples were analyzed in the 1100–2500 nm region. A spinning sample module was used. Each sample was repacked and analyzed five times. This repetition was done to ensure that any spectral differences seen were associated with chemical differences, not sampling error. Differences were seen in the 1975 to 2125 nm region, and the 1475 to 1625 nm region. Both regions are associated mainly with amine absorptions, however, aldehyde or ketone absorptions can also occur there.

Results

The results indicate that NIR can be used to detect chemical differences, although the exact causes of the absorptions are uncertain.

No. 9: Distinguishing between different capsules of piroxicam

Summary

This NIR application is used to distinguish between different capsules of Piroxicam. Six capsules were provided for comparison.

System

Model 5000, transmission detector module, fiber optic bundle setup module, interactance fibers and reflectance probe was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The samples were analyzed in the 1100–2500 nm region in reflectance. The RCA was used for whole capsule analysis. The fiber optic interactance probe was also used for analysis of the piroxicam powder. Significant spectral differences can be seen around 2400, 2100, 1775, and 1450 nm.

Results

The results indicate that NIR can be used to locate significant spectral differences in these capsules. Using just the powder, stronger absorptions are seen.

No. 10: Qualitatively distinguishing naproxen tablets from a placebo

Summary

This NIR application is used to qualitatively distinguish naproxen tablets from a placebo. Several tablets were provided of various shapes and sizes. Also provided were four unknowns.

System

Model 5000, reflectance detector module, sample transport module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The samples were analyzed in reflectance mode in the 1100–2500 nm region. The tablets were placed into an aluminum cup, and the remote reflectance module was used for analysis. The spectra of the placebos are easily distinguishable from that of the tablets containing naproxen. A library was developed using these spectra.

Results

Based on these results, it appears feasible to identify individual tablets as either a placebo or a tablet containing the active ingredient.

No. 11: Qualitatively distinguishing between four samples: A, B, Diazepam, and meprobamat

Summary

This application shows that NIR spectroscopy can be applied to distinguish between A, B, diazepam, and meprobamat. Four samples were provided.

System

Model 5000, transmission detector module, fiber optic bundle setup module, interactance fiber and reflectance probe was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS SmartProbe Analyzer 2m Fiber	2.921.1610

Sampling

The samples were analyzed using a fiber optic interactance reflectance probe in the 1100–2500 nm region. Spectral differences could be seen throughout the spectrum. Spectrally, the most similar samples were A and diazepam (small differences could be seen between these samples). IQ2 was not used for this analysis.

Results

The results indicate that NIR can be used to distinguish between these samples.

No. 12: Quantitatively monitoring the active in nicardipine hydrochloride powder blends and qualitatively determining content uniformity

Summary

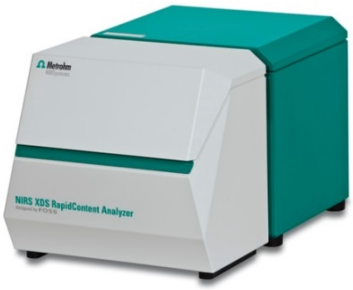
This NIR application is used to quantitatively determine the active drug in nicardipine hydrochloride powder blends (range from 48 to 130). Also to determine content uniformity.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

The samples were analyzed in reflectance mode in the 1100–2500 nm region. The blend samples were measured using a standard sample cup at three different orientations. Nicardipine absorptions are found at 1620 and 1680 nm and 2250 nm (other components are isosbestic). A regression was performed at 2152 (SEC of 3) and 1680 nm (SEC of 2 with a lower slope term). IQ2 was used for content uniformity. The results were close to 1 indicating that there is very little difference between the samples.

Results

The results indicate that NIR can be used to monitor the level of nicardipine in a powder blend. Also demonstrated was the use of the spectral matching algorithm to look for compositional differences in the samples. The results of close to 1.00 for all samples indicate that they are very similar.

No. 13: Qualitatively determining moisture, peroxide, carbonate, and bicarbonate

Summary

This NIR application is used to determine moisture, peroxide, carbonate and bicarbonate content in efferdent. The components of efferdent were sodium perbonate, oxone, sodium carbonate and sodium bicarbonate.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

All NIR spectra were collected in the reflectance mode with only the efferdent tablets requiring any sample preparation (grinding). The samples were analyzed in the 1100–2500 nm range. No calibrations were developed. The component spectra collected show that these compounds exhibit absorptions in the NIR spectral region and that they are sufficiently different to be measured with NIR. Also, moisture is visible not only in the finished product (efferdent) spectrum but also in the component spectra.

Results

The results indicate that NIR can be used to determine not only the components of product but also moisture.

