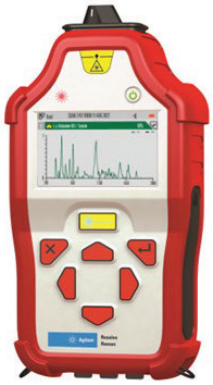
Application Note

Drugs

Direct Identification of Street Drugs using an Agilent Resolve Handheld Raman Analyzer

Identification of drug samples directly through the wrapping without decanting



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Abstract

The Agilent Resolve handheld Raman analyzer uses traditional Raman and spatially offset Raman spectroscopy (SORS) through-barrier Raman techniques to probe the contents of wrapped or contained materials. No sample preparation is required, enabling fast, remote analysis of samples.

The Resolve analyzer was used to analyze 42 wrapped drug samples that had been seized, surrendered, or confiscated. The various samples were analyzed either in traditional surface mode or SORS through-barrier mode. All samples yielded excellent matches to known compounds in the onboard spectral reference library. All but two samples contained significant narcotic content. Twenty-one samples were identified as ketamine, eleven as cocaine, eight as MDMA, and two as caffeine. All samples were examined in their native wrapper, with or without an outer evidence bag. Leaving the original packaging in place protected the operator from any potential inhalation or contact hazards when handling the samples.

To further investigate the selectivity and sensitivity of the Resolve analyzer, the spectra of the 42 samples were analyzed by Principal Components Analysis (PCA). PCA can reveal any inter and intra narcotic class variance relationships and distributions. Narcotic class separation using the spectral data was clearly achieved and the potential for quantitative analysis was also indicated by the intra-sample spread patterns. The spectral dataset was extracted using the Agilent Command software fleet management tool for Resolve and then examined and analyzed using Agilent MicroLab Expert spectroscopic software.

Introduction

According to a recent United Nations report, drug use remains high worldwide. An estimated 5.8% of the global population aged between 15 and 64 used a drug during 2021.[1] In the European Union, cannabis, cocaine, and 3,4-methylenedioxymethamphetamine (MDMA, also known as ecstasy) are the most widely used recreational drugs.[2]

Analysts can use a wide variety of techniques to identify illicit drugs, ranging from portable GC/MS and spectroscopic methods to colorimetric single-use targeted compound tests. All hyphenated techniques and some lab-based spectroscopic require sample preparation, power supply, technical ability, and a safe place to operate. However, battery operated portable spectroscopic instruments[3,4] with on-board spectral libraries and simplified workflows have simplified the analysis of recreational drugs in the field. Instruments such as the Agilent Resolve handheld Raman analyzer can be operated by non-expert users, leading to its widespread adoption by law enforcement and border control agents.

The Resolve analyzer can be used to test a sample in conventional surface or Spatially Offset Raman Spectroscopy (SORS) through-barrier modes (Figure 1). Conventional Raman spectroscopy involves illuminating a sample with a laser followed by the detection of the scattered light whereas SORS through-barrier mode uses multiple measurements to probe the subsurface of a sample.[5] SORS often allows materials to be identified inside sealed, thick, colored, and opaque containers, which is not achievable using conventional surface mode Raman spectroscopy.

To identify the sample, the acquired Raman spectrum is compared with reference spectra of compounds in various onboard spectral libraries. The comparison is performed automatically by the Agilent Raman Resolve software and the libraries are regularly updated to cover novel psychoactive substances (NPS), cutting agents, and precursors. Users can also create, manage, and deploy their own spectral libraries. Agilent also provides a reachback service for users who have any data queries. These queries are answered by Agilent experts. The service can be accessed online with a few simple steps.

To analyze the content of a suspect package using most analytical techniques, it would be necessary to take a small subsample from the package. In contrast, the Resolve analyzer can directly measure samples through clear to semi-opaque materials in conventional surface scan mode. This mode is called “Clear bag or None” in the software (Figure 1). Samples behind thicker barriers can be analyzed in SORS mode, which is called “Thick, Colored or Opaque” in the software (Figure 1).

