NanoRam®-1064 Fast Facts: Botanical Verification

Introduction

Before the technological advancements of science, botanical medicine laid the groundwork for pharmaceutical advantages that exist today. Botanicals are dervied from plant materials and are used for their medicinal and therapeutic properties. They are the primary aspect of the dietary supplement market called nutraceuticals that is promoted to the public as a holistical alternative to typical pharmaceutical drugs. The nutraceutical market is not as heavily regulated by the U.S. Food and Drug Administration (FDA) as the pharmaceutical drug market. However, under the FDA nutraceuticals manufacturers of botanicals follow Good Manufacturing Practice (GMP) requirements to ensure identity, purity, quality, strength and, composition, which qualifies for necessary testing before consumption.

Raman can be utilized in the testing of botanical samples. Each sample varies with different chemical components, and some fluoresce greater than others. A typical handheld Raman device with a 785 nm laser is unable to identify the grape seed extract due to strong fluorescence (**Figure 1, red trace**). B&W Tek's NanoRam®-1064 is able to minimize some of the fluorescence from the grape seed extract (**Figure 1, blue trace**), permitting visibility of a few peaks for quick handheld Raman analysis.

The NanoRam-1064 is a handheld Raman device fully compliant with all major pharmacopeias. Its records management software is 21 CFR Part 11 compliant with complete audit trail.