No. 14: Monitoring the level of naproxen in pharmaceutical tablets

Summary

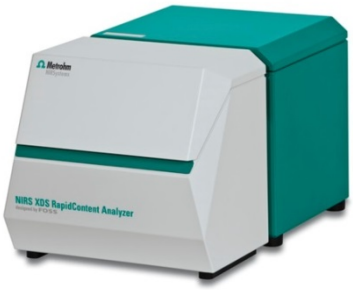
This NIR application is used to monitor the level of Naproxen in pharmaceutical tablets. All samples (tablets) were 250 mg, with the concentration of the naproxen ranging from 96 LS to 102% LS (237.5 to 255 mg).

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The tablets were crushed using a mortar and pestle to a fine powder, and approximately equal weights of each sample were placed into a micro-sample cup. The spectral range was 1100–2500 nm. Calibrations for Naproxen were developed at 3 separate wavelengths: 1356, 1686, and 2254 nm (SEC of 6, 7, and 6mg, respectively). A divisor term in the 1820 nm region was added to each calibration equation to correct for the change in penetration depth, associated with changes in excipient concentrations. The SEC was reduced to 2, 1, and 2 mg, respectively.

Results

The results indicate that NIR can be used to monitor the presence of Naproxen in pharmaceutical tablets. These results also suggest one possible method which may be used to overcome the difficulties associated with changes in excipient concentrations. Once these sampling problems have been minimized, improvements in the results are seen.

No. 15: Monitoring stearic acid in microcrystalline cellulose formulation tablets

Summary

This NIR application is used to monitor stearic acid (SA) in microcrystalline cellulose (MCC) formulation tablets. Approximately ten tablets of each sample were provided.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS MasterLab Analyzer	2.921.1310

Sampling

Each set of samples were placed in a sample cup with an aluminum foil backing to provide for total reflectance. The samples were analyzed in the 1100–2500 nm region. The 1750 nm region shows an increase in SA concentration while at 1927 nm the MCC concentration decreases. It appears that the spectral changes which are being seen are caused by the melting of the SA in the formulation. The melted SA, in turn coats the formulation tablets.

Results

The results indicate that NIR can be used to scrape the top portion of each tablet off. Then the relative amounts of MCC would increase in the center of the tablets.

No. 16: Monitoring moisture in aspirin granulations and tablets

Summary

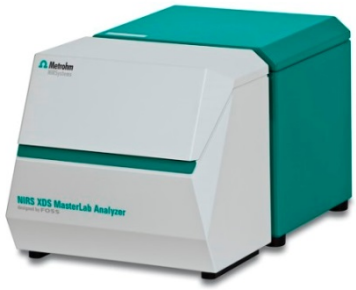
This NIR application is used to determine whether NIR could be used to monitor moisture in aspirin granulations and tablets. Fifty tablets were analyzed from each granulation (virgin granulation and composite granulation).

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS MasterLab Analyzer	2.921.1310



Sampling

The samples were analyzed in reflectance mode, using the spectral region from 1100 to 2500 nm. For moisture determination, two regions are useful: 1920 and 1440 nm. Significant differences between virgin granulation and composite granulation are seen in these two regions. The tablet form from each granulation showed the same results, but not as large as with the granulations.

Results

The results indicate that NIR can be used to determine differences between virgin granulations/tablets and composite granulations/tablets. No calibrations were developed. With the preliminary moisture content values provided, it would be reasonable to expect that quantitative determinations of moisture content could be made using NIR.

No. 17: Monitoring calcium carbonate levels in antacid tablets

Summary

This NIR application is used to determine calcium carbonate levels in antacid tablets. The first part of this study was to develop a calibration for the lab prepared samples. Then, the calibration was tested by predicting on process samples.

System

Model 5000, rapid content analyzer module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS MasterLab Analyzer	2.921.1310

Sampling

The lab prepared tablets were prepared to cover 75, 90, 100, 110, and 125% of the theoretical calcium carbonate content. Spectra were collected in the 1100–2500 nm region in reflectance mode. At 2344 nm, calcium carbonate exhibits a strong band in the second derivative, whereas the placebo does not. A least-squares regression was performed at this wavelength (SEC of 0.9%). Good agreement between NIR and reference calcium carbonate levels was obtained. In order to predict on the process samples, only a bias adjustment was necessary. All components in the lab samples were present in the process.

Results

The results indicate that NIR can be used to determine calcium carbonate in antacid tablets.

No. 18: Determining the thickness of a lacquer coating on tablets

Summary

This application shows that NIR spectroscopy can be applied to determine the thickness of a lacquer coating on tablets.

System

Model 5000, transmission detector module, sample transport module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS MasterLab Analyzer	2.921.1310

Sampling

The tablets were analyzed in reflectance mode in the 1100–2500 nm region. The tablets were placed into a coarse sample cell for analysis. The pure lacquer was measured in transmittance mode. Lacquer thickness can be monitored at 1185 nm where the two types of talc and the tablet are isosbestic, and the lacquer has an absorption. At 1665, 1690, 1750, 2230, and 2330 nm, an absorption for the lacquer is observed while all other components are isosbestic.