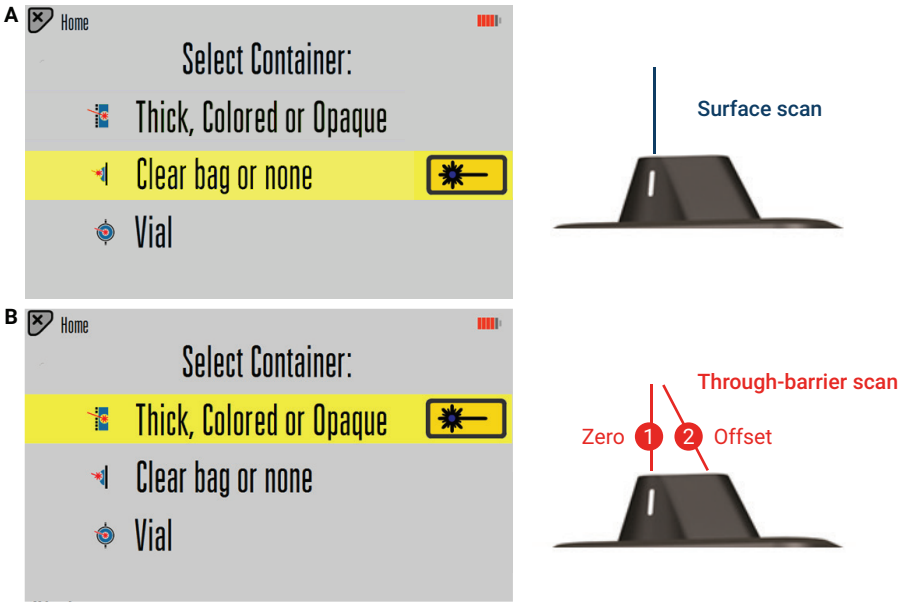

Figure 1. Agilent Raman Resolve software screen showing how to conduct a surface scan by selecting "Clear bag or none" mode (A). Resolve software screen showing how to conduct a SORS/through-barrier scan by selecting "Thick, Colored or Opaque" mode (B). The 830 nm laser is an invisible NIR laser and the blue and red colors are used for illustration purposes only.

In this study, 42 samples that were either seized or surrendered at a large European social event were analyzed using the Resolve handheld Raman analyzer. All suspect powder samples were contained in low-density polyethylene (LDPE) zip lock bags, paper, or plastic wrap (cellophane). The samples were all correctly identified without the need to open any of the packages, demonstrating the high selectivity of the Resolve analyzer. The data was also examined by Principal Components Analysis (PCA) to mathematically illustrate the clustering of each sample per class of drug.

Experimental

Instrumentation

The Resolve handheld Raman analyzer is a flexible spectrometer that is widely used for the identification of chemicals, including hazardous materials. Details of the instrument and its key attributes are outlined in Figure 2.

The Resolve analyzer was used to identify 42 samples in surface and SORS through-barrier modes. The data was exported to a PC installed with Agilent MicroLab Expert spectral analysis software via a USB using the optional Agilent Command Resolve fleet management software designed for fleet management. The Command software can be used to create and manage libraries on a single or multiple (a fleet of) Resolve instruments. It can also export the spectra in the spectroscopic .spc format, spreadsheet compatible .csv format, or .pdf portable document format (PDF). The PDF file contains all instrumental details, scan details, graph of the suspect/query scan, and match results.

The results for the 42 samples were exported to the MicroLab Expert spectral analysis software as .spc files for statistical analysis by Principal Component Analysis (PCA). PCA is a Multivariate Analysis (MVA) technique.

