Application Note

Cosmetics

Cosmetic Raw Material Identification Testing Through Transparent and Opaque Containers

For more efficient and convenient adherence to current and future GMP requirements

Authors

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Abstract

With the adoption of stricter requirements for the manufacturing of cosmetic products, the Good Manufacturing Practice landscape has evolved and impacted quality control (QC) processes to meet quality, costs, and efficiency requirements. In particular, raw material identification (ID) testing has seen the adoption of at-the-point-of-need solutions in the warehouse. The Agilent Vaya Raman is the latest generation Raman handheld spectrometers for raw material ID testing directly through containers. This application note discusses the capability of Vaya for cosmetics raw material ID testing through transparent and opaque containers and describes the impact on raw material receipt processes.

Introduction

In response to the evolving landscape of the cosmetics industry, cosmetics manufacturing organizations have witnessed an uptick in their costs. This trend is driven by a growing demand for high-quality cosmetic products and heightened government scrutiny fueled by public health concerns. The pharmaceutical sector encountered a similar scenario and responded by optimizing resource allocation and streamlining time-intensive manufacturing processes to restore economic viability.

Within this context, QC in manufacturing has emerged as a focal point. Its impact on production schedules and overall output cannot be overstated. Specifically, the management of raw materials—essential components of production—has been under scrutiny. Large quantities of raw materials may take more than a week to become available for use, prompting efforts to enhance cost efficiency and operational effectiveness.

How is raw material identification at receipt performed?

The process of receipt and ID testing of solid raw materials can be broken down into multiple steps, as shown in Table 1.

Table 1. Multiple steps at receipt and ID testing of raw materials.

Identification at Receipt Process	
1. Unloading and quarantine area 	Raw materials, typically shipped by truck, are unloaded and stored in a quarantine area to await further inspection. In the quarantine area, the raw material containers are visually inspected for obvious defects. Labels are placed onto each container for tracking purposes.
2. Sampling room 	A fraction of all containers (up to 100%) are selected for further verification. These containers are then moved to a dedicated sampling room or booth.
3. Container inspection 	In the sampling room, an operator opens the container or its secondary, outer packaging. The raw material inside is directly verified through the transparent primary package. This verification is done using a conventional handheld Raman spectrometer, capable of acquiring the chemical fingerprint of a raw material through a transparent container.
4. Alternative verification 	If direct verification through the transparent package is not feasible, a few alternative approaches exist. 1. The primary container is opened, and subsequently, an NIR-based analysis is performed. This analysis typically requires either sampling of the raw material or introduction of a probe directly into the raw material. 2. Alternatively, the primary container is opened and sampled. All of the samples are then sent to a QC lab for mid-IR analysis. In these cases, cleaning and cleaning validation processes are introduced as the instrument is in contact with the raw material and therefore must be cleaned.
5. Return to quarantine 	Once sampled or analyzed, all containers (primary and secondary) are once again sealed and moved back to the quarantine area. For some packaging (e.g. paper sack), container resealing and closing may be time-consuming. After relocating the containers, cleaning and cleaning validation processes of the sampling booth are typically performed.
6. Approval and addition to production stock 	While the containers are back in quarantine, the analytical data are reviewed for approval. On approval, the quarantined raw materials are mixed with production stock.

The conventional process often lacks cost-effectiveness and struggles with scalability and flexibility when accommodating increased testing or novel combinations of raw materials and containers. However, recent advancements have revolutionized the identification of raw materials upon receipt, resulting in significant reductions in container handling, sampling, and overall production release time. The process overhaul was made possible by progress in Raman spectroscopy. Pavel Matousek, a professor at the Rutherford Appleton Lab in the United Kingdom, devised the groundbreaking concept of deep subsurface noninvasive chemical analysis using Raman spectroscopy and the property of light travel through turbid media, called spatially offset Raman spectroscopy. Deep surface analysis with no to minimal interference from the surface of the analyte has extraordinary repercussions for through-barrier analysis.