Results

The results indicate that NIR can be used to determine lacquer thickness on tablets without interference from the other materials in the tablet.

No. 19: Monitoring solutions in gelatin capsules

Summary

This application shows that NIR spectroscopy can be applied to distinguish between solutions used to fill soft gelatin capsules. Four different solutions were submitted for examination.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The spectra of the fluids were measured in the 1100–2500 nm range using cuvettes. The spectra were collected in transmittance mode. Spectral differences occur in at least four regions: 2050, 2125, 2180, and 2280 nm.

Results

The results indicate that NIR can be used to quantify the components filled into capsules.

No. 20: Determining the amount of phase 2 and phase 3 spheroids in cold relief capsules

Summary

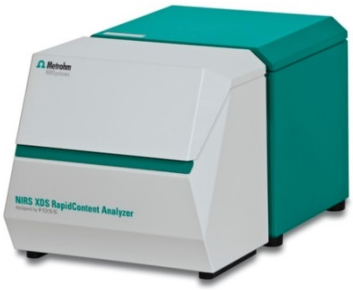
This application shows that NIR spectroscopy can be applied to determine the amount of phase 2 and phase 3 spheroids in cold relief capsules. Phase 1 was a powder, therefore phase 2 and 3 mixtures were made without phase 1 added (mixtures 35/65 to 65/35 of phase 2/3).

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

Mixtures of phase 2 and 3 spheroids were prepared by simply weighing the material on a balance, then mixing by agitating the spheroid in a beaker for one minute. The samples were analyzed in reflectance mode in the 1100–2500 nm region. A calibration for phase 2 was developed at 2254 nm (phase 1 and 3 were isosbestic). A SEC of 1% was obtained. A calibration for phase 3 was developed at 2270 nm (phase 1 and 2 were isosbestic). A SEC of 2% was obtained.

Results

The results indicate that NIR can be used to determine the percentage of phase 2 and 3. The relative error in the study is somewhat high, because the static charge on the spheres interfered with mixing, and the amount of sample was small.

No. 21: Monitoring the ethyl cellulose coating thickness on pharmaceutical spheres

Summary

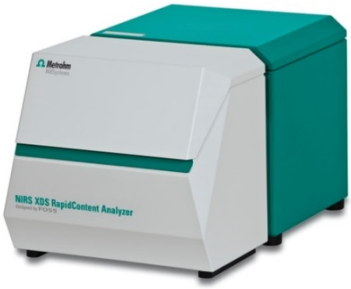
This application shows that NIR spectroscopy can be applied to monitor the ethyl cellulose coating thickness on pharmaceutical spheres. Provided were samples of the uncoated spheres, ethyl cellulose coating, and spheres coated at three different levels.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

All spectra were collected in the 1100–2500 nm range. The spheres were measured in reflectance mode using a standard powder cup, whereas the coating material was analyzed in transmittance in a 0.5 mm cuvette. Coating differences can be seen in the region above 2000 nm. An absorption at 2350 nm appears for the coating. Differences between the three different coatings can be seen at this wavelength. No calibrations were developed.

Results

The results indicate that NIR can be used to quantify the components filled into capsules.

No. 22: Monitoring the level of an ethyl cellulose coating on pharmaceutical beads

Summary

This NIR application is used to monitor ethyl cellulose coating on pharmaceutical beads. Provided were the ethyl cellulose, the uncoated beads and the coated beads up to 6% weight.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples were analyzed in reflectance mode in the 1100–2500 nm region using a powder cup. The most promising region occurs around 2350 nm. The uncoated beads are not interfering with the ethyl cellulose absorption at this wavelength. A calibration was performed (SEC of 0.07%).

Results

The results indicate that NIR can be used to monitor ethyl cellulose on pharmaceutical beads.

No. 23: Monitoring protein and fat levels in synthetic dietary powder

Summary

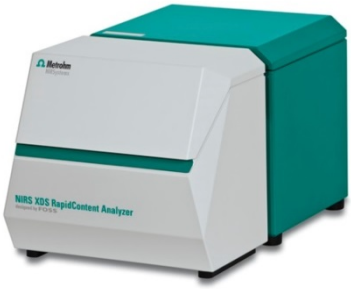
This application shows that NIR spectroscopy can be applied for quantitative analysis of protein and fat levels in a synthetic dietary powder.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

Samples were labeled numbers 1–10 with values for protein and fat ranging from 1.82–2.78% and 0.97–1.32% respectively. The spectra were recorded in the 1100–2500 nm region using a standard sample cup. A calibration was developed for fat at 2327 nm yielding a SEC of 0.1%. A calibration was developed for protein at 2164 nm yielding a SEC of 0.09%.

Results

The results indicate that NIR can be used to quantitatively determine protein and fat in a synthetic dietary powder, and that the analyses can be performed without sample preparation.

