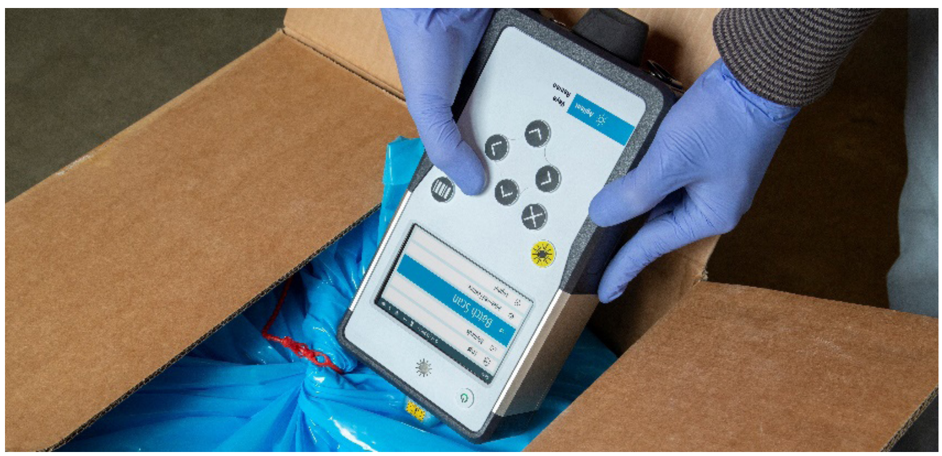
Application Note

Pharma and Biopharma

Verification of Nutraceutical Raw Ingredients Directly Through Packaging

Simple, fast, and accurate identification using Agilent Vaya handheld Raman spectrometer



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Abstract

This study explores how the Agilent Vaya Raman handheld spectrometer can be used to perform material verification of a range of nutraceutical materials through transparent and nontransparent (opaque) packaging. Vaya uses Spatially Offset Raman Spectroscopy (SORS) to provide easily interpretable pass/fail results for through-barrier identification tests. The nutraceutical materials tested in this study include fatty acids, vitamins, amino acids, and nutritional markers extracted from botanicals. The results demonstrate the suitability of Vaya SORS for product identification testing of raw ingredients in current Good Manufacturing Practice (cGMP) environments. Vaya meets current verification testing requirements for nutraceuticals, enabling fast turnaround of raw ingredients in a warehouse without the need to open packaging.

Introduction

Nutraceuticals testing

Nutraceuticals are dietary supplements that provide nutritional and/or physiological benefits when taken as part of a healthy and balanced diet. Nutraceuticals are often referred to as dietary supplements, health food supplements, traditional medicines, herbal medicines, or complimentary medicines. To ensure the safety, quality, and authenticity of these products, many countries have tightened regulations over recent time, as the popularity of dietary supplements has increased. Typically manufacturers and distributors must adhere to regulations within the jurisdiction where the products are sold.

Many countries consider nutraceuticals as foods and do not have separate testing requirements for supplements, while other countries' regulations are more similar to the testing requirements of pharmaceuticals. Jurisdictions including the United States (US) require the verification of both raw ingredients and finished products. Specifically, the US Food and Drug Agency (FDA) requires firms that manufacture, package, or hold dietary supplements follow current Good Manufacturing Practices (cGMP) under CFR 21 part III.[1] Section 75(a)(1) of 21 CFR 111 states that firms must conduct at least one appropriate test or examination to verify the identity of any component that is a dietary ingredient. The FDA regulations also contain a requirement to test batches of raw ingredients using scientifically valid analytical methods. In the European Union (EU), it is the responsibility of the nutraceutical provider (importer, supplier, or distributor) to ensure the safety of the product according to the EU General Food Law Regulation 178/2002.[2]

Testing of incoming raw ingredients using a suitable verification technique is increasingly deemed good industry practice, bringing health supplement testing more in line with established practices within the pharmaceutical industry.

In this study, an Agilent Vaya Raman system was used to identify fatty acids, vitamins, amino acids, and nutritional markers extracted from botanicals in clear glass containers and two samples inside a white high density polyethylene (HDPE) bottle.