Spatially offset Raman spectroscopy (SORS)

SORS uses light propagation through diffusely scattering materials theory, in combination with Raman spectroscopy to achieve through-opaque container analysis. SORS introduces a spatial offset between the region of the sample being excited by the laser light and the region of the sample from which the detector is collecting information. When analyzing a material through a container in the offset configuration, the CCD-detected Raman photons originate mostly from beneath the analyte surface, providing a spectrum rich in information about the subsurface – i.e., the raw material. In contrast, the spectrum with no or zero physical offset yields a spectrum that is rich in the top layer information – i.e., the container. The scaled subtraction of the container-rich zero spectrum from the raw material-rich offset spectrum provides a container-free raw material spectrum that can be used for identification verification purposes.

Unlike conventional Raman back-scattering spectroscopy, SORS can reliably perform identification tests through a variety of transparent and opaque containers. Examples include amber glass bottles, multilayer paper sacks, colored and transparent plastic liners, and opaque plastic containers made from polyethylene (PE), polyethylene terephthalate (PET), polypropylene (PP), or polycarbonate (PC). Agilent SORS-based spectrometers are effective at conducting measurements through light-filtering containers such as amber glass bottles for two main reasons: First, sensitive CCD detectors capture the weaker (attenuated) offset signal and, therefore, the light that the amber glass lets through. Second, an algorithm completely subtracts the zero spectrum (i.e., container) signal, including the container fluorescence, eliminating any fluorescence interference from the analyte signal.

Vaya, a portable spatially offset Raman spectrometer for ID testing through barriers

Agilent developed a handheld solution based on SORS to optimize the receipt of raw materials and their chemical identification for quality control purposes. The Agilent Vaya Raman can verify raw materials through opaque and transparent containers such as white or colored plastic drums, flexible intermediate bulk bags (FIBC), paper bags, or amber bottles. The Vaya onboard software requires minimal training. Non-spectroscopists can develop robust identification test methods using the wizard-based software. A dedicated raw material ID workflow, combined with PASS/FAIL answers ensures that Vaya operators in the warehouse can perform ID tests with minimal errors. Vaya has been designed to be used in a cGMP pharmaceutical environment, as it supports compliance with 21 CFR Part 11 and EU Annex 11 and meets requirements set forth in national pharmacopeias (USP <858>, USP <1858>, EP 2.2.48, Japanese Pharmacopeia 7th Edition Supplement II chapter 2.26, and Chinese Pharmacopeia 2020 Attachment D Chapter 0421).

The impact of the Vaya on the raw material ID process

Using the Vaya in the warehouse can streamline raw material receipt by reducing or removing a number of steps in the process, as shown in Table 2.

Table 2. Impact of the Agilent Vaya on the raw material ID process.

Identification at Receipt Process	
1. Unloading and quarantine area 	Raw materials, typically shipped by truck, are unloaded then stored in a quarantine area to await further inspection. In the quarantine area, the raw material containers are visually inspected for obvious defects. Labels are placed onto each container for tracking purposes.
2. Container inspection 	In the quarantine area, an operator verifies the ID of the raw material directly through the container with an Agilent Vaya Raman spectrometer.
3. Approval and addition to production stock 	Once the required number of containers are verified, the analytical data are reviewed for approval. On approval, the quarantined raw materials are mixed with production stock.

With Vaya, shuttling raw materials from the quarantine area to the sampling booth and back is no longer necessary. Container handling is drastically reduced as primary or secondary containers do not need to be opened, sampled, or resealed. The use of sampling consumables such as glassware, sample thieves, and PPE (gloves and booties) is reduced. Hazardous materials exposure is also kept to a minimum. With Vaya, it is estimated that 50% less time is spent in the warehouse, while costs are reduced by 50%.

Regulatory landscape

The International Organization for Standardization (ISO) 22716 is a set of comprehensive guidelines for good manufacturing practices (GMP) for the cosmetics and personal care sector. Introduced in 2007, the International Cooperation on Cosmetic Regulations (ICCR), formed by the United States (US), Canada, European Union (EU), and Japan, determined this standard would be used when recommending or publishing cosmetics GMP guidelines for each country. Since 2013, the EU officially requires that all cosmetic products sold on the EU market comply with the GMP for cosmetics as set out in the ISO 22716 standard (Cosmetics Regulation 1223/2009). In 2013, the US Food and Drug Administration (FDA) followed suit and published a non-enforceable GMP guidance for cosmetics manufacturing as a draft, considering the recommendations stated in ISO 22716. US GMP requirements for cosmetics are expected to be available toward the end of 2025. The FDA currently encourages cosmetics manufacturers to follow ISO 22716. In 2022, adopting in large part ISO 22716 requirements, the People Republic of China's State Food and Drug Administration released its own GMP regulation for cosmetics manufacturing.