No. 24: Monitoring the level of laidlomyxin propionate in a pharmaceutical product

Summary

This application shows that NIR spectroscopy can be applied to monitor the level of laidlomycin proprionate (active) in product.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

Samples which had active levels ranging from 9 to 12% were sent as milled and unmilled form. Samples were measured in the 1100–2500 nm range. The samples were placed into a standard sample cup, and analyzed in a spinning module.

Results

The results indicate that NIR can be used to measure active level in this product. The ability to quantitatively monitor the active level was demonstrated using the active levels supplied with each calibration sample.

No. 25: Measuring acetaminophen, dextromethorphan, doxylamine succinate, and pseudoephedrine in cough syrup

Summary

This application presents the NIR test results of monitoring acetaminophen (APAP), dextromethorphan (DM), doxylamine succinate (DOX), and pseudoephedrine (PSEPH) in cough syrup. Twenty-four samples were provided for calibration, as well as placebo and four samples of individual actives (1%) in the placebo. ADAP concentration ranged from 1.9 to 3%, DM ranged from 0.05% to 0.1%, DOX ranged from 0.01% to 0.02%, and PSEPH ranged from 0.1% to 0.19%.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The samples were analyzed in transmission mode in the 1100–2500 nm region. A 2 mm pathlength quartz cuvette was used for analysis. Unique absorptions could not be located for the individual components. Therefore, PLS regression was used in the 1612 to 1844 nm region. For APAP, a PLS regression using two factors was required (SEC of 0.02%). For PSEPH, a four factor PLS model was required (SEC of 0.01%). For DM, five PLS factors were required to describe this system (SEC of 0.01%). For DOX, five factors were required (SEC of 0.002%).

Results

The results indicate that NIR can be used to monitor APAP, PSEPH, DM, and DOX in cough syrup.

No. 26: Monitoring percent oil in erythromycin fermentation broth, and monitoring level of erythromycin in recovery solutions

Summary

This application shows that NIR spectroscopy can be used to monitor percent oil in an erythromycin fermentation broth. Oil levels ranged from 1.0 to 9.1%. Also, to monitor the level of erythromycin in recovery solutions. The level of erythromycin ranged from 52.967 to 56.008.

System

Model 5000, transmission detector module, fiber optic bundle setup module, interactance fiber and reflectance probe was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110
NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The fermentation broth was analyzed in reflectance mode by placing the broth into a 20 mm cuvette. The recovery solutions were analyzed in transmission mode using a 1 mm cuvette. The samples were analyzed in the 1100–2500 nm region. A unique absorption was located for the oil at 1718 nm. A regression at this wavelength yielded a SEC of 0.9%. An absorption due to the erythromycin was located at 2252 nm. A regression performed at this wavelength yielded a SEC of 1.4.

Results

The results indicate that NIR can be used to monitor the percent oil in an erythromycin fermentation broth.

No. 27: Monitoring glucose in water

Summary

This application shows that NIR spectroscopy can be applied to monitor glucose in water.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

A saturated solution along with four samples of varying concentrations of glucose and water were provided. The concentrations ranged from 0.33 to 1.50%. The samples were analyzed in the 1100–2500 nm region. The samples were analyzed in transmission mode. Spectral features due to glucose are present at 2060, 2276 (strongest band), 2342, and 2434 nm.

Wavelength: A least-squares calibration was developed at 2276 nm (SEC of 0.007% for four samples).

Results

The results indicate that NIR can be used to monitor glucose in water.

No. 28: Measuring polydimethylsiloxane (PDMS, simethicone) in antacid/antigas liquids

Summary

This application presents the NIR test results of quantitative analysis of PDMS (simethicone) in antacid/antigas liquids. The calibration samples ranged from 0.5 to 1.33% total simethicone. The five validation samples ranged from 0.57 to 1.1% total simethicone.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The samples were analyzed in transmission mode in the 1100–2500 nm region. A 0.5 mm pathlength was used. The samples were made by spiking antacid/antigas with one to eleven drops of pure simethicone. Changes in intensity due to the simethicone are evident at 1694 and 1744 nm. A least-squares regression was performed at 1694 nm (SEC of 0.1%). Tablets were also scanned, and a simethicone peak at 1694 nm was also evident, but only on one side of the tablet.

Results

The results indicate that NIR can be used to monitor simethicone.

No. 29: Monitoring total reducing sugars (TRS) in extra strength cough drops

Summary

This NIR application is used to determine the total reducing sugars (TRS) in your Extra Strength cough drops. Five samples were analyzed having a representative range of TRS from 12.73 to 13.77%.

System

Model 5000, rapid content analyzer was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The spectral region used for this study was 1100 to 2500 nm. The rapid content analyzer was used to scan the tablets. This setup employs a reflectance module and a template specifically designed for the tablets analyzed. A calibration model was developed at 1454 nm (SEC of 0.2%) for TRS.

