Application Note

Raw Material Identification

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Through-Container Identity Verification of Polysorbates 20, 40, 60, and 80 with the Agilent RapID Raman System

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Abstract

Polysorbates are often packaged in a sealed, oxygen-free environment to prevent degradation. Amber glass bottles are common containers for polysorbates, often used in large numbers, making identification difficult and time-consuming. Manufacturers of polysorbates typically make different grades, so reliable identity verification is essential to mitigate mistakes in supply. This Application Note describes how the Agilent RapID Raman system can unambiguously verify the identity of the four common pharmaceutical grades of polysorbates through unopened amber glass bottles.

Introduction

Polysorbates are used as excipients and as reagents in bioreactions, and in all applications degradation by atmospheric exposure is particularly important to avoid. Polysorbates 20, 40, 60, and 80 are often packaged in transparent amber glass bottles, which, although not opaque, are difficult to identify through using conventional (handheld) Raman instruments. Polysorbates have a weak Raman signal and all variants have similar spectra. The added difficulty of measuring through amber glass therefore significantly increases the probability of a false positive or failed identification using conventional technology.

The Agilent RapID Raman system uses spatially offset Raman spectroscopy (SORS) technology to verify the identity (ID) of raw materials through unopened opaque packaging, but glass containers can also benefit. Fluorescence from amber glass is intense, making the Raman spectrum noisy (Figure 1). This means that 100 % confidence of a positive ID may be impossible using conventional instruments, even at longer excitation wavelengths.

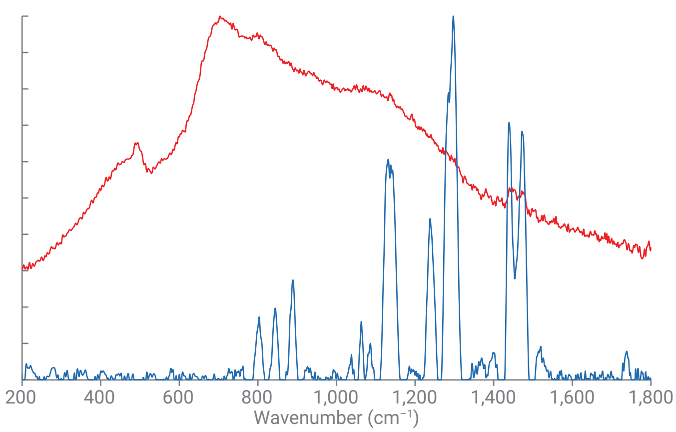

Figure 1. Raman spectra through amber glass at 830 nm: Conventional Raman (red) and using the Agilent RapID system (blue).

Verifying Different Polysorbates

Raman spectra provide a chemically specific fingerprint of each polysorbate that can be used to differentiate these similar chemicals. The spectra in Figure 2 show a significant difference for only one material, PS 80. The other three are similar, and require both a high-quality measurement and a robust algorithm for unambiguous verification. Figure 2 shows the high quality of Raman signal that can be measured through unopened amber glass bottles using the RapID system in approximately 20–30 seconds per container. Not all amber glass is the same, even though it may look similar; containers can have variable absorption and fluorescence. This impacts the ability of conventional Raman to measure contents through apparently transparent glass. The RapID system avoids collecting fluorescence from the bottle, rather than trying to remove its contribution by data processing, as conventional Raman instruments do.

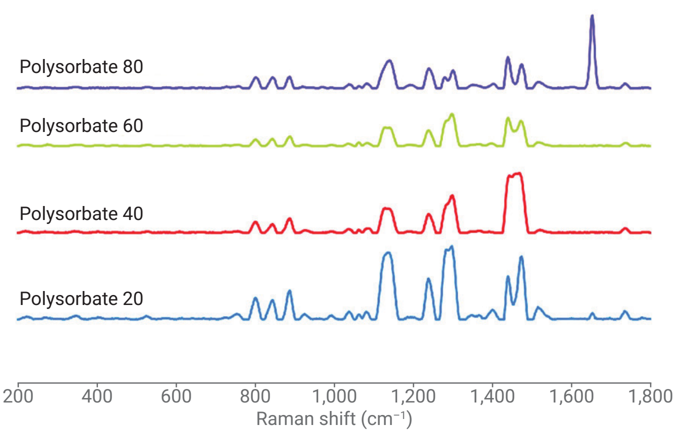

Figure 2. Spectra of polysorbates 20, 40, 60, and 80 acquired through amber glass with an Agilent RapID Raman system.