Requirements for raw materials testing – ISO 22716

According to ISO 22716, raw materials testing is part of the quality management system for cosmetics products. The standard states that purchased raw materials and packaging materials used for the manufacturing of cosmetic products should meet defined acceptance criteria relevant to the quality of the finished products. This means that cosmetics manufacturers should at a minimum ensure that the correct raw materials are received and used in the manufacturing process. Certificates of analysis may be used in lieu of testing performed at receipt if raw materials suppliers are vetted and regularly audited by cosmetics manufacturers. In this case, the raw materials quality testing can be executed by the supplier.

In practice, many providers of cosmetic products prefer to perform testing in-house for several reasons:

- Providers may manufacture at the same location regulated and unregulated products, and decide to apply the same raw material ID process to both products. The regulated products require 100% ID testing for many countries in accordance with legislation controlling the release of pharmaceutical ingredients.
- Compliance with quality requirements is improved when testing is performed in-house.
- Providers may wish to prepare their operations for the future to account for further tightening of regulations governing the testing and safety of cosmetic products.

Vaya and cosmetics raw materials

To demonstrate the potential of the Vaya for QC of cosmetics manufacturing, cosmetics excipients and active ingredients were probed with Vaya directly through their original containers. The following excipients and active ingredients were tested:

Emollients and occlusives – Emollients are substances used to hydrate the skin. Occlusives are used to "lock-in" the moisture and provide a protective barrier or film.

Humectants – These moisturize the skin by drawing moisture from the air, rather than providing moisture directly (as in the case of emollients).

Preservatives – Commonly used to prevent the growth of mold and bacteria within cosmetic products.

Surfactants – Primarily used for cleansing and foaming and as emulsifying agents.

Essential oils – Used typically to add fragrance to cometic products.

Vitamins – These have a variety of effects when used on skin ranging from neutralizing free radicals, to increasing collagen production.

Experimental

All materials used in this experiment were procured from Sigma-Aldrich (UK), Holland and Barrett (UK), and BulkSupplements.com. A unique Vaya ID method was established for each of the raw materials listed in Table 3. For every method, the settings (including acquisition time and exposure time) were automatically configured by the built-in computer. The individual developing the method was only asked to select the type of container that housed the raw material (neat, thick plastic, thin plastic, glass vial, glass, or paper sack). Based on this selection, the built-in software chose, and, if necessary, optimized the container subtraction algorithm/process to remove the container signal from the raw material Raman spectrum. The spectral models from each developed method were overlaid for the purpose of comparison.

Results and discussion

Figures 1, 2, and 4 show that SORS is an effective technique to verify ID through transparent and opaque containers alike for cosmetics raw materials such as emollients and occlusives, humectants, preservatives, surfactants, essential oils, and vitamins. For ID testing or verification directly through opaque containers, SORS correctly removes the container contribution of nontransparent containers to yield a container-signal-free content spectrum – as shown for urea, SDS, and vitamin C stored in white HDPE containers.[1] The major bands for the HDPE polymer and the TiO_2 pigments are not visible on the material SORS spectra acquired through the white and transparent HDPE container (i.e., HDPE: 1,065, 1,129, 1,295, and 1,440 cm^{-1}, TiO_2: 451 and 611 cm^{-1}). For the materials acquired through white PP, Raman bands (403, 807, 845, 1,089, 1,154, 1,326, and 1,460 cm^{-1}) have also been subtracted correctly.

Table 3. Raw materials identified.

Cosmetic Ingredient Class	Example Ingredients Verified
Emollients and Occlusives in Amber Glass Bottles	Castor oil, linseed (flaxseed) oil, olive oil, almond oil
Humectants in opaque and semitransparent High Density Polyethylene (HDPE) Containers and White Polypropylene (PP) Flexible Intermediate Bulk Containers (FIBC)	Glycerol, PEG, sorbitol, urea, ethylene glycol, propylene glycol
Preservatives in Amber Glass and Opaque HDPE Containers	Ethanol, benzyl alcohol, cetyl stearyl alcohol mix, citric acid, hexamethylenetetramine, stearic acid
Surfactants in Amber Glass and Opaque and Semitransparent HDPE Containers	Sodium dodecyl sulfate (SDS), Triton X100, PS20, PS80
Essential Oils in Amber Polycarbonate Containers	Citronella oil, eucalyptus oil, juniper berry oil, lavender oil, orange oil, tea tree oil
Vitamins in Clear Glass Bottles	Vitamin A palmitate, vitamin B3 in bovin gelatin capsules, vitamin C

[1] Spectra of semitransparent HDPE, white HDPE, and white FIBC (PP) are added to the figures of the different classes of cosmetic ingredients for comparison purposes.