Results

The results indicate that NIR can be used to determine total reducing sugars in cough drops. However, it should be noted that the peak which gave good results is very near the water absorption bands in the NIR region. To insure that we were actually calibrating for the TRS value, a second wavelength was sought.

No. 30: Monitoring lysine in lysine final product

Summary

This application shows that NIR spectroscopy can be applied to monitor lysine levels on final product. The lysine concentration ranges from 98.58 to 99.78%.

System

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples had particle size variations ranging from a fine powder to fairly large grains (2 mm diameter) so the samples were initially ground using a krups mill. The samples were placed into a powder cell, and scanned in the 1100–2500 nm range. A calibration was developed at 2224 nm, assignable to a N-H functional group. A SEC of 0.3% was obtained.

Results

This study as yet does not prove the feasibility for monitoring lysine levels in the final lysine product. In developing a calibration for lysine, a standard error equal to about half the range of the lysine values was obtained, the source of which has not been determined, but appears not to be due to any sampling problems with the NIR. Since samples analyzed closely in time produce substantially better calibration equations, it appears that there may be a systematic error in the laboratory analysis. Further evaluation should be done.

No. 31: Determining if laidlomycin propionate (active) in pharmaceutical products could be detected

Summary

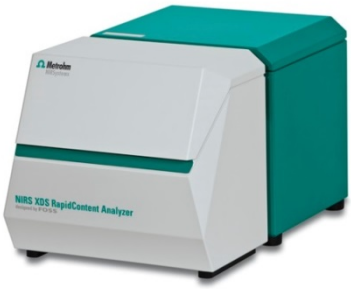
This NIR application is used for detecting Laidlomycin Proprionate (active) in pharmaceutical product. The samples used in this evaluation were two lots of the placebo, laidlomycin propionate (neat), and the levels of active in the product.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The spectra were collected in the 1100–2500 nm range. Each sample was measured in reflectance using a small powder cell. Regions throughout the spectrum were identified where the active ingredient absorbed with little or no interference from the placebo. No calibrations were developed.

Results

From this study, it appears to be feasible to monitor the level of Laidlomycin Proprionate in your pharmaceutical product using NIR spectra. The rest of the materials in the sample do not appear to have any effect on the overall spectrum, and will therefore not affect the ability to quantitate the active ingredient in this product.

No. 32: Monitoring the amount of heparin complex in an isopropanol solution of heparin

Summary

This application shows that NIR spectroscopy can be applied to monitor the amount of Heparin complex in an isopropanol (IPA) solution of Heparin. Nine solutions containing Heparin from 0.4 to 2.7% were used for this study.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

All spectra were collected in transmission mode from 1100–2500 nm. Samples were placed in a 1 mm cuvette and analyzed. The Heparin shows an absorbance maximum at 1724 nm while the IPA crosses zero. The absorbance changes at this wavelength should be due only to the solute and not the solvent. A calibration was developed at 1726 nm yielding a SEC of 0.04%.

Results

The results indicate that NIR can be used to monitor the level of Heparin in isopropanol based solutions.

No. 33: Monitoring aluminum chlorohydrate and salicylic acid in foot powders

Summary

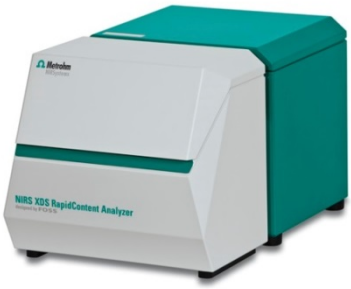
This application shows that NIR spectroscopy can be applied to monitor the levels of several active ingredients (aluminum chlorohydrate and salicylic acid) in three different foot powders. The samples provided for analysis were the components of each foot powder in their neat form.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120	NIRS XDS RapidContent Analyzer



Sampling

The samples were analyzed in the 1100–2500 nm region using a standard powder cell. The spectra were collected in reflectance mode. Aluminum chlorohydrate has very few spectral features, and most of those are attributable to hydrated water (1940 and 1450 nm). The band at 2150 nm is due to the active, where the inactives do not absorb. This band might be used for quantitation, but the other components have absorptions near this band. The salicylic acid can be monitored in many areas.

Results

The results indicate that NIR can be used to measure several of the active ingredients in the three different foot powders. The measurement for aluminum chlorohydrate is questionable, since it has very few absorption bands to use in measuring the level of this component.

No. 34: Quantifying magnesium hydroxide and calcium carbonate in antacid powders

Summary

This application presents the quantitative analysis of magnesium hydroxide and calcium carbonate in antacid powders. Ten samples were prepared using the raw materials provided. Eight samples were used for calibration, and two for validation. The magnesium hydroxide concentration ranged from 4.04 to 4.9%, and the calcium carbonate ranged from 19.42 to 23.71%.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples were analyzed in the 1100–2500 nm region using a standard powder sample cup and a spinning sample module. For magnesium hydroxide, a calibration was developed at 1390 nm (SEC of 0.2%). For calcium carbonate, a calibration was developed at 2342 nm (SEC of 0.6%).

