ASSESSING SELECTIVITY OF THE ASSURx® G7 HANDHELD RAMAN ANALYZER

APPLICATION NOTE RAMAN-009 (A4)

Abstract

Selectivity is the measure of an analyzer's ability to distinguish chemically-similar materials. It is important to evaluate the selectivity of a Raman instrument especially in the pharmaceutical, nutraceutical, and cosmetic industries to ensure proper material verification, and ultimately, material quality. This short application note will demonstrate the high selectivity of the ASSURx® G7 Handheld Raman Analyzer to distinguish a variety of similar sugars, and not confuse any of these sugars with one another. An experiment analyzing polymorphs, i.e., same molecule with different crystalline forms, will also be described where the ASSURx analyzer demonstrated high selectivity to separate such materials.

Introduction

Selectivity of a Raman device is a key performance metric that is evaluated during method development for raw material verification in the pharmaceutical manufacturing process. When verifying incoming raw materials, the verification tool should be able to distinguish "chemically-similar" materials from one another. Chemically-similar materials should include different molecules, with the same empirical formula, and even the same molecules with different crystalline structures. A good Handheld Raman analyzer for material verification distinguishes these materials with very low false positives.

If a Raman instrument has high selectivity it produces a low number of false positives (i.e., does not erroneously verify materials as a pass, when it is different material); while if it has low selectivity it produces a high number of false positives. In this brief application note, an experiment used to demonstrate the selectivity of the ASSURx Raman Analyzer will be described.

Method

Experiment 1. Sugars

The experimental setup in this first experiment to demonstrate selectivity of the ASSURx analyzer was as follows: eleven different sugars (sucrose samples) were acquired from unique manufacturers and distributors. Each of the sugar samples w scanned into the ASSURx analyzer's library. The search mode and the "Top 5" feature was used to re-scan each material and identify nearest matches, and to look for potential false positives. A cross validation matrix was then created using the "Top 5" feature.

Experiment 2. Calcium Carbonate

The experimental setup in this second experiment to demonstrate selectivity for polymorphs was as follows: two forms of Calcium Carbonate were acquired, Aragonite and Calcite. Each of these $CaCO_3$ samples were scanned into the ASSURx analyzer's library. A cross-validation matrix was then created using the "Top 5" feature.

Selectivity Results

Experiment 1. Distinguishing Sugars

Upon scanning the eleven sugars into the ASSURx analyzer's library and then utilizing the search mode and "Top 5" feature to rescan each material and identify the nearest match, spectral similarities (Figure 1) were evaluated as well as a cross validation matrix of HQI scores (Figure 2).

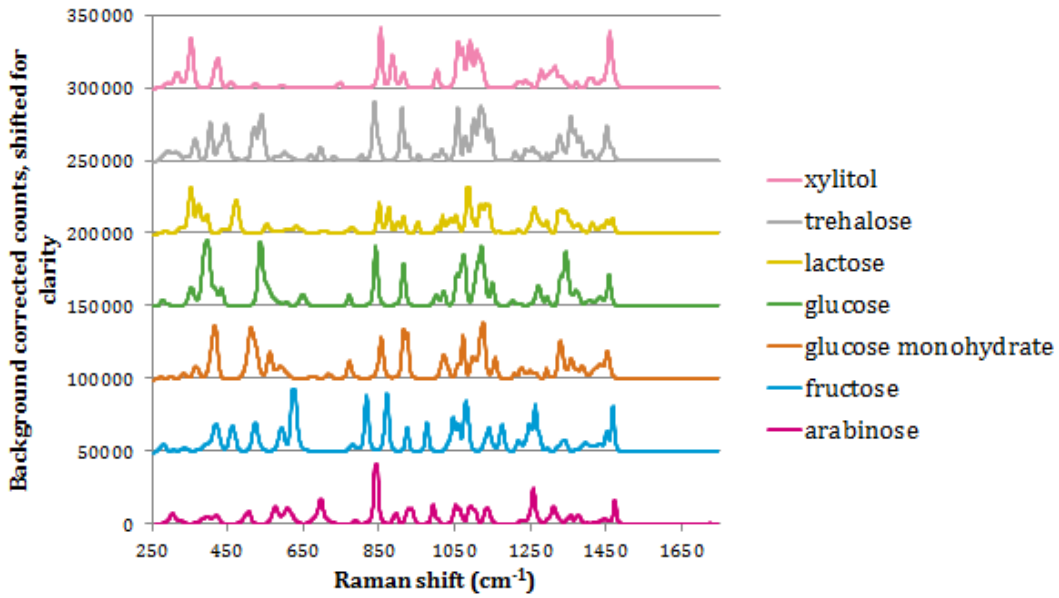

Figure 1. Raman spectra of various sugars

Method Used in ASSURx Analyzer	Material analyzed: arabinose	fructose	d-xylose	mannitol	trehalose	lactose	xylitol	mannose	glucose mono	sorbitol	glucose
arabinose	0.962	0	0	0	0	0	0	0	0	0	0
fructose	0	0.965	0	0	0	0	0	0	0	0	0
d-xylose	0	0	0.984	0	0	0	0	0	0	0	0
mannitol	0	0	0	0.964	0	0	0	0	0	0.62	0
trehalose	0	0	0	0	0.979	0	0	0	0	0	0.43
lactose	0	0	0	0	0	0.960	0.19	0	0	0	0
xylitol	0	0	0	0	0	0	0.953	0	0	0	0
mannose	0	0	0	0	0	0	0	0.986	0	0	0
glucose mono	0	0	0	0	0.20	0	0	0	0.985	0	0
sorbitol	0	0	0	0.59	0	0	0	0	0	0.968	0
glucose	0	0	0	0	0.44	0	0	0	0	0	0.974