Identification testing of ingredients

The Vaya Raman handheld spectrometer is designed for raw material identification applications. It is widely used within the pharmaceutical industry to identify and differentiate raw materials on receipt at the warehouse or manufacturing facility. Testing can be performed through transparent and nontransparent containers—avoiding the need to open containers—enabling "pass/fail" results to displayed on the Vaya screen in a few seconds. Based on Spatially Offset Raman Spectroscopy (SORS), Vaya simplifies and accelerates the verification of raw materials, including materials used to manufacture nutraceuticals. A single operator can easily receive and release large volumes of containers in a matter of hours rather than days, as needed by other techniques such as Fourier transform infrared. The SORS technique eliminates the bottlenecks associated with sampling and quality control (QC) laboratory processes, facilitating simpler, faster, less resource-intensive, and more cost-effective testing of raw materials.

Spatially Offset Raman Spectroscopy

SORS technology is unique to Agilent. It uses the property of light propagation through diffusely scattering media with Raman spectroscopy to achieve through-barrier analysis. Unlike conventional Raman back-scattering, SORS introduces a physical offset between the area that is excited by the monochromatic light/laser and the area of detection. In "laser offset" mode (Figure 1), with the propagation of the laser inside the material (sample), the Raman photons collected in the detection area originate mostly from the subsurface layers. This offset geometry provides a spectrum rich in the subsurface material. In contrast, the spectrum with no or "zero" physical offset (Figure 1) produces a spectrum rich in the top layer material.

For identification testing of a raw material through a container, the container-rich zero spectrum is subtracted from the raw material spectrum yielding a container-free raw material spectrum. A simplified representation of the principles of SORS is illustrated in Figure 1.

Unlike conventional Raman back-scattering spectroscopy, SORS can reliably perform identification tests through transparent and opaque containers like amber bottles, multilayer paper sacks, colored and transparent plastic liners, and opaque polyethylene containers.

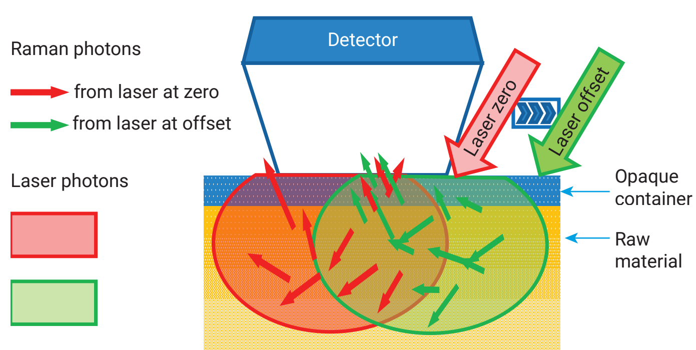

Figure 1. Principles of SORS for the identification of a raw material in an opaque container.

Experimental

To explore the capability of the Vaya handheld SORS spectrometer to verify nutraceutical materials in containers, 15 samples from four classes of materials were investigated. All samples were analyzed inside clear glass containers (Figure 2). The samples were supplied as powders, liquids, or capsules. The classes of materials and samples analyzed in this study included:

- **Fatty acids:** olive oil, rapeseed oil, flaxseed oil, fish oil, and conjugated linoleic acid (CLA).
- **Vitamins:** vitamin A palmitate, vitamin B3, and vitamin C.
- **Amino acids:** L-carnitine, L-arginine base, and lysine HCL (hydrochloride salt of L-lysine).
- **Nutritional markers extracted from botanicals:** D-glucosamine, hydrolyzed collagen, resveratrol, and turmeric.

D-glucosamine and vitamin C were also analyzed inside a white HDPE bottle.

Figure 2. Image of some of the nutraceutical raw ingredients in glass containers that were analyzed in this study.

Results and discussion

Figures 3 to 6 show SORS spectra for the 15 samples obtained by Vaya through a clear glass container. Strong, well-defined spectra were acquired for most of the samples. Figure 7 shows SORS spectra for D-glucosamine and vitamin C measured through a white HDPE container. The sample spectra are clearly distinct from the container reference spectrum, indicating excellent container subtraction by SORS.

SORS is a highly selective technique, as shown by the characteristic "fingerprint" for each material, even when there are significant chemical similarities between some samples.