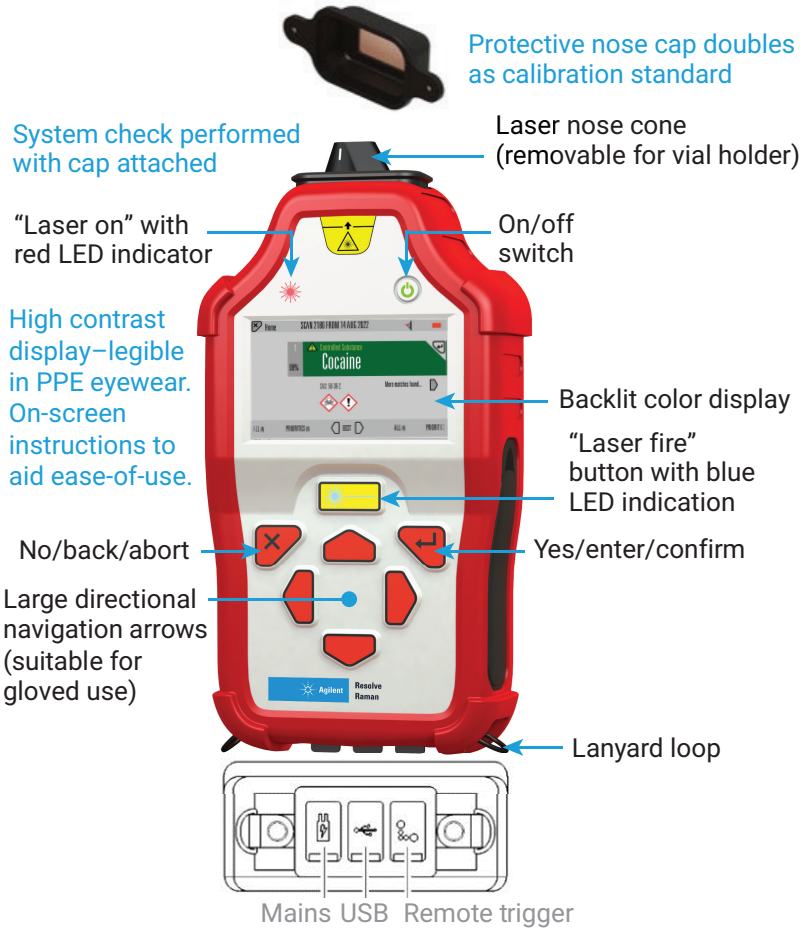

Figure 2. Overview of the Agilent Resolve handheld Raman analyzer.

Key attributes

- Choice of modes
  - Surface (conventional)
  - SORS (through-barrier)
  - Vial
  - Stand off (non-contact)
- Low power consumption
- Built-in libraries
  - Updated regularly
- User custom library options
  - Easy addition of spectra
  - Shock-resistant and IP67
- 830 nm Class 3B laser
- Auto-scheduled system checks
- On-screen guidance
- Reachback contact service to Agilent for queries

Samples

The seized suspect samples comprised powdered samples that were contained in a zip lock bag, plastic wrap, or paper. Most of the 42 suspect samples were further contained within an evidence bag. Sample contents varied from 2 to 5 g and were white to off-white powders with many grain sizes and shapes.

Workflow

The data collection to PCA analysis workflow is outlined in Figure 3. The Resolve analyzer was used to collect the data for each sample. The results were then exported as a database to a PC via a USB. The Command software was used to open the database, locate the relevant files, and export the data set as .spc file format to the MicroLab Expert software. The MicroLab Expert software was used to create an MVA-PCA model using project and modeling tools. The model can be saved for classification of future samples.

Results and discussion

Narcotics identification through original wrappers

All 42 samples were measured as provided (in their original wrapping and most inside an evidence bag, adding an extra layer) using the Resolve analyzer. Conventional mode was used for samples in clear packaging (most samples) and SORS through-barrier mode was used for the small number of samples in opaque packaging. A summary of the onscreen results by category (ketamine, cocaine, MDMA, or caffeine) is shown in Figure 4.