Figure 1 also shows that SORS and Vaya retain minor spectral features, as shown by the small differences in the different SORS spectra obtained for the emollients and occlusives class.[2] The challenge matrix depicted in Figure 1 visually demonstrates how Vaya fares in discriminating the different oils in the emollients and occlusives class. In such a matrix, an ID test is performed for each analyte in the class using the ID verification method specifically developed for each analyte within the same class. Ideally, a challenge matrix should only display pass rate scores (represented by the color green) along the diagonal of the matrix, indicating that the method accurately identifies its corresponding material. Off the diagonal, the matrix should ideally show only fail score rates (represented by red tiles), signifying that the method correctly rejects incorrect materials.

In situations where the chemistry and resulting spectra of a sample set are so alike that perfect separation is challenging, Vaya allows the addition of spectra from similar samples to the method build. By incorporating these additional spectra, the instrument's algorithm adjusts the decision criteria to achieve flawless identification without any false positives. The challenge matrix in Figure 1 demonstrates that the combination of SORS and the two-criteria decision/comparison algorithm of the Vaya delivers excellent discrimination power.

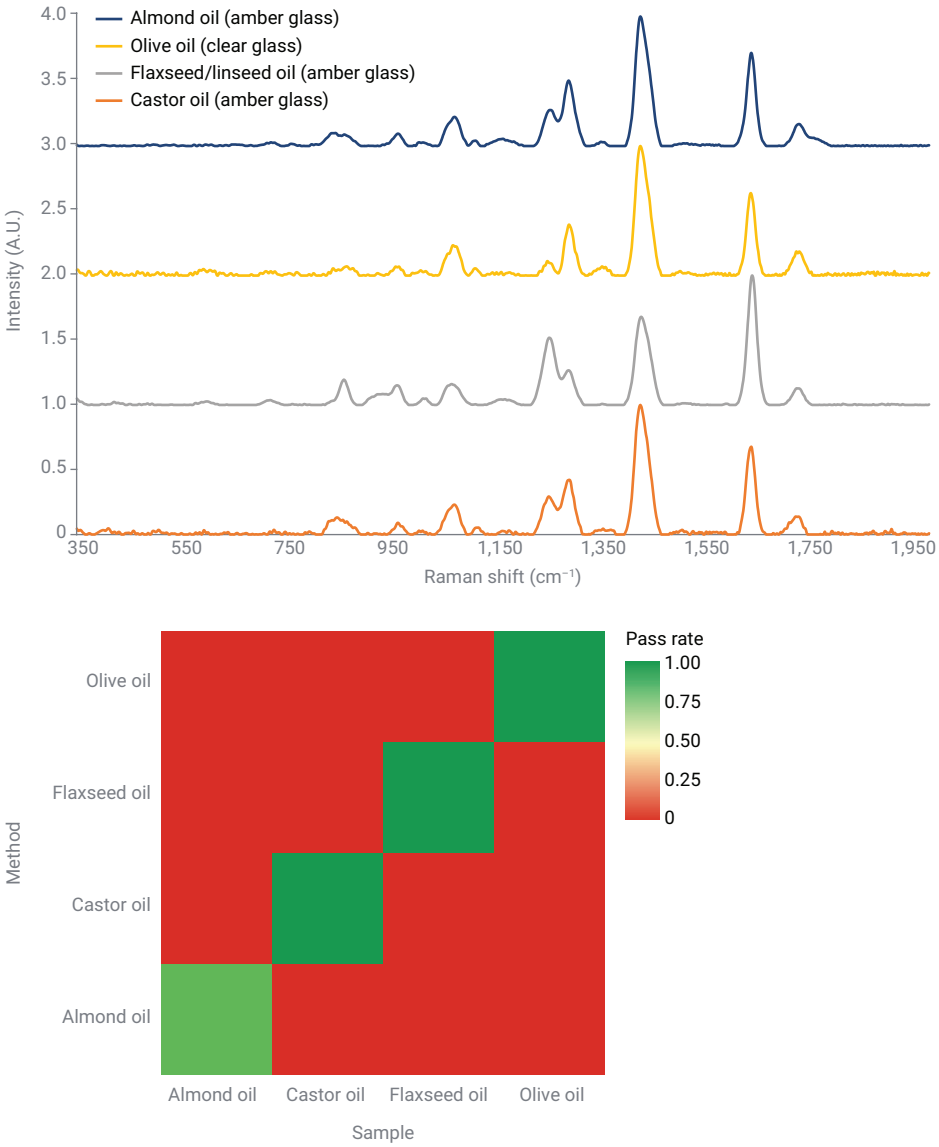

Figure 1. Agilent Vaya Raman spectra and associated challenge matrix – emollients and occlusives.

[2] Challenge matrices were not developed for other classes of cosmetic raw materials in this application note as none of the other classes included raw materials with similar composition or structure and a subsequently similar Raman spectrum.

[3] The spectra were visually overlayed with spectra available from the Agilent Resolve Library.