Results

The results indicate that NIR can be used to monitor magnesium hydroxide and calcium carbonate.

No. 35: Performing in-situ moisture determinations of pharmaceutical powders in sealed vials

Summary

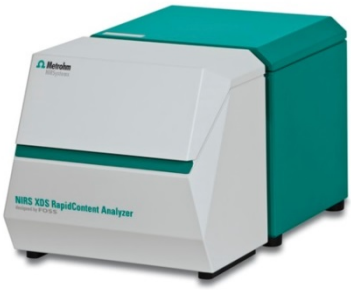
NIR spectroscopy is applied to monitor moisture in pharmaceutical powders in sealed vials. The samples were provided in sealed glass vials, with moisture ranging from 0 to 12%. Also six samples with approximately the same moisture levels were provided for examining the precision of the NIR method.

System

Model 5000, reflectance detector module, horizontal setup module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The samples were analyzed in the 1100–2500 nm region in reflectance mode. The spectrophotometer was oriented so that the vials sat directly on the beam (the instrument was placed on its back). A calibration for moisture was performed at 1444 nm (SEC of 0.3%). The precision for the six samples containing the same amount of moisture was +/- 0.55%. The precision within each individual vial was +/- 0.1%.

Results

The results indicate that NIR can be used to monitor moisture through glass vials.

No. 36: In-situ monitoring of moisture content in lyophilized pharmaceuticals

Summary

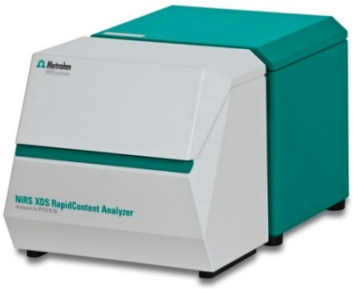
The in-situ monitoring of moisture content in lyophilized pharmaceuticals can be performed using NIR spectroscopy. The samples provided for this study included samples of a pharmaceutical powder in glass vials which varied in moisture content from 7.7 w/w to 12% w/w. Also included was a sample which had been dried to remove essentially all traces of moisture.

System

Model 5000, rapid content analyzer was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The samples were analyzed directly through the glass vials using the rapid content analyzer. The vials were oriented so that the sample was illuminated from the bottom of the vial. The samples were shaken to homogenize the sample, and the sample was leveled by tapping the vial several times prior to each NIR measurement. The samples were analyzed in reflectance mode in the 1100–2500 nm region. A calibration for moisture was developed at 1444 nm (SEC of 0.2%).

Results

The results indicate that NIR can be used to measure in-situ moisture content in lyophilized pharmaceuticals. Variability seen in the data collected indicate the observed differences can be attributed to variability in the physical appearance of the samples (e.g. clumping) which was only observed at high moisture levels.

No. 37: Measuring moisture in lyophilized samples

Summary

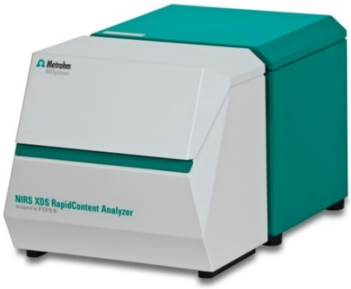
This NIR application is used to measure moisture in lyophilized samples. Eight glass container samples were provided with moisture concentration ranging from 0.25 to 2.35%. Also provided were three blanks, and five unknown samples.

System

Model 5000, reflectance detector module, horizontal setup module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110



Sampling

The spectrophotometer was oriented so that the NIR beam illuminated the samples from the bottom of the glass container. The areas of interest were around 1450 and 1940 nm where water absorbs in the NIR spectrum. Each sample was analyzed five times, rotating the sample between scans. A calibration for water was developed at 1940 nm (0.2% SEC).

Results

The results indicate that NIR can be used to monitor moisture concentration in lyophilized samples through glass containers. It is also apparent from this study that cracks in the lyophilized cake sample or the sample being in pieces affects the obtained spectra. The accuracy and precision may also have been affected by the glass containers. A standard glass vial with no writing imprinted on the bottom, and of consistent thickness could improve the accuracy and precision.

No. 38: Detecting different water concentrations in bleomycin sulfate

Summary

This NIR application is used to detect differences in water concentrations in Bleomycin Sulfate. A total of eight samples were analyzed. Four samples are of known concentration with water values of 0 – 7%.

System

Model 5000, rapid content analyzer was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer	2.921.1110

Sampling

The NIR spectra were measured in sealed glass vials, using a diffuse reflectance fiber optic probe. The samples were analyzed in the 1100–2500 nm region. A moisture calibration was developed at 1930 nm yielding a SEC of 0.3%.