The high match scores obtained for ketamine, cocaine, and MDMA negated the need for secondary analysis. If either the sample was large and/or prosecution was being considered, a secondary confirmatory technique would be requested.

Figure 3. Workflow for the PCA analysis of the 42 suspected drug samples.

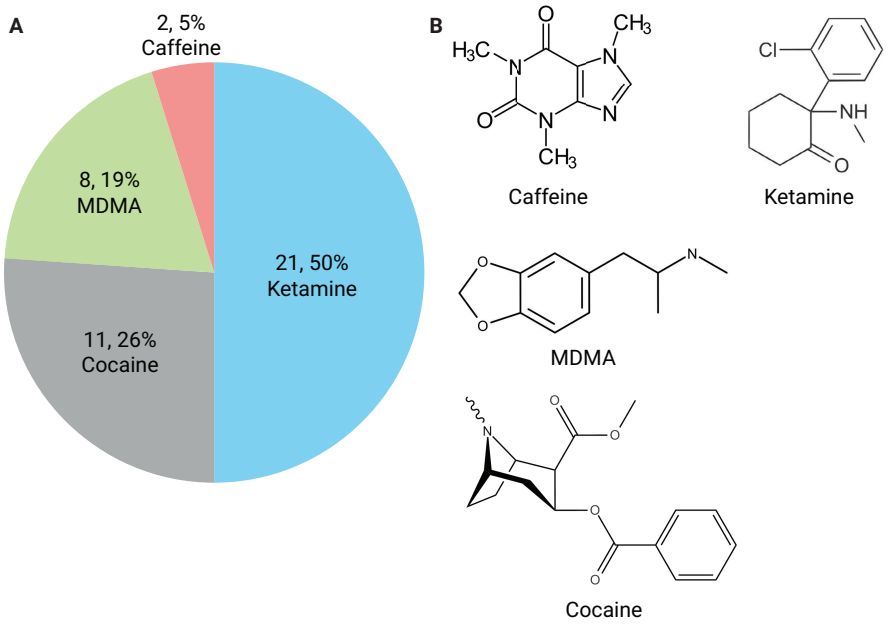

Figure 4. (A) Pie chart showing the identity of the 42 samples as a number and percentage. (B) Base chemical structures of caffeine, ketamine, MDMA, and cocaine.

Figure 5 shows a typical Resolve analyzer screenshot following the analysis of one of the drug samples. The software displays the best match for the sample compared to the reference spectra from the instrument's standard library (ketamine HCl + taurine in the example) and a percentage confidence value of the match (96% in this case). Taurine is a common cutting agent. Cutting agents are adulterants that are deliberately added to illegal drugs to increase their volume.

By pressing the right arrow button on the pad, all the best matches that meet the threshold (% match) criteria are shown (Figure 5B). The spectral match for any of the user adjustable threshold criteria can be seen on the screen by highlighting and pressing the return button (↵). The software displays the spectrum for the best library match in black and the spectrum for the sample in green (Figure 5C). When the spectral match is excellent, the green (sample) scan line takes precedence, as shown in the example.

The spectra acquired by the Resolve analyzer following the analysis of some of the other samples are shown in Figure 6. The match quality of the scans was excellent, ranging from 93 to 99%. Some of the samples were relatively pure, some were a mixture of narcotic with a single cutting agent, and some had been adulterated or mixed (cut) with other substances, e.g., caffeine and ketamine.

Optional statistical data analysis

If more analytical information is needed, highly detailed spectra and spectral features relating to each sample can be viewed in more detail in the Command Raman Resolve software. The software can also be used to export the spectra to MicroLab Expert for further analysis using MVA techniques.

