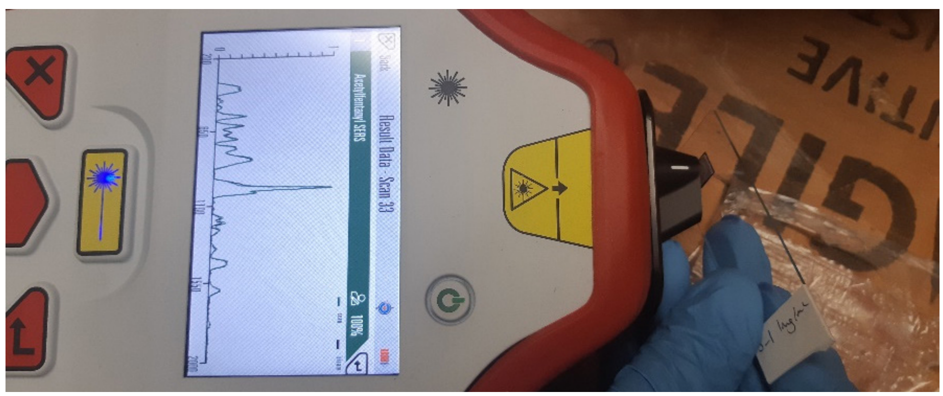
Application Note

Forensics

Surface Enhanced Raman Spectroscopy Analysis of Low Concentration Fentanyl Street Samples

Low concentration narcotics detection with a handheld Resolve Raman analyzer using SERS substrates



Authors

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Abstract

Street-bought narcotics can contain a variety of active materials and cutting agents, some of which can cause fatalities, even when present at very low dosages. For example, trace amounts of fentanyl analogs can result in an overdose. The low concentration of fentanyl found in some street drugs makes detection by bulk techniques, such as conventional Raman spectrometry, challenging.

This study shows the capabilities of the Agilent Resolve Raman handheld analyzer with Nikalyte gold Surface Enhanced Raman spectroscopy (SERS) substrates for the trace detection of fentanyl analogs in street drug samples. First, a user SERS library of narcotics was created using the Agilent Command Fleet Management software. This library was then used to identify fentanyl compounds in a range of street drug samples. The workflow outlined in the application note demonstrates the ease of use of Command to build a detection library and the compatibility of the Resolve with SERS for trace detection of various fentanyl compounds.

Introduction

Fentanyls are highly potent synthetic opioids (10 to 1,000 times more potent than heroin), which have contributed to many overdose deaths around the globe in recent years.[1] Due to their potency, fentanyl analogs are typically present at trace-level concentrations in street samples and often in complex mixtures. These characteristics make the detection of fentanyl in these types of samples challenging by typical spectroscopic techniques.

Raman spectroscopy is a well-established analytical technique that provides molecular specific data, enabling the identification of bulk concentration narcotics. As a bulk technique, identifying trace-level concentrations of drugs, such as fentanyl in street samples, can be difficult. This limitation can be overcome to some extent, by combining Raman spectroscopy with a metallic surface, in a technique termed Surface Enhanced Raman spectroscopy (SERS). Adsorbing the drug sample onto the metallic surface can enhance the Raman signal of the drug. SERS is a simple way to increase the sensitivity of a Raman spectrometer, such as the Agilent Resolve Raman handheld analyzer, enabling trace-level detection of narcotics.[2]

This study explores the compatibility of SERS substrates bought from Nikalyte with the Resolve Raman spectrometer to detect fentanyl analogs at a range of concentrations in street drug samples. A small selection of fentanyl analogs and other drug-related materials were analyzed using the SERS technique. From this data, the Agilent Command Fleet Management software was used to build a custom Resolve library of SERS narcotics spectra. This custom-built library was then used to identify fentanyl analogs in a range of street samples.