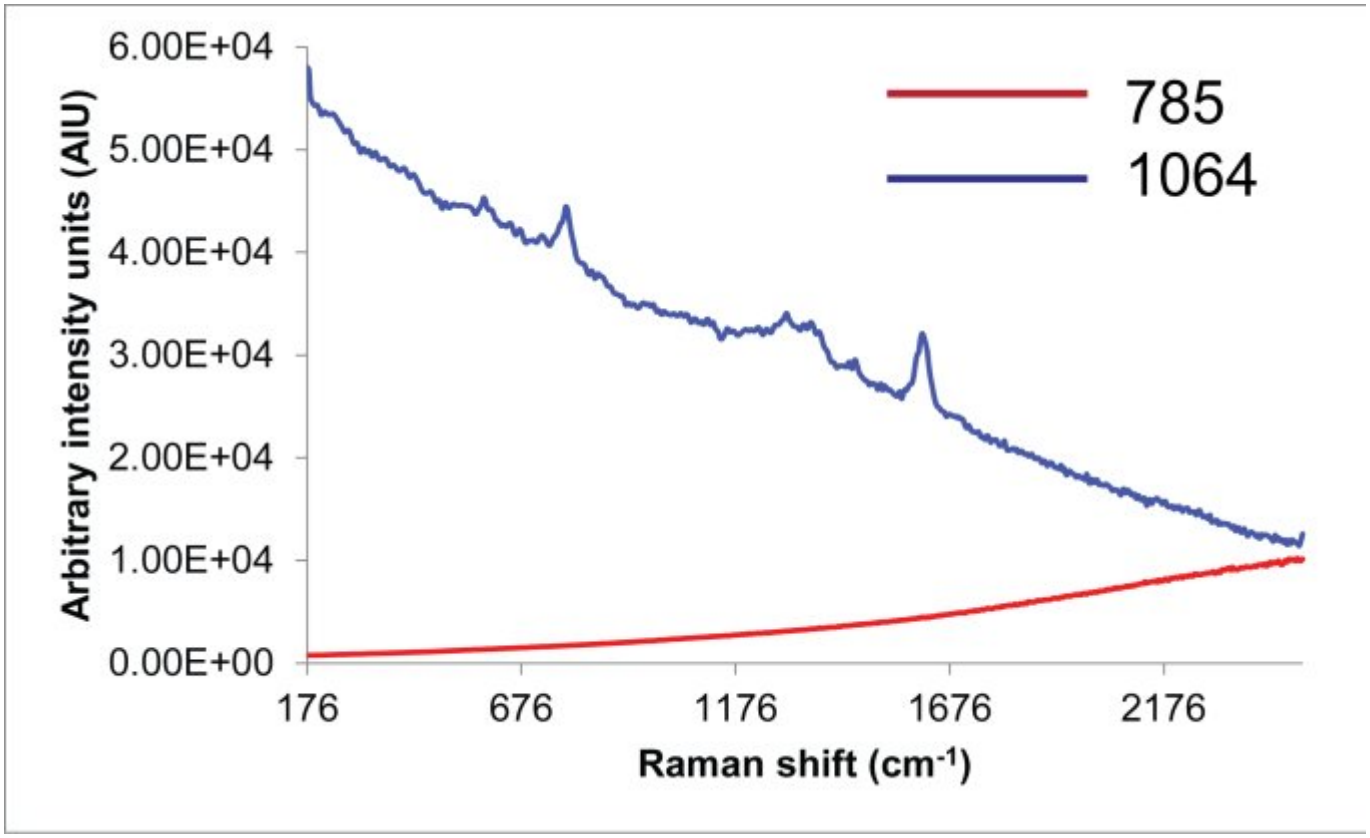

Figure 1. Raman spectra of grape seed extract collected with 785 nm and 1064 nm laser excitations.

Configuration

BWT-840000953 - NanoRam-1064 Handheld Raman Spectrometer
The NanoRam-1064 is a high-performance handheld Raman Spectrometer for nondestructive identification and verification of incoming raw materials, such as APIs, excipients, and intermediates, regardless of their color. Compact and agile, the NanoRam-1064 can be used by non-technical users to rapidly identify samples in the warehouse, on the loading ramp, in the field or in the laboratory, minimizing quarantine areas and expediting materials through the manufacturing lifecycle. Utilizing Raman technology, the NanoRam-1064 minimizes fluorescence and can identify a large range of samples by distinguishing between different grades of cellulose, polysorbate and Opadry®. Rapid incoming material testing with the NanoRam-1064 can be performed through transparent containers, all the while maintaining sample volume and integrity. The unit also offers full onboard library and method validation, making a complinat workflow for methods and library development.The NanoRam is fully compliant with the US FDA 21 CFR Part 11 and Part 1040.10, and can play an integral role in cGMP-compliant facilities. The NanoRam-1064 meets the requirements of Raman spectroscopy methods including the US Pharmacopeia <858>, European Pharmacopeia 2.2.48, Japanese Pharmacopeia 2.26, as well as the People’s Republic of China Pharmacopeia Directives on Raman Spectroscopy. Raman is a recognized method for complying with the PIC /S & GMP directives regarding 100% identity assurance for starting materials. A complete range of training courses and support services is available, including IQ/OQ/PQ/DQ implementation services, as well as method and/or new library development support.

Methodology

A NanoRam-1064 with a point and shoot adapter was utilized to analyze four different types of botanical samples sealed in plastic sample bags (**Figure 2**). The samples include vitamin K2 and pomegranate, rhodiola rosea, and grape seed extracts. Laser power was set at 90% of the

maximum power (~380 mW) for the Vitamin K2 sample with a yellow pigmentation. The laser power was set at 10% (~42 mW) for the remaining three samples because of darker colored samples. For this case study the NanoRam-1064 Identification mode was utilized because it provides a robust algorithm based on a multivariate method. For each botanical sample an individual method was created. To create a method each sample was scanned five different times in alternate spots. All samples were tested against each method to prove validity.

Figure 2. Analyzing grape seed extract with 1064 nm laser with point and shoot adapter.

Results

The validity of a method is dependent on each method having to prove its “specificity” via the correct sample passing and all other samples failing. The statistical significance (p-value) determines the samples passing or failing the method. The NanoRam-1064 p-value threshold is p = 0.05, which corresponds to the default significance level set for the botanical methods.

Calculated p-values over p = 0.05 are indicative of a “Pass” result, and p-values below p = 0.05 result in a “Fail” result. **Table 1** displays a matrix of pass/fail results for each individual botanical method. Each botanical method is able to selectively pass its own sample, while failing all other samples.

Method / Sample	Vitamin K2	Rhodiola rosea ext	Pomegranate ext	Grape ex
Vitamin K2	PASS p=0.999996	FAIL p=0	FAIL p=0	FA p=
Rhodiola rosea ext	FAIL p=0	PASS p=0.999971	FAIL p=7,79692 x10^{-4}	FA p=
Pomegranate ext	FAIL p=0	FAIL p=3.33067 x10^{-16}	PASS p=0.999992	FA p=
Grape seed ext	FAIL p=0	FAIL p=0	FAIL p=0	PA p=0.9

Table 1. Botanicals specificity matrix

Conclusion

The NanoRam-1064 is an effective pharmaceutical device for the minimization of fluorescence in raw materials identification. In this case study the NanoRam-1064 was able to reduce the fluorescence in different botanical ingredients, allowing them to be analyzed and tested against each individual sample method for robust identification.

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