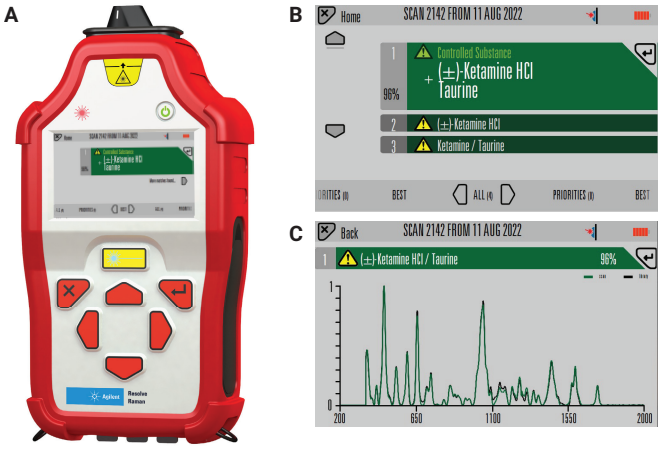

Figure 5. (A) The primary best match result for a mixture of ketamine HCl + taurine is shown on the screen of the Agilent Resolve handheld Raman analyzer. (B) Three matches meeting the search criteria. (C) Best match result (ketamine HCl/taurine), Raman scan in green, and composite library match scan in black. The green sample scan takes precedence over the black library scan when the two spectra are highly similar (high % match).

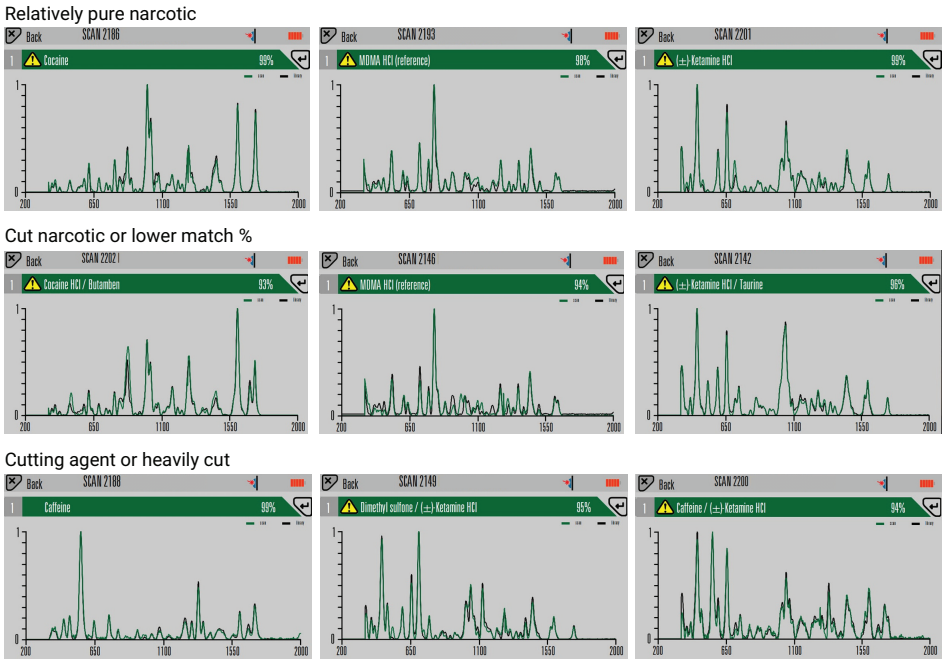

Figure 6. Agilent Resolve handheld Raman analyzer best match scans and their corresponding match % score together with their spectral scan and library match. Top row: High match %, suggesting high purity drug. Middle row: Cut (mixed) or lower purity drugs. Bottom row: Cutting agent or heavily cut narcotic. All samples >93% match. Note for the heavily cut samples, the cutting agent is named first in the mixture.