Experimental

Workflow

Figure 1 shows the overall workflow for the trace analysis of narcotics using the Resolve handheld Raman analyzer. The process is the same as a standard library creation workflow, with the addition of the SERS substrates that were used to enhance the Raman signal from low concentration samples. To create a library for a target set of chemicals, suitable materials (preferably certified standards or samples of confirmed composition) are measured with the portable Resolve analyzer. The data is exported via a USB to a PC installed with Command Management software. Once Command has created the custom library, the library file is then loaded onto the Resolve analyzer (or deployed to a fleet of analyzers), ready for the identification of unknown samples.

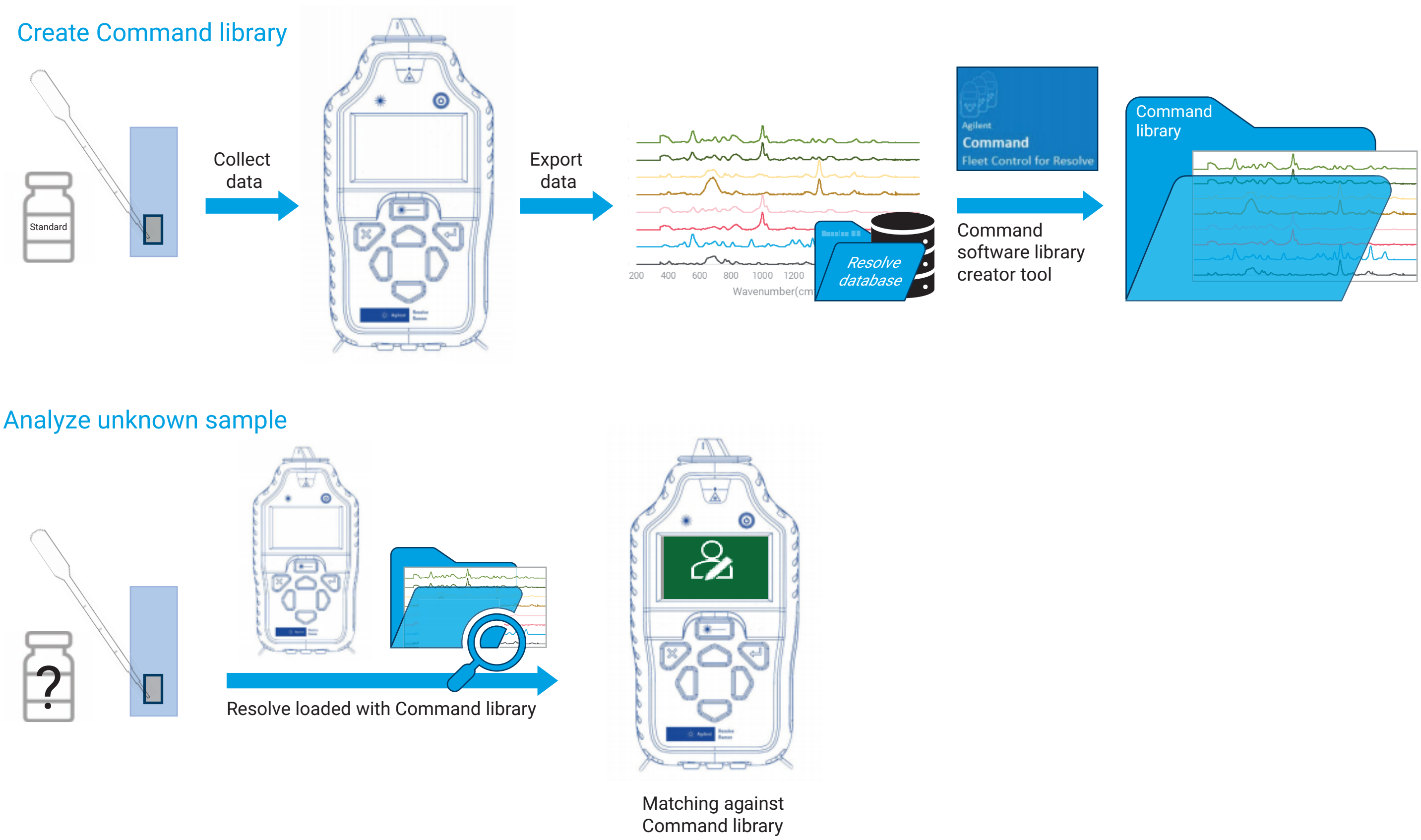

Figure 1. Method for trace detection of compounds using SERS substrates with the Agilent Resolve Raman spectrometer through library creation and deployment using the Agilent Command Fleet Management software.

SERS substrate

Gold nanoparticle SERS substrate slides were used for all SERS trace experiments (Nikalyte Ltd, Bicester, UK).

The substrates were selected as gold nanoparticles are expected to produce a stronger Raman signal with the 830 nm laser used by Resolve. Nikalyte Ltd worked with Agilent to develop these substrates for use on the Resolve analyzer.

Figure 2. Nikalyte gold SERS substrates used to enhance the sensitivity of the Agilent Resolve handheld Raman analyzer. Photo courtesy of Nikalyte Ltd, https://www.nikalyte.com/sers-substrates.

Standards and samples

Eleven narcotic certified standards were used to build the custom Command library for fentanyl compounds. The standards included: lorazepam, nimetazepam, heroin HCl, phencyclidine HCl (PCP), 3, 4-methylenedioxyamphetamine HCl, DL-methylamphetamine, DL-amphetamine, fentanyl HCl, alfentanil HCl, remifentanil HCl, and acetylfentanyl.