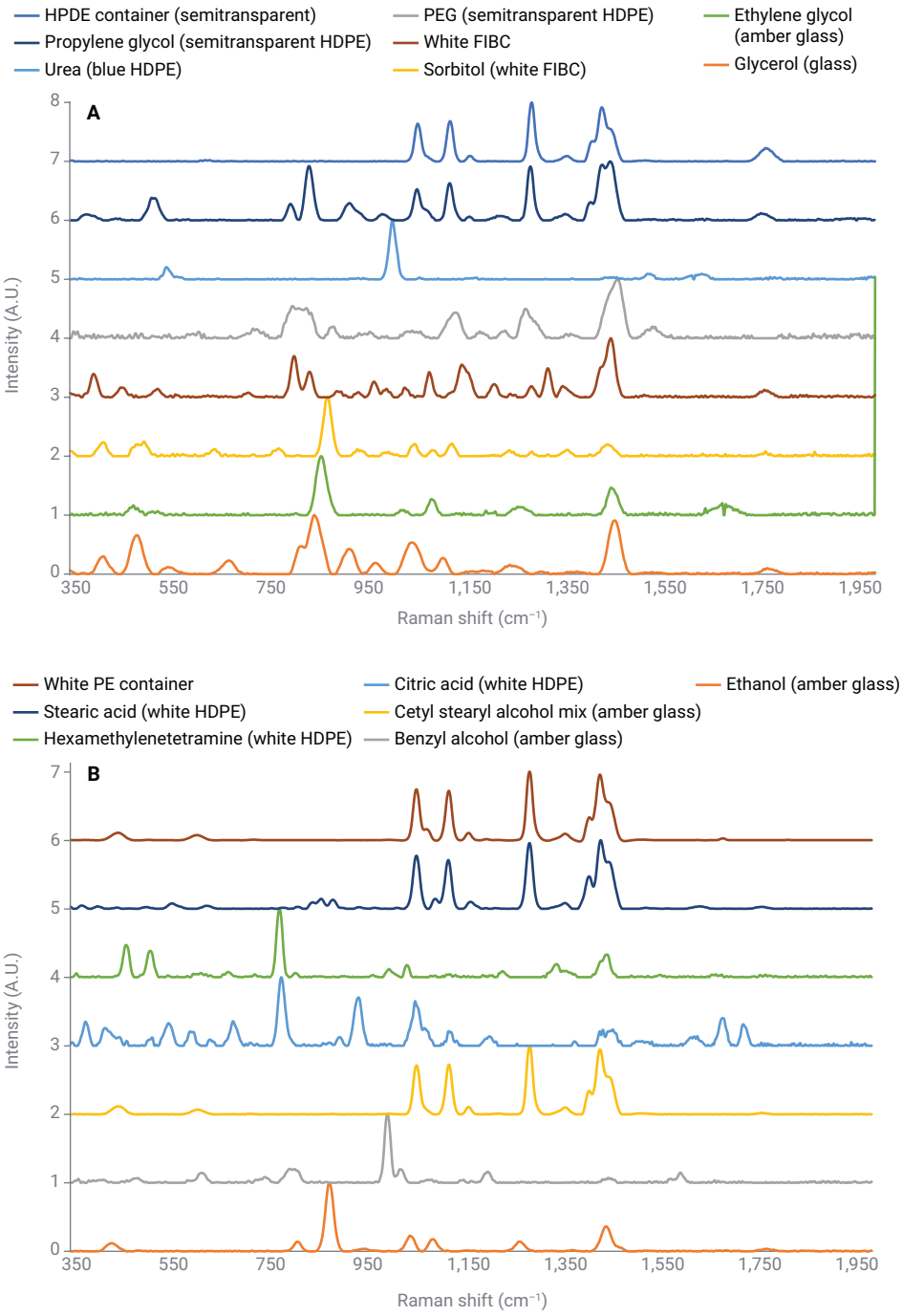

Figure 2. Agilent Vaya Raman spectra – humectants (A) and preservatives (B).

Figure 3 compares the Raman spectra for stearic acid acquired through a white HDPE container and the same empty white HDPE container. It shows that the identification of stearic acid through a white PE container is possible despite large similarities between the stearic acid and the white HDPE container Raman bands. The best evidence for the absence of the container in the stearic acid spectrum is the absence of the TiO_2 bands in the 300 to 600 cm^{-1} region.

Figure 4 shows the Raman spectra for surfactants, essential oils, and vitamins. The vitamins class spectra demonstrate the sensitivity of the Vaya, and its ability to detect low Raman signals. The vitamin B3 spectrum was acquired through a glass bottle