Fatty Acids

Raman spectra of a range of fatty acids are shown in Figure 3. These samples share several bands in common, notably the carbonyl groups at 1,650 cm^{-1}, and the methylene and methyl groups at 1,450 cm^{-1}. However, each fatty acid sample has a unique signature, which the Vaya's decision engine system[3] can differentiate, ensuring excellent specificity and protection against false positive results.

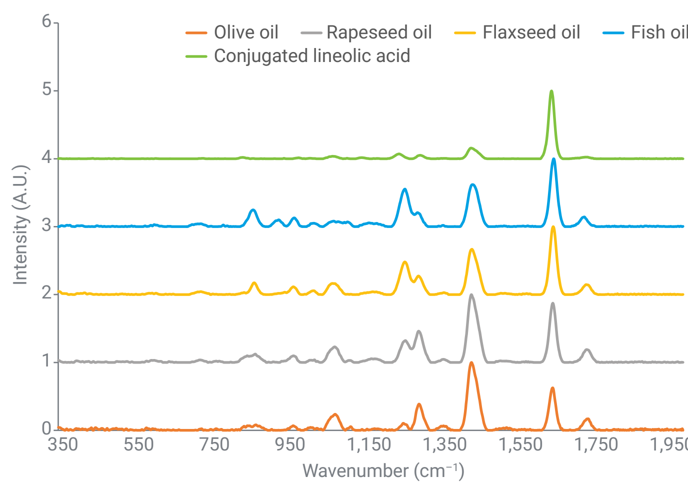

Figure 3. Agilent Vaya Raman spectra of fatty acids obtained through clear glass.

Vitamins and amino acids

The Raman spectra for the three vitamins shown in Figure 4 have clear, well-defined bands with little similarity, making them highly specific. Likewise, the spectra acquired for the three amino acids are distinct, as shown in Figure 5.

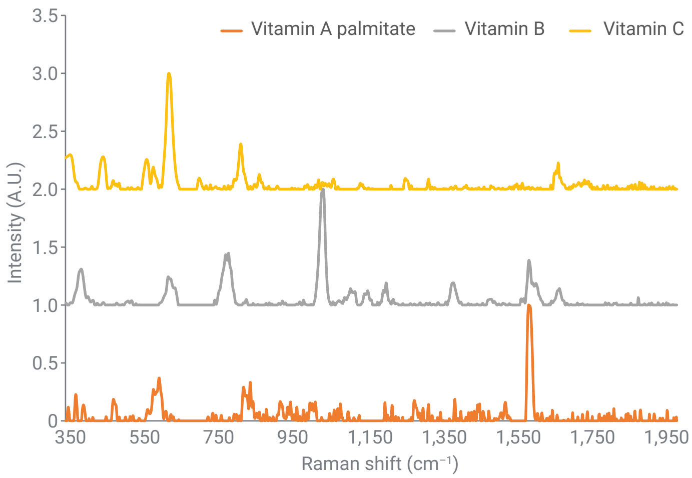

Figure 4. Agilent Vaya Raman spectra of vitamins obtained through clear glass.

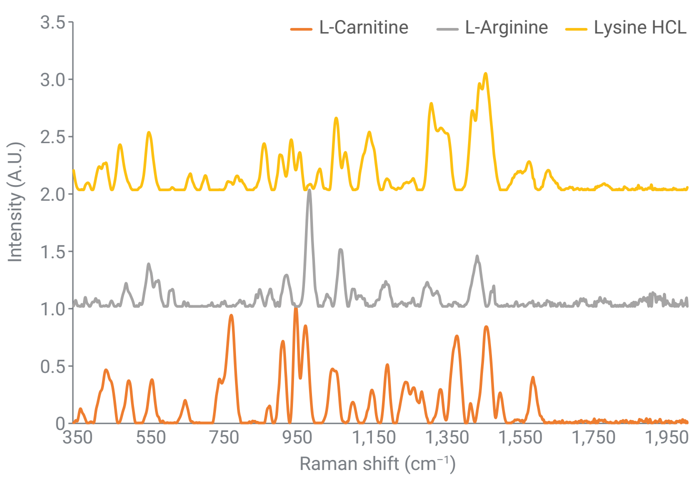

Figure 5. Agilent Vaya Raman spectra of amino acids obtained through clear glass.