The Command-generated library was tested using the Resolve to analyze street samples containing fentanyl analogs at a range of concentrations from 0.26 to 40% and with varied compositions (Table 1). The composition of the street samples had been verified by paper spray mass spectrometry.

Collecting SERS spectra of narcotic standards and samples

Solutions of the 11 certified standard narcotics were prepared at 1 mg/mL in de-ionized water. Solutions of the street samples were prepared by dissolving 3 to 5 µg of the drug sample in 3 mL of distilled water.

For analysis of both standards and samples, 14 µL of each solution was slowly added to the bottom corner of the nanoparticle pad on a Nikalyte slide using a pipette (Figure 3A). Care was taken not to oversaturate the pad. The loaded nanoparticle pad was positioned in front of the Resolve nose cone (Figure 3B). Three continuous measurements were collected using the glass vial setting and the highest laser power setting of 475 mW. To ensure the generation of robust reference and sample spectra, the process was repeated using three separate Nikalyte glass slides for each narcotic standard and sample.

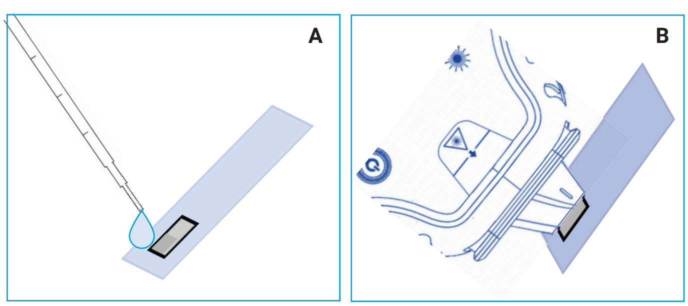

Figure 3. Illustration of loading a sample onto a SERS substrate (A) and alignment of the loaded nanoparticle pad with the nose cone of the Agilent Resolve handheld Raman analyzer (B).

Creating a command library

A custom library was made using the "Library Build Functions" in the Command Fleet Management software. Scans corresponding to each measured item were averaged to make a robust library entry using the "Add library Item" option in the software. The name of the chemical, hazard class, and any further information was logged in the metadata screen before the chemical entry was complete. Once this process had been repeated for each standard material, the library items were compiled into a library labeled as SERS Narcotics, using the "Build Library" option.