Figure 7 shows stacked plots of each sample by group (caffeine, ketamine, MDMA, and cocaine), all Raman active compounds. Their chemical structures are highly distinct from each other. Notably, the benzene ring of cocaine, ketamine, and MDMA, is affected strongly by its chemical surroundings and is shifted (positively or negatively) depending on the attached groups. For cocaine, the benzene ring is detected at ~1,000 cm^{-1}. In ketamine, the chloride group on the benzene ring shifts the peak to ~1,100 cm^{-1}. For MDMA, the benzene ring is connected to a methylenedioxy group (see Figure 4), which causes the peak to shift to ~800 cm^{-1}. The chemical structure of caffeine consists of a heterocyclic ring system, not a benzene ring, as shown in Figure 4. Heterocyclic rings do not absorb highly in the region of 800 to 1,100 cm^{-1}.

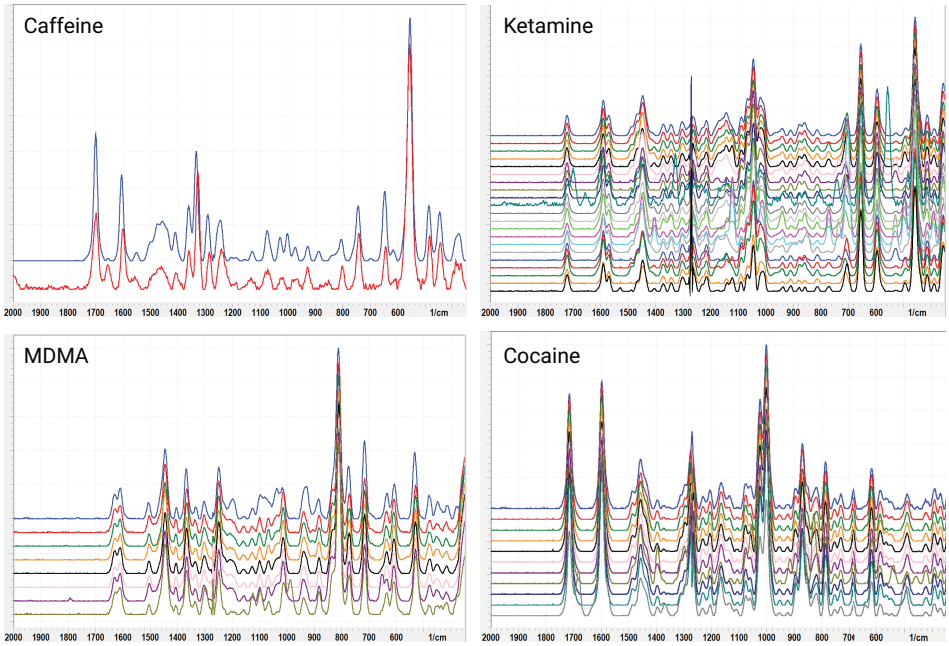

Figure 7. Agilent Resolve handheld Raman analyzer spectra for the four classes of compounds identified in this study, with each sample grouped into by its class (caffeine, ketamine, MDMA, or cocaine). The results are ordered by quality of match %, from best match at the top (shown in blue in each class) to the spectra with lowest match % at the bottom.

Multivariate data analysis

The Resolve analyzer spectral data sets were analyzed using PCA, a multivariate data analysis method within the MicroLab Expert software. The technique is useful for the analysis of high-density data sets such as spectra, where there is no Y quantifiable value or attribute. In this PCA analysis, the spectra were grouped into four classes, as shown in Figures 4 and 7. Figure 8 displays the 3D scores plot of the PCA analysis of the 42 sample spectra produced by the MicroLab Expert software. Factors 1, 2, and 3 in the graph are also called principal components 1, 2, and 3 (principal components are typically abbreviated to PC1, PC2, and PC3 in other data analysis software).

PCA analysis is often used as a means to interrogate variable-rich data like spectral data (Raman spectra) to elucidate the clustering within a group or class, and also the distances between classes and related compounds in the K-dimensional space. Spectra that share similar spectral characteristics will group closely in the PCA scores plots and PCA will often highlight any outliers, such as misidentified samples, misclassed sample spectra, diluted samples, and potentially altered samples.