Results

The results indicate that NIR can be used to monitor water content in Bleomycin Sulfate by using diffuse reflectance fiber optic probe. This could be performed for samples contained in sealed vials, eliminating direct human contact with this material.

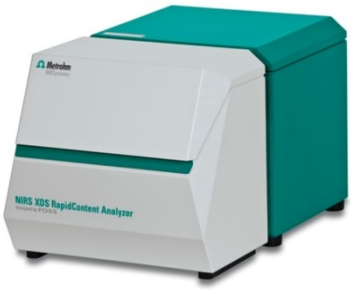
No. 39: Monitoring an active ingredient on a substrate

Summary

This application presents the NIR test results of monitoring an active ingredient on a substrate. Thirty samples were analyzed: two groups with concentration ranging between 83-109, and 490-636 micrograms/cm^2.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

All spectra were collected in reflectance mode in the 400–2500 nm region. A spinning sample module was used for analysis. The 2312 nm wavelength is a region of the spectrum where the active has an absorption band with no interference from the substrate sheet. A calibration was developed at this wavelength (SEC of 14 micrograms/cm^2).

Results

It appears that NIR can be used to monitor active on a substrate.

No. 40: Methylphenidate in transdermal patches

Summary

This application shows that measuring the potency of methylphenidate in transdermal patches can be performed by NIR spectroscopy.

System

A NIRSystems model 6500 monochromator equipped with a Spinning Sample module was used to scan the samples in reflectance, from 1100–2500 nm. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The second derivative (segment 10, gap 0) spectra of 10 lab prepared samples with varying coat weight and potency levels (1.2–3.4 mg/cm2) were included in the calibration set. The application of a simple linear regression produced a correlation of 0.99 and Standard Error of Calibration (SEC) of 0.09 at wavelength 2090 nm.

Seven samples of a single coat weight (15), again using the second derivative and a linear regression, produced a correlation at wavelength 2090 nm, of 0.999 and SEC of 0.04.

Results

Near-infrared spectroscopy can be successfully used to measure the potency level of methylphenidate in transdermal patches. Calibrations for samples of varying coat weights can be developed; however, calibrations for samples of a specific coat weight show improved results.

No. 41: Measuring nitroglycerin in transdermal patches

Summary

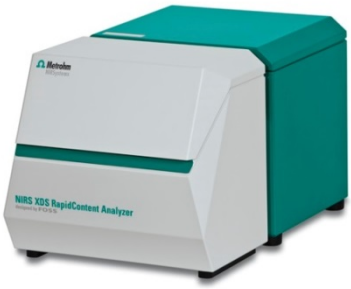
This application shows that NIR spectroscopy can be applied to measure nitroglycerin in transdermal patches. The samples ranged in nitroglycerine concentration from 12.1 to 16.41 mg/patch. Ten lots of patches (five pump speeds/lot, ten patches/pump speed) were provided for analysis.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120



Sampling

The samples were analyzed in reflectance mode in the 1100–2500 nm region using a spinning sample module. Two regions of the spectrum, 1650 and 2270 nm, were identified as regions containing spectral difference between the placebo patch and the nitroglycerine sample. A calibration was developed at 2266 nm (SEC of 0.4 mg/patch).

Results

The results indicate that NIR can be used to measure nitroglycerine in transdermal patches.

No. 42: Analysis of nicotine patches

Summary

This application presents the NIR test results of monitoring the active nicotine on a patch.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

Sample spectra were collected in the 1100–2500 nm region. The samples were scanned in reflectance mode using the sample transport mechanism. All sample spectra were collected with the PVC cover on and then sent for HPLC analysis. 2188 nm appears to be the most intense peak for nicotine. However, a regression was performed at 2280 nm (SEC of 0.02 mg/c m^2 for a range of 0.78 to 0.9 mg/cm^2). A second term was added to this equation because the foil backing reflected NIR radiation back through the sample. Calibrations were developed at 2280/1768 nm corrects for varying thickness, and yields a SEC of 0.02 mg/cm^2.

Results

The results indicate that NIR can be used to monitor nicotine on patches.

No. 43: Monitoring an active on a substrate

Summary

This application shows the test results of monitoring an active ingredient on a substrate. Ten samples were provided: four samples from 84.3 to 95 mg, four samples which ranged in active concentration from 509 to 602.0 mg, and one unknown sample.

System

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples were analyzed in reflectance mode using the scan range from 1100 to 2500 nm. The only sample preparation required involved the cutting of the substrate sheet into a smaller sample. It could be avoided if the remote reflectance sampling module is used rather than the horizontal setup module. Two calibration equations will be needed: one for the low range, and one for the high range. For the low concentration, a calibration for the active was developed at 2314 nm (SEC of 1 mg). For the high concentration, a calibration was developed at 2328 nm (SEC of 21 mg).