The Command-made custom SERS Narcotics library was then exported and loaded on to a Resolve analyzer. The Command library was set as "Matchable" on the Resolve handset, making it available for spectral matching of Resolve measurements of "unknown" fentanyl compounds.

Instrumentation

Two Resolve Raman spectrometers were used in this study. One of the instruments was used at TICTAC Communications in London, UK, to collect the SERS reference spectra listed in Figure 4. The spectra were used to create a Command custom library. The library was installed on a second Resolve analyzer, which was then used at various North American sites to collect standard Raman and SERS spectra of the street samples listed in Table 1.

Results and discussion

Building a SERS library

The 11 narcotic certified standards were used to build the SERS Narcotics custom library. The standards included a few fentanyls, plus narcotics likely to be found alongside fentanyls in street samples and which may share spectral features. The SERS spectra of each material were collected in triplicate with the Resolve analyzer. An averaged spectrum for each sample is shown in Figure 4. All fentanyl analogs show the typical peak at around 1,000 cm^{-1} with small variations in the rest of the spectrum. Noticeably, the 1,000 cm^{-1} peak is also prominent in the amphetamine samples, making them a risk item for false alarms in the trace detection of fentanyls using spectroscopic techniques.

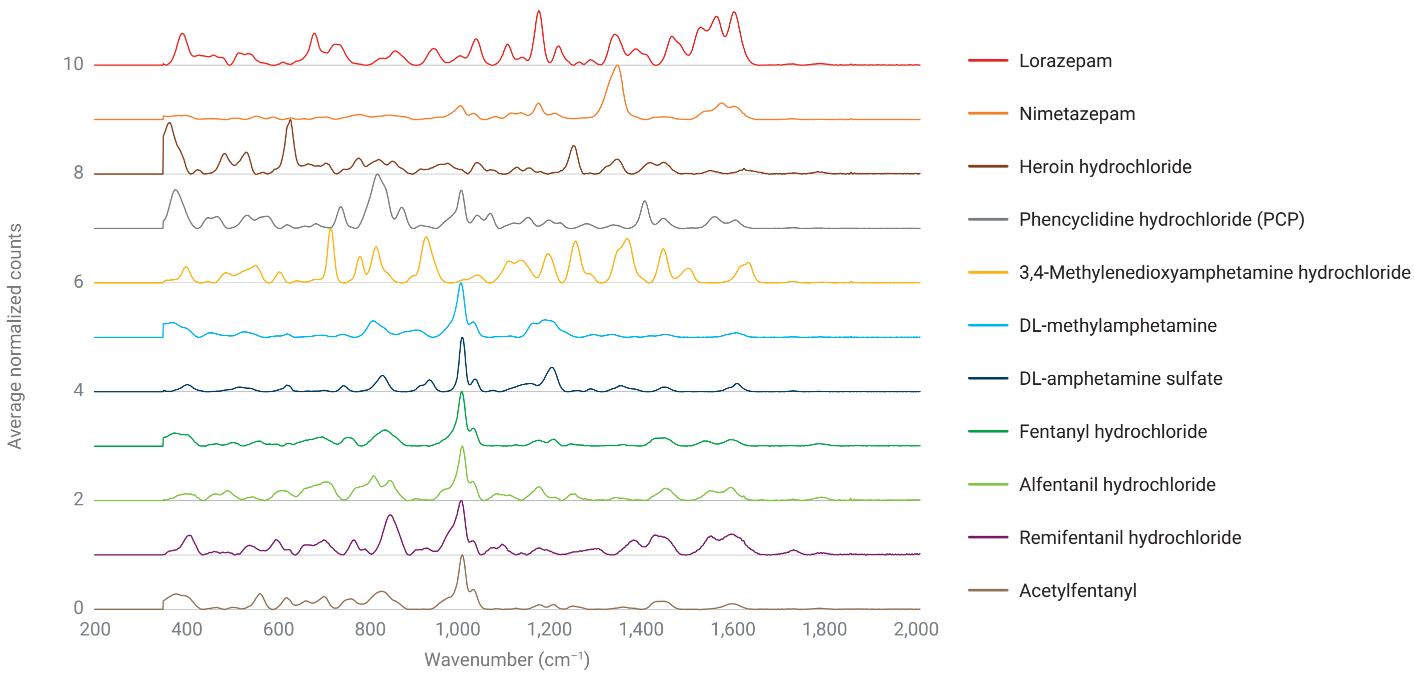

Figure 4. Averaged normalized spectra of the 11 narcotic certified standards used to build the SERS library.

Identification of fentanyls in street samples using the Command-built library

A selection of street samples with fentanyl concentrations ranging from 0.26 to 40% (Table 1) were used in this study. First, the samples were measured directly, without the SERS enhancement, to determine if the standard Raman signal could identify the presence of fentanyl analogs. Only sample 20, with 40% content of fentanyl in the mixture, was identified correctly using standard Raman.