Nutritional markers extracted from botanicals

Materials that are derived from plants can fluoresce under the laser and obscure Raman signals. However, these transitions can be reduced using a higher wavelength laser. Vaya uses an 830 nm laser, which mitigates sample fluorescence. The Raman spectra obtained from the nutritional markers extracted from botanicals (Figure 6) illustrate the ability of Vaya to acquire quality Raman data from potentially fluorescent materials.

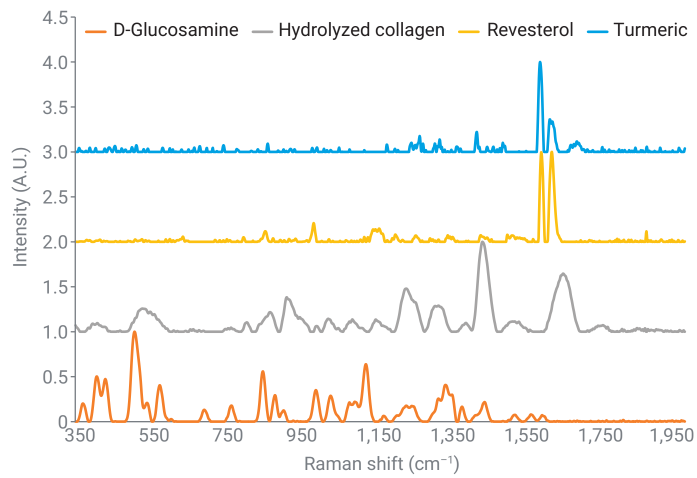

Figure 6. Agilent Vaya Raman spectra of nutritional markers extracted from botanicals through clear glass.

Verification through nontransparent containers

Figure 7 demonstrates the ability of the Vaya to verify both d-glucosamine and vitamin C inside a nontransparent HDPE bottle. There is no evidence of the HDPE spectrum (Figure 7, top) interfering with the sample-spectra, confirming the performance of SORS, which automatically subtracts the scaled container spectrum from the materials spectra.

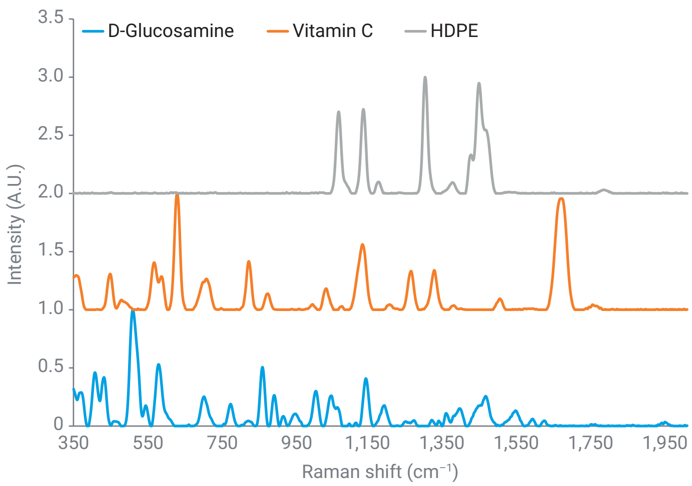

Figure 7. Raman spectra of D-glucosamine and vitamin C measured through HDPE (top spectrum).

Conclusion

The handheld Agilent Vaya Raman spectrometer successfully verified nutraceutical materials including fatty acids, vitamins, amino acids, and nutritional markers extracted from botanicals through transparent and nontransparent containers. Using SORS technology, which automatically subtracts the container spectrum from the sample spectra, distinct spectra were obtained for 15 samples in clear glass containers and two samples in white HDPE containers.

As regulations relating to nutraceuticals and dietary supplements evolve, Vaya can accelerate and future-proof raw material identification workflows for regulatory, safety, and quality purposes. Using a simple pass/fail result display, Vaya provides a unique capability to identify variations in batch quality, delivery mistakes, and willful substitutions of materials. A fast, simple check of materials directly in their containers using Vaya that takes a few seconds can prevent wrong, and potentially dangerous materials being sent from the warehouse into production.

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