containing vitamin B3 niacin in gelatine capsules, and exhibited a good signal-to-noise ratio (S/N) despite the capsules' loose packing in the glass bottle, and subsequent greater loss of Raman photons compared to that of powder-based niacin.

The polysorbate 20 and 80 spectra acquired through light-blocking amber glass bottles also exhibited good S/N and low fluorescence. By combining excellent fluorescent mitigation of the amber bottle and good photon sensitivity, the Vaya can discriminate the two polysorbates using the monooleate band at 1,650 cm^{-1} only present in the polysorbate 80. The spectra for all materials match reference spectra published elsewhere.[3]

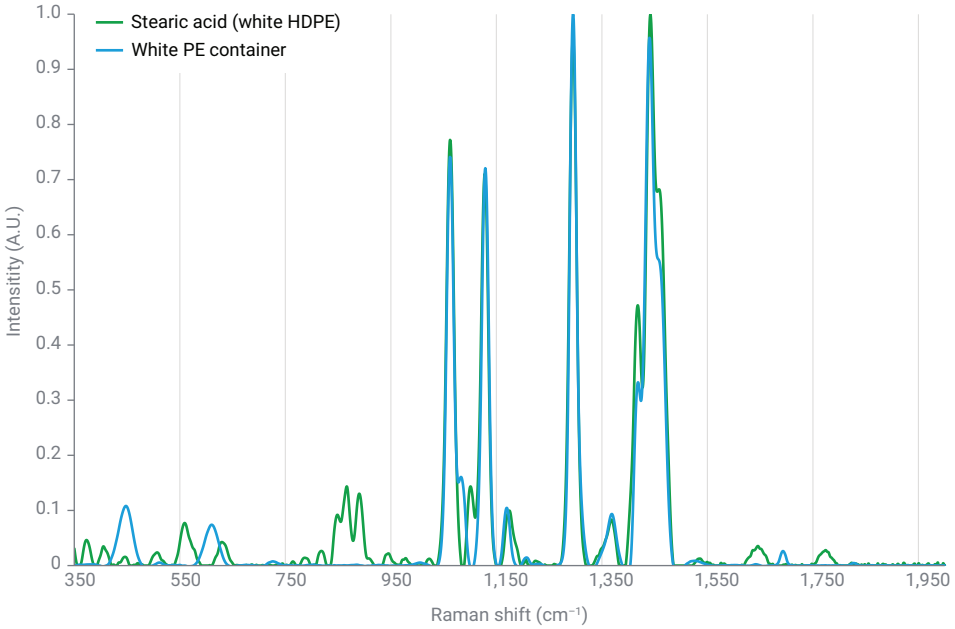

Figure 3. Agilent Vaya Raman spectra of stearic acid through a white HDPE container and an empty white HDPE container.