The samples were reanalyzed using the SERS workflow and the spectra were matched against the newly created Command SERS Narcotics library. Only the Command SERS library was used for matching (all standard Agilent libraries were switched off). The SERS technique detected fentanyl analogs in 12 out of the 20 samples, as shown graphically in Figure 5. In most cases of correct fentanyl detection, the system mostly reported the fentanyl HCl variant.

The addition of a set of cutting agents and other drugs that are commonly found in fentanyl-based street samples to the SERS library would further improve the detection performance of the Resolve.

Table 1. List of street samples containing fentanyl and the Raman and SERS fentanyl identification results.

Sample	Composition	Result	
		Raman	SERS
1	0.26% Fentanyl, 99% caffeine	×	×
2	0.5% Carfentanil, 99% xylitol, 0.14% ANPP	×	✓
3	0.5% Fentanyl, 99% caffeine	×	✓
4	0.55% Fentanyl, 99.5% caffeine	×	×
5	0.44% Fentanyl, 0.23% carfentanil, 32% heroin, 4% etizolam, 60% caffeine	×	×
6	0.12% Fentanyl, 0.43% carfentanil, 0.23% ANPP, 50% caffeine, 49% xylitol	×	×
7	1.6% Fentanyl, 64% etizolam, 34% caffeine, 0.4% erythritol	×	×
8	0.61% Fentanyl, 50% caffeine, 49% erythritol	×	✓
9	0.25% Fentanyl, 0.4% carfentanil, 0.5% Heroin, 2% etizolam, 96% caffeine	×	×
10	1.52% Fentanyl, 0.29% carfentanil, 0.47% ANPP, 0.1% erythritol, 98% caffeine	×	✓
11	1.7% Fentanyl, 0.13% carfentanil, 58% caffeine, 40% erythritol	×	✓
12	2% Fentanyl, 98% caffeine	×	✓
13	4% Fentanyl, 96% caffeine	×	×
14	6.82% Fentanyl, 0.11% etizolam, 0.15% flualprazolam, 90% caffeine	×	✓
15	7.54% Fentanyl, 0.11% etizolam, 2% mannitol, 90% caffeine	×	✓
16	7.85% Fentanyl, 5.7% cocaine, 44% caffeine, 44% erythritol	×	✓
17	11.8% Fentanyl, 19.2% etizolam, 60% caffeine, 20% sugar	×	×
18	12.6% Fentanyl, 3% fluorofentanyl, 2.9% etizolam, 80% caffeine	×	✓
19	13.7% Fentanyl, 3.98% xylazine, 1.64% etizolam, 0.31% alprazolam, 80% caffeine	×	✓
20	40% Fentanyl, 60% caffeine	✓	✓

In a final test, 13 street drug items containing no fentanyl were analyzed using the Resolve with SERS to determine if any samples would produce false positive results. A false fentanyl reading was seen for two samples containing methamphetamine and cocaine, showing, as previously indicated, that some materials can be misidentified as fentanyl with the SERS technique. Building a more robust SERS library based on typically found materials and mixtures would improve the accuracy of the Resolve.