Ensuring Reliable Identification Using SORS

The RapID system software builds a library model for each material from through-container scans. The method validation step verifies a material against positive and negative matches. For screening polysorbates, it is important to demonstrate that all models correctly identify only the polysorbate in their respective model, and reliably reject all others in the validation protocol. To add a further degree of assurance during validation (Figure 3), the RapID system's built-in validation check tool automates that checking against all models in the database.

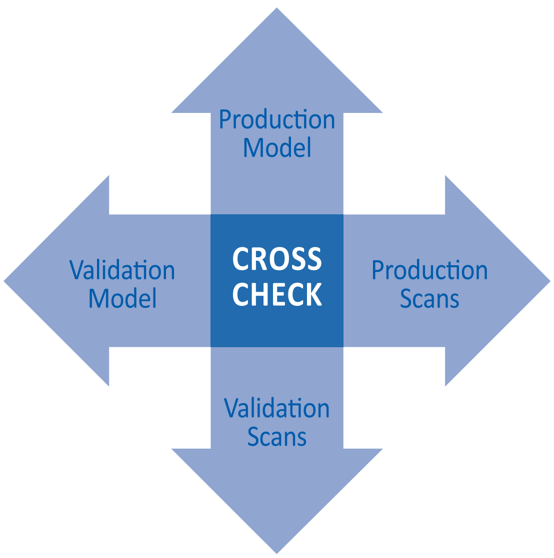

Figure 3. Cross-checking process.

Methods

To demonstrate correlation performance, models were built using polysorbates 20, 40, 60, and 80 sourced from Sigma-Aldrich. A model was built for each material in Sigma-Aldrich amber glass containers. These models were manually validated and automatically cross-checked before ID verification testing. The process was repeated using JT Baker PS 20 and 80 (the most common variants) in amber glass. It is known that JT Baker's amber glass has a different absorption profile from Sigma-Aldrich containers, and causes problems with 1,064 nm Raman (cf. Rapid at 830 nm).

Results and Discussion

Table 1 indicates the correlation of through-container scans of polysorbates 20, 40, 60, and 80 against all models for Sigma-Aldrich-sourced materials and bottles. The results show that, despite their similar molecular structure, all polysorbates will pass their respective ID verification tests when the genuine material is tested. When the incorrect material was scanned, the RapID system correctly identified fails against each incorrect material. The JT Baker samples were also identified correctly, with no false positives or negatives.

Table 1. ID validation for the different polysorbate methods in percentage of positive ID. Procedure: repeat validation measurements using a model (left) tested against each material (top) 30 times over three different days, recording each positive ID.

Sample	Polysorbate 20	Polysorbate 40	Polysorbate 60	Polysorbate 80
Polysorbate 20	100	0	0	0
Polysorbate 40	0	100	0	0
Polysorbate 60	0	0	100	0
Polysorbate 80	0	0	0	100

Conclusions

The Agilent RapID system combines high-quality through-container Raman measurements with a robust analytical method for unambiguous ID verification of polysorbates 20, 40, 60, and 80. The validation demonstrates that even the very similar 20, 40, and 60 grades can be verified routinely.

By avoiding opening the bottles for ID testing, shelf-life can be managed, sterility is maintained, and expensive nitrogen-purged testing equipment can be avoided. High-throughput testing with the RapID system means that a batch of 100 bottles can be processed in less than 1 hour by one person in a warehouse environment.

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