Application Note 410000049-A

NanoRam®-1064 Fast Facts: Botanical Verification

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.

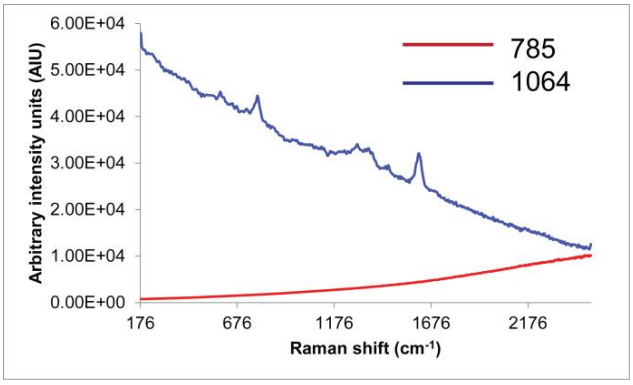

Figure 1. Raman spectra of grape seed extract collected with 785 nm and 1064 nm laser excitations.

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 seed ext
Vitamin K2	PASS p=0.999996	FAIL p=0	FAIL p=0	FAIL p=0
Rhodiola rosea ext	FAIL p=0	PASS p=0.999971	FAIL p=7,79692 x10^{-4}	FAIL p=0
Pomegranate ext	FAIL p=0	FAIL p=3.33067 x10^{-16}	PASS p=0.999992	FAIL p=0
Grape seed ext	FAIL p=0	FAIL p=0	FAIL p=0	PASS p=0.999997

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.

CONTACT

Metrohm Deutschland
In den Birken 3
70794 Filderstadt

info@metrohm.de

CONFIGURATION

NanoRam-1064 Raman-Handspektrometer

Das NanoRam-1064 ist ein leistungsstarkes Raman-Handspektrometer zur zerstörungsfreien Identifikation und Verifizierung von angelieferten Rohmaterialien wie pharmazeutischen Wirkstoffen, Hilfsstoffen und Zwischenprodukten, unabhängig von ihrer Farbbeschaffenheit. Das kompakte und flexible NanoRam-1064 kann von technischen Laien eingesetzt werden, um Proben im Lager, an der Laderampe, im Aussendienst oder im Labor rasch zu identifizieren, sodass Quarantänebereiche möglichst klein gehalten und Herstellungszyklen beschleunigt werden können. Mithilfe der Raman-Technologie reduziert das NanoRam-1064 Fluoreszenz auf ein Minimum und kann eine grosse Auswahl an Proben identifizieren, wobei zwischen verschiedenen Qualitätsstufen von Cellulose, Polysorbat und Opadry® unterschieden werden kann. Schnelle Tests angelieferter Materialien können mit dem NanoRam-1064 durch transparente Behälter erfolgen, ohne die Integrität der Probe oder deren Volumen zu beeinträchtigen. Das Gerät bietet ausserdem eine vollständig integrierte Bibliothek und eine Methodenvalidierung, was bei der Entwicklung von Methoden und Bibliotheken einen konformen Ablauf ermöglicht.

Das NanoRam erfüllt sämtliche Anforderungen gemäss 21 CFR Part 11 sowie Part 1040.10 der US-amerikanischen Behörde FDA und kann eine zentrale Rolle in Einrichtungen einnehmen, die sich nach der cGMP (in den USA aktuell gültige gute Herstellungspraxis) richten. Das NanoRam-1064 erfüllt die Anforderungen an die Methoden der Raman-Spektroskopie laut Kapitel <858> des Amerikanischen Arzneimittelbuchs, Europäischer Pharmakopöe 2.2.48, Japanischer Pharmakopöe 2.26 sowie den Richtlinien der Pharmakopöe der Volksrepublik China zur Raman-Spektroskopie. Raman ist eine anerkannte Methode zur Einhaltung der Richtlinien gemäss PIC/S und GMP, wenn es um die 100%ige Identitätssicherung bei Ausgangsstoffen geht. Schulungen und Supportleistungen sind in vollem Umfang verfügbar, darunter auch Implementierungsleistungen zu IQ/OQ/PQ/DQ sowie Unterstützung bei der Entwicklung von Methoden und/oder neuen Bibliotheken.