Conclusion

The study has shown that the Agilent Resolve handheld Raman spectrometer can be used as part of a SERS workflow to detect low concentrations of fentanyl compounds in street narcotics.

The Agilent Command Fleet Management software is a powerful addition to Resolve, allowing users to create their own detection libraries to deploy on any Resolve analyzer. The use of gold SERS substrates and the Command-created SERS library improved the correct detection of fentanyl in street samples from 5 to 60%, compared to a non-SERS method.

To maximize the performance of the SERS technique and reduce the number of false alarms, a more robust SERS Command library is needed. As outlined in this paper, a custom library that is built on a more comprehensive selection of materials (including cutting agents and commonly observed drugs) can be easily created and deployed.

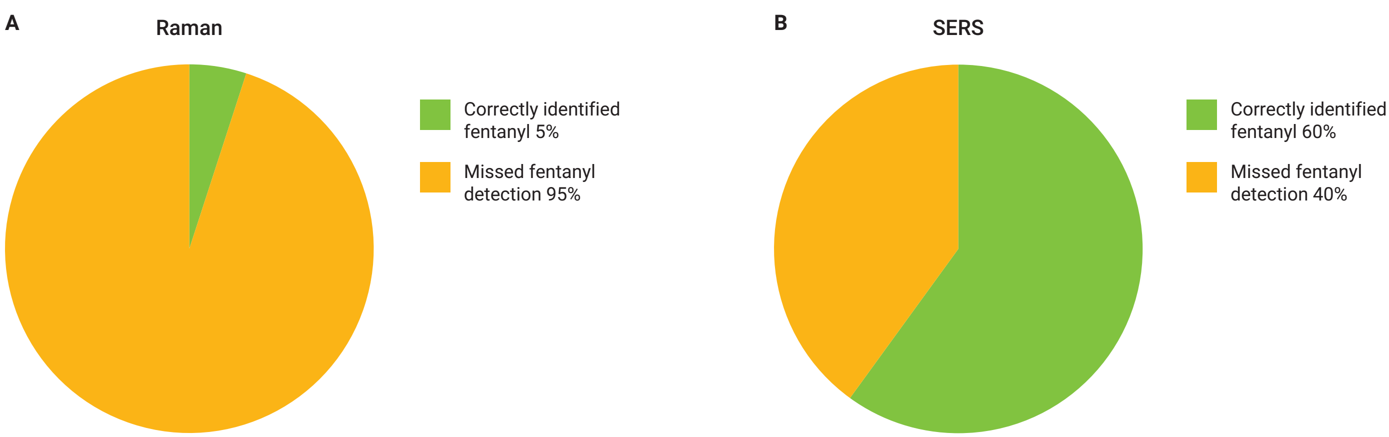

Figure 5. Comparison of fentanyl detection in a range of street samples using standard Raman (A) versus the SERS technique using the Command-built SERS library (B).

References

1. Jones, C. M. *et al.* The Evolving Overdose Epidemic: Synthetic Opioids and Rising Stimulant-Related Harms. *Epidemiol. Rev.* **2020**, *42(1)*, 154-166. doi:10.1093/epirev/mxaa011
2. Smith, M. A Semi-Quantitative Method for the Detection of Fentanyl Using Surface-Enhanced Raman Scattering (SERS) with a Handheld Raman Instrument. *J. Forensic Sci.* **2021**, *66(2)*, 505–519. doi: 10.1111/1556-4029.14610

Further information

Resolve Handheld Raman Analyzer

Command Fleet Management Software

Resolve Handheld Raman Analyzer FAQs

Raman Spectroscopy FAQs

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