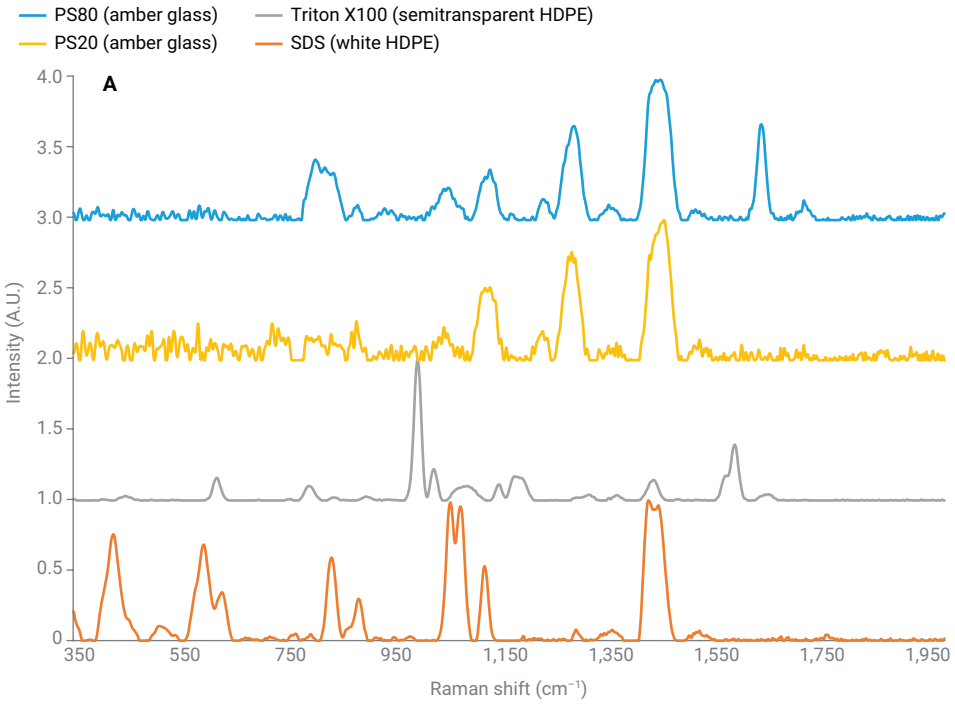

Figure 4A. Agilent Vaya Raman spectra of surfactants.