Figure 2. Cross-validation matrix of HQI scores for the tested sugars

Figure 1 shows the spectral similarities between the sugar samples. As would be expected, many of the spectral features are similar between the different sugars. However, Figure 2 shows the high selectivity of the ASSURx Raman analyzer to be able to distinguish all the sugars from one another, with no false positives (HQIs off-axis were all <0.8). For off-axis results that were 0.4–0.8, not a pass but measurable HQIs, for example, glucose and trehalose, it can be seen that the spectra are very similar in Figure 1. However, in Figure 2, when Glucose is the method being run, and the sample is Trehalose that is being analyzed, the HQI scoring method combined with the high resolution and sensitivity of the ASSURx Raman, showed the correct failing verification, with a HQI score of 0.44. Similarly, when Trehalose was the method being run, and the sample being analyzed was Glucose, the ASSURx Raman again, correctly showed a failing verification, with a HQI score 0.43. The ASSURx analyzer was clearly sufficient to make the distinction between the sugars in this experiment, and even very similar ones.

Experiment 2. Distinguishing Polymorphs

The spectral results of the two polymorphs of calcium carbonate show that they have similarities (Figure 3). However, the ASSURx analyzer can distinguish these polymorphs (Figure 4).

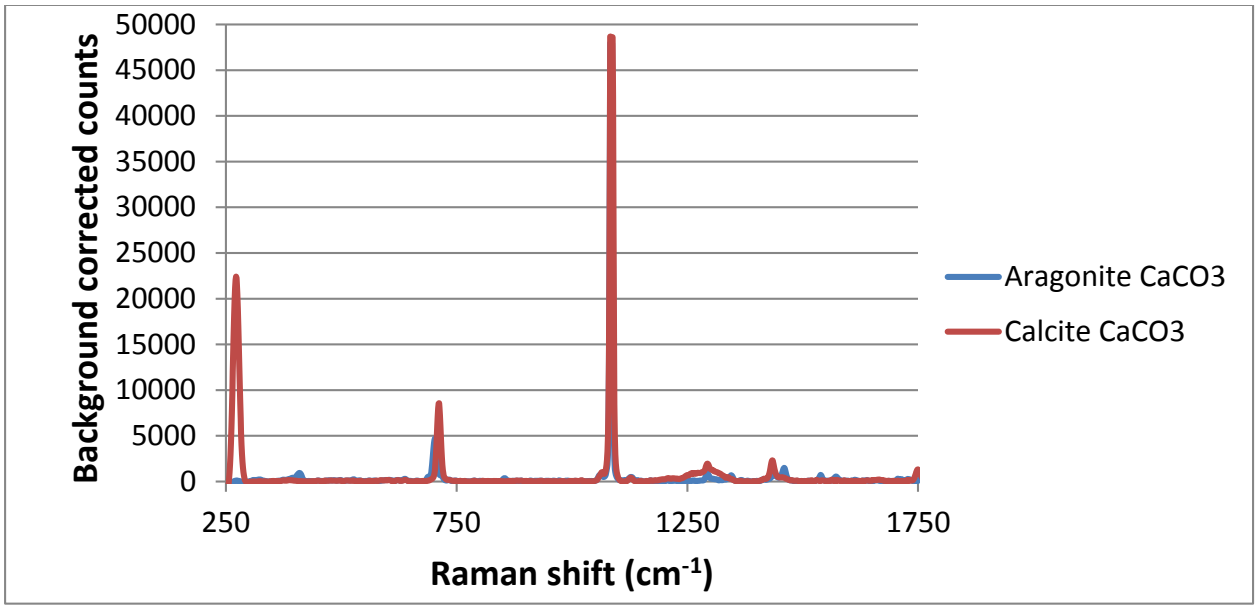

Figure 3. Spectra of 2 polymorphs of Calcium Carbonate

	Aragonite	Calcite
Aragonite	0.967	0.74
Calcite	0.74	0.963

Figure 4. Cross-validation matrix of HQI scores for polymorphs of Calcium Carbonate

There are overlaps of major spectral features in Figure 3. But again, the ASSURx analyzer's high selectivity is capable of uniquely identifying and verifying these materials.

Conclusion

These simple experiments easily demonstrate the high selectivity of the ASSURx Raman analyzer. As such, users can expect a low number of false positives when running chemically-similar, but different materials. The ASSURx analyzer's high selectivity ensures for accurate raw material verification and identification in pharmaceutical cGMP processes.

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