Results

The results encourage further investigation of NIR. It was recommended that a full feasibility study be performed to demonstrate more accurately and precisely NIR can be used.

No. 44: Monitoring the levels of bisulfate, carbonate and oxone in crystalline toilet cleaner

Summary

This application shows that NIR spectroscopy can be applied to monitor levels of bisulfate, carbonate and oxone in crystalline toilet cleaner.

System

Model 5000, reflectance detector module, spinning sample module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples were analyzed in reflectance mode in a standard sample cup in the 1100–2500 nm region. Without interference from the other components, the following are optimum regions for measurement: oxone (near 1620 nm), carbonate (2350 nm), and bisulfate (1724 nm).

Results

From the spectra of the pure components in crystalline toilet cleaner, several spectral regions looked promising for monitoring the levels of oxone, bisulfate and carbonate. Unfortunately, the sampling error is large. However, if an appropriate sampling method can be developed, it should be possible to monitor the levels of each component at the above wavelengths.

No. 45: Measuring the Concentration of cocamide MEA and diazolidinyl urea in a complex matrix of crystalline toilet cleaner

Summary

The application shows the possibility of using NIR to measure the concentration of cocamide MEA and Diazolidinyl Urea in the complex matrix of crystalline toilet cleaner. Twenty samples were provided with cocamide MEA concentration ranging from 33 to 36 grams, and diazolidinyl urea concentration ranging from 0.25 to 0.55 grams.

System

Model 5000, reflectance detector module, sample transport module was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidContent Analyzer Solids	2.921.1120

Sampling

The samples were analyzed in the 1100–2500 nm range using a coarse sample cell. The instrument was equipped with a sample transport mechanism. Due to the large number of constituents in the product , PLS was used to monitor cocamide MEA and diazolidinyl urea. Three spectral regions were used for cocamide MEA: 1150–1300, 1520–1850, and 2275–2350 nm (SEC of 0.2). Two regions were used for diazolidinyl urea: 1600–1850 nm, and 2000–2200 nm (SEC of 0.01).

Results

The results indicate that NIR can be used to monitor the amount of Cocamide MEA and Diazolidiny1 Urea in crystalline toilet cleaner.

No. 46: Monitoring isopropyl alcohol (IPA) and chlorhexidine gluconate (CHG) in antibacterial soap

Summary

NIR Spectroscopy is used to study measuring isopropyl alcohol (IPA) and chlorhexidine gluconate (CHG) in antibacterial soap samples. Thirty-one spiked antibacterial soap samples were provided with varying concentrations of IPA and CHG, ranging between 3.52 and 4.63%, and 3.51 and 4.54%, respectively. The calibration set consisted of twenty-five antibacterial soap samples, and the remaining five samples were used for validation. Also provided were the two active ingredients, 100.0% IPA and 20.0% CHG, and a blank containing 0% IPA and 0.05% CHG.

System

Model 5000, liquid sampling system was used for this application. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS RapidLiquid Analyzer	2.921.1410

Sampling

The analysis was performed in transmission mode in the 1100–2500 nm range using a 1 mm pathlength quartz cuvette. A calibration was developed for IPA at 1692 nm (SEC of 0.06%). For CHG, PLS was used because no regions in the spectrum could be found free of interferences. PLS was done in the 1626–1820 nm, and 1936–2052 nm. A 6 factor model was developed with a SEC of 0.05%.

Results

The results indicate that NIR can be used to monitor IPA and CHG in antibacterial soap.

No. 47: Propionic acid in fermentation broth

Summary

Measuring propionic acid in fermentation broth using transmission Near-infrared spectroscopy is the objective of this report.

System

A NIRSystems model 6500 monochromator with an OptiProbe fitted with a transflectance tip having a 1 mm pathlength, was used to collect all sample spectra. Spectra were collected at room temperature. This analyzer is no longer available.

The equivalent and recommended instrument

NIRS XDS Interactance OptiProbe Analyzer	2.921.1510

Sampling

Four samples having a propionic acid concentration range of 0.03–1.3 mg/ml, were taken from one fermentation tank. A simple linear regression model was developed on the second derivative spectra of the samples. Using the signal at 1672 nm produced an equation with an r^2 =0.99 and Standard Error of Calibration (SEC) of 0.04 mg/ml.

Five samples, having a propionic acid range of 0.2-1 mg/ml, were taken from a second tank. Again a simple linear regression was applied to the second derivative spectra of the samples. This regression, at wavelength 1682 nm, yielded an r^2 = 0.98 and SEC = 0.06 mg/ml.

Results

Near-infrared spectroscopy can be successfully used to measure propionic acid in fermentation broth at levels below 1.3 mg/ml. It is believed that a larger dataset, in which all fermentation tanks are equally represented, could be used to generate one calibration equation that could be applied to product from all tanks. This approach would probably require the application of partial least squares regression technique.