In the PCA algorithm, every data point is considered a variable and projected into a dimension referred to as K-space. The primary aim is to attempt to explain the variance in a reasonable number of factors (principal components).[6] The five factors of the model explain 50.5, 29.7, 9.3, 4.3, and 2.7% of the variance, respectively (a total of 96.5%). For visual interpretation, Figure 8 shows the Resolve analyzer match results, scan number, and the corresponding 3D scores plot for the first three principal components. Note that PCA is an iterative algorithm, where each factor typically mathematically reduces the amount of available variance it can explain. Therefore, during each pass of the algorithm, the explained variance tends to be higher in the first pass compared to subsequent passes.

The ketamine class (shown in blue) has the highest number of related spectral library matches and the highest compositional diversity. Some of the samples indicated by the bold scan number have been labeled in the plot to highlight their scores distance from the main clustered group. Although sample 2,200 was assigned to ketamine based on partially containing ketamine, the Resolve analyzer reported that the sample contained more caffeine spectral characteristics than ketamine (94% caffeine and ketamine HCl). Therefore, ketamine scan number 2,200 was expected to be the furthest score distance from the main ketamine matches. The scores plot confirms that this ketamine sample had been significantly diluted with caffeine.

The clustering of the all the cocaine samples, except for scan 2,202, represents samples that had a high spectral match to cocaine. Sample 2,202 was the only mixture-matched drug in its

Scan No.	Resolve Match
2,147	100% Cocaine
2,138	99% Cocaine
2,158	99% Cocaine
2,173	99% Cocaine
2,181	99% Cocaine
2,186	99% Cocaine
2,191	99% Cocaine
2,156	99% Cocaine
2,159	99% Cocaine
2,167	96% Cocaine
2,202	**93% Cocaine HCl + butamben**
2,188	99% Caffeine
2,165	93% Caffeine
2,143	100% (±)-Ketamine HCl
2,148	100% (±)-Ketamine HCl
2,157	100% (±)-Ketamine HCl
2,145	99% (±)-Ketamine HCl
2,154	99% (±)-Ketamine HCl
2,199	99% (±)-Ketamine HCl
2,201	99% (±)-Ketamine HCl
2,139	98% (±)-Ketamine HCl
2,190	98% (±)-Ketamine HCl
2,194	98% (±)-Ketamine HCl
2,183	97% (±)-Ketamine HCl
2,142	**96% (±)-Ketamine HCl, taurine**
2,170	96% (±)-Ketamine HCl
2,184	96% (±)-Ketamine HCl
2,166	94% (±)-Ketamine HCl
2,172	**92% Ketamine**
2,171	**91% Ketamine**
2,189	**91% (±)-Ketamine HCl**
2,149	**95% Dimethyl sulfone, (±)-ketamine HCl**
2,168	**95% Dimethyl sulfone, (±)-ketamine HCl**
2,200	**94% Caffeine + (±)-ketamine HCl**
2,193	98% MDMA HCl
2,141	96% MDMA HCl
2,153	96% MDMA HCl
2,155	96% MDMA HCl
2,197	96% MDMA HCl
2,140	95% MDMA HCl
2,179	95% MDMA HCl
2,146	**94% MDMA HCl**

