APPLICATION NOTE

FT-NIR Spectroscopy

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Analysis of Pharmaceutical Raw Materials Through Packaging Using an FT-NIR Fiber Optic Probe

Introduction

The analysis of all incoming pharmaceutical raw materials is a key part of 21CFR compliance (section 211.84).[1] It is therefore important to have a high-throughput method by which raw materials may be analysed in a loading bay or warehouse, while also preventing sample exposure. The PerkinElmer Spectrum Two N™ Remote Sampling Module, also referred to as the Fiber Optic Probe, provides a means by which raw materials may be analyzed through different thicknesses and types of packaging, allowing a rapid and non-destructive method.

In this application, various commonplace pharmaceutical raw materials have been analyzed and identified through both one and two layers of clear polyethylene (PE) bags using the Spectrum Two N Remote Sampling Module and Spectrum Touch™ software.

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Experimental

42 spectra were collected while pressing the fiber probe tip against either one or two layers of clear PE bag containing the raw material. Prior to sample collection, a background was taken using the probe holder containing a NIR reference material (Spectralon®). Measurements were carried out using the scan parameters shown in Table 1 with the PerkinElmer Spectrum Two N FT-NIR and Remote Sampling Module (Figure 1).

Table 1. Experimental parameters used for scanning of raw material spectra with Remote Sampling Module.

Scan Range	10000 – 4000 cm^{-1}
Accumulations	64
Resolution	16 cm^{-1}

Figure 1. PerkinElmer Spectrum Two N with Remote Sampling Module.

This method allows for pharmaceutical raw materials to be analyzed inside their packaging and thus requires no sample preparation or handling. Sample integrity is protected as there is no requirement to open packaging and, therefore, no exposure to airborne contaminants and moisture.

Results and Discussion

As with the raw materials, polyethylene (PE) absorbs in the near-infrared region (10,000 – 4,000 cm^{-1}), therefore a method must be developed which incorporates the removal of this interference. Spectrum™ 10 software is capable of performing this with the 'Arithmetic' function with which the user may add, subtract, multiply and divide spectra using a constant value or spectrum as the operand. In this case, a spectrum of either one or two layers of the PE bag (measured against Spectralon® 99% diffuse reflectance standard) is subtracted in order to leave a spectrum of the pharmaceutical raw material. An example showing spectra of D-Mannitol, a single layer of PE and the resulting spectrum is shown in Figure 2.

This method allows for all spectral information relating to the raw material itself to be retained while removing interference from the PE bag (especially at the lower wavenumber region around 4000 cm^{-1}).

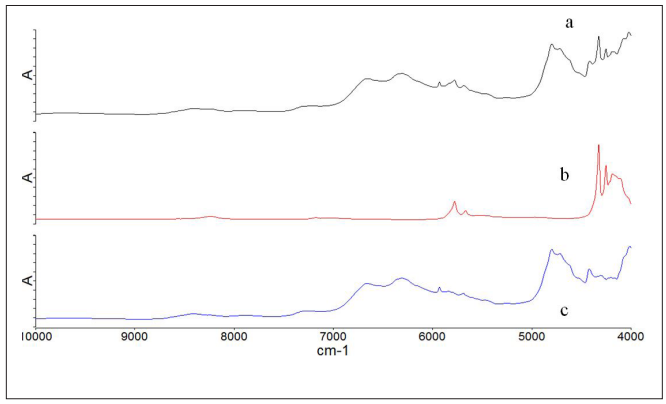

Figure 2. NIR Spectra of a) D-Mannitol though single PE layer. b) Single layer of polyethylene. c) Result when spectrum of single PE layer is subtracted from spectrum of D-Mannitol through single PE layer.

By removing the polyethylene interference, the spectra may be used with the variety of identification tools available in Spectrum 10 including COMPARE, Search, MultiSearch and Verify.

After the appropriate PE spectrum is subtracted, the resulting spectrum is analyzed using a COMPARE algorithm with a library of pharmaceutical raw materials with correlation coefficient for a material to pass set at 0.9800. The COMPARE algorithm determines the correlation between the sample spectrum and spectra from a library, producing a 'best hit'.

Touch Method Validation

The method was validated using 14 spectra of seven different raw materials in the two thicknesses of PE packaging (30 µm and 60 µm), the results of which are shown in Table 3. In each case, the raw material was correctly identified with a high correlation.

Table 2. Validation results from 14 raw materials in packaging.

Sample	Packaging Thickness (µm)	Compare Result	Correlation
Avicel	30	Pass	0.9978
	60	Pass	0.9995
Calcium Phosphate	30	Pass	0.9977
	60	Pass	0.9989
Dextrin from Corn	30	Pass	0.9975
	60	Pass	0.9980
Dextrin from Maize	30	Pass	0.9999
	60	Pass	0.9998
Dextrin from Potato	30	Pass	0.9998
	60	Pass	0.9988
D-Mannitol	30	Pass	0.9997
	60	Pass	0.9998
Talc	30	Pass	0.9969
	60	Pass	0.9911

Spectrum Touch software enables users to access methods from a menu and run them with detailed step-by-step instructions, thus eliminating the need for costly and time-consuming training. An example result from a Touch method successfully identifying D-Mannitol in a double layer PE bag is shown in Figure 3.

This method may also be implemented into a QA/QC pharmaceutical environment using Spectrum Touch, with the enhanced security (ES) version of the software ensuring 21CFR part 11 compliance.

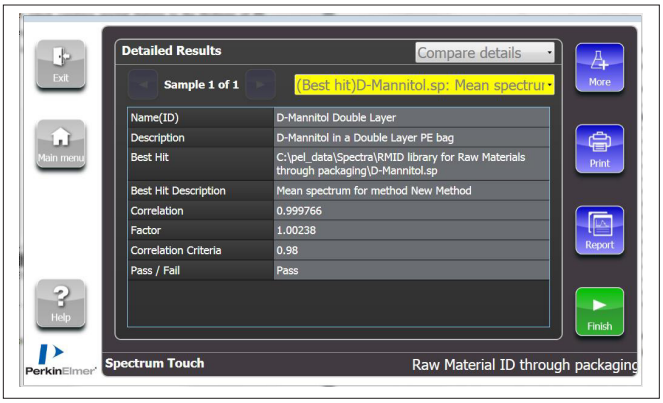

Figure 3. Touch method result from the analysis of D-Mannitol in a double layer PE bag.

Conclusion

The PerkinElmer Spectrum Two N FT-NIR spectrometer with Remote Sampling Module ensures rapid and non-destructive identification of raw materials through multiple layers of PE packaging. Analysis can be conducted anywhere, including loading bays without concern for potential contamination. Additionally, when used in conjunction with Spectrum Touch, a workflow-oriented method is implemented allowing users of any background to analyze materials.

Reference

1. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm (Accessed 14/02/18)

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