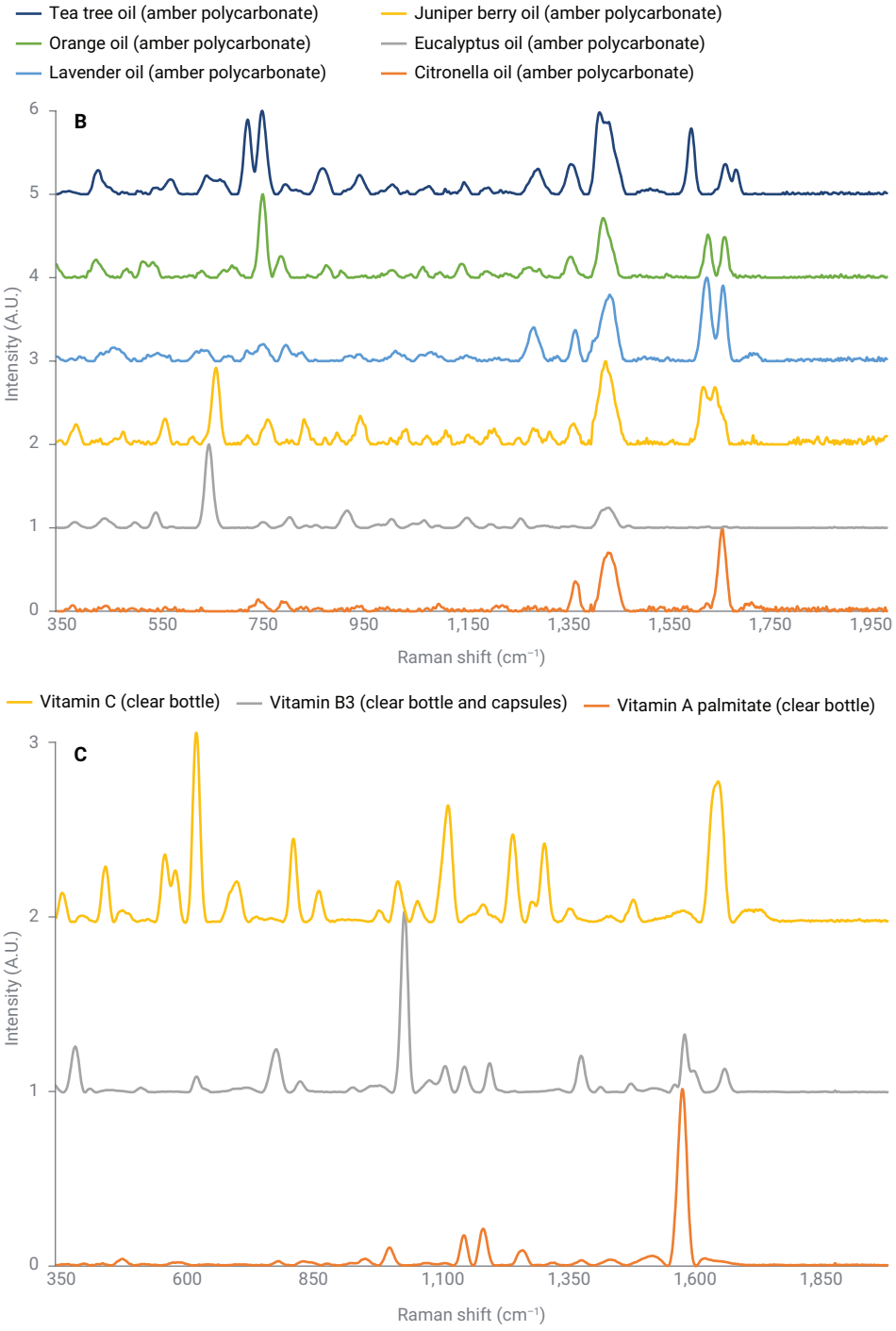

Figure 4B,C. Agilent Vaya Raman spectra of (B) essential oils and (C) vitamins.

Note that the spectrum of vitamin A palmitate was acquired using a mixture of 7% vitamin A palmitate compounded with other excipients (modified starch, maltodextrin, sucrose, corn oil, tocopherol, sodium ascorbate, and silicon dioxide). The spectrum mostly matches one of pure vitamin A palmitate with some Raman bands in the 480 to 1,500 cm^{-1} region (480 cm^{-1} v:w, 595 cm^{-1} v:w, 860 cm^{-1} v:w, 942 cm^{-1} v:w, and 1,121 cm^{-1} v:w (wide)) belonging to starch.

The presence of the other excipients cannot be ascertained. The concentration of the excipients was not provided by the vitamin manufacturer, however, starch is typically used as a bulking agent/filler, and therefore should be the excipient with the largest concentration and be among the most visible in the spectrum. Vitamin A palmitate dominates the spectrum, given the difference in polarizability potential compared to that of starch. Other excipients are not expected to be detectable due to their much lower concentration.

Conclusion

The Agilent Vaya Raman spectrometer has the capability to distinguish a unique Raman spectrum for each material in this study, enabling their direct ID verification while in quarantine. There is no need for sample or container preparation before scanning a the contents of a container using the ID verification feature of the Vaya. Users are simply asked to place the Vaya directly against the container and initiate the process. The instrument remains stationary during the spectrum acquisition phase. On average, the scanning time for through-transparent is 10 to 15 seconds, and for opaque containers, 35 to 40 seconds.

The Vaya Raman raw material identity verification system, with its rapid analysis times and capability to measure through both transparent and opaque containers, is perfectly adapted for handling large quantities of raw materials used in the formulation of cosmetic products. It enables immediate identification of raw materials in quarantine upon receipt. The Vaya Raman instrument simplifies the process by reducing or eliminating many steps required in FTIR or conventional Raman spectroscopy, such as cleaning instrumentation and the sampling booth or moving containers to and from the quarantine area for sampling and analysis. Using Vaya allows for future preparation of raw material receipts and can accommodate increased production volumes or new sampling requirements such as 100% ID, all with minimal investment.

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