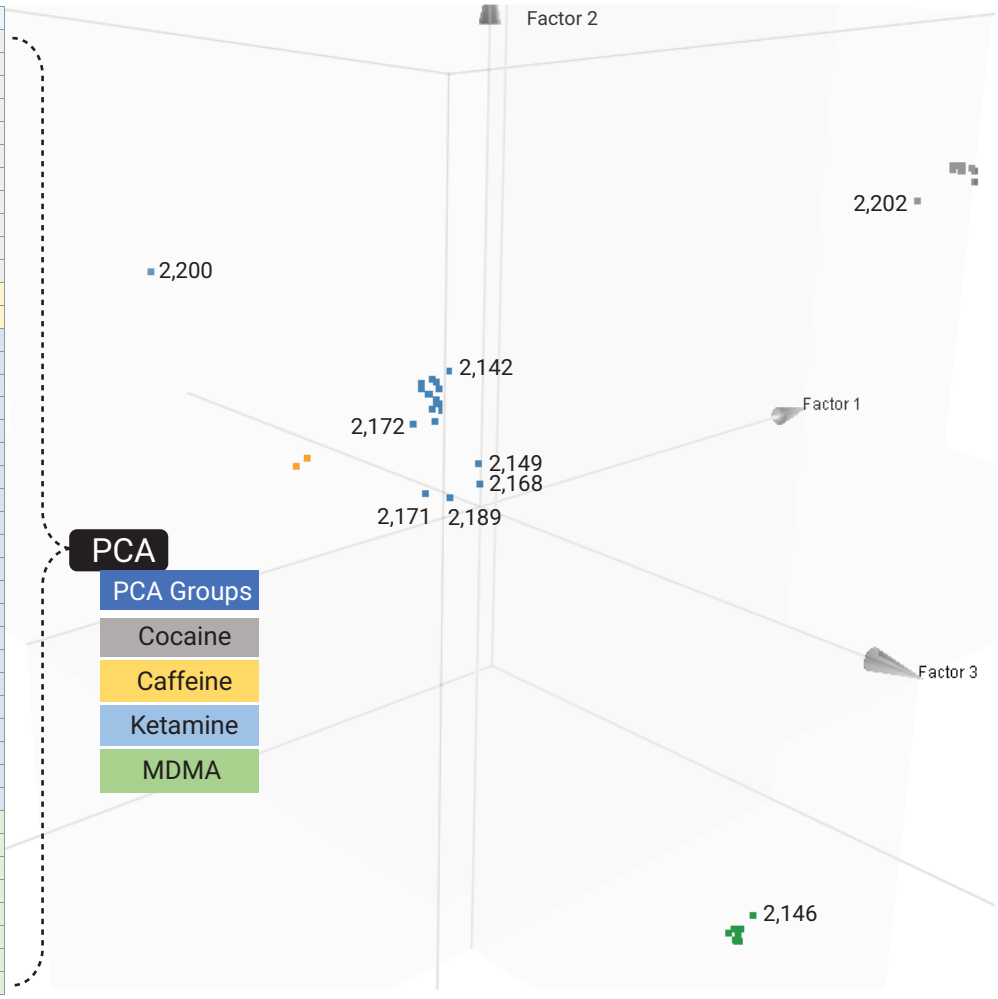

Figure 8. 3D scores plot for first three factors (principal components) of the 42 narcotic samples. The model spectra were grouped as ketamine (blue), cocaine (grey), MDMA (green), and caffeine (yellow). The scan numbers shown in the table in bold have been identified in the plot. All emboldened samples and scan numbers have been cut and diluted.

class, with a 93% match to cocaine and butamben, a known cutting agent, which explains its distance from the group of single compound-matched samples (shown in grey). The lowest spectral match for MDMA (scan 2,146) also sits outside the main MDMA group cluster (shown in green).

The excellent separation of both interclass and intraclass signifies that, with suitable standards, quantitative models can be built using the Resolve analyzer data. Also, the degree of separation of each class of drug graphically demonstrates the high degree of selectivity inherent in the Raman spectra of the Resolve analyzer. The clear separation within each class of drug based on the library match % of the Raman spectra demonstrates the sensitivity of the Resolve analyzer.

Conclusion

The Agilent Raman Resolve analyzer identified 42 suspected drug samples seized at a live music event using the instrument's standard option spectral library containing ~1,100 Raman spectra. All the spectral acquisitions were performed without opening or unzipping the sample bags or removing the wrapping, ensuring the safety of the operator.

If more information is needed, the data can be exported to a PC via USB. Agilent Command software can then be used to show more spectral detail for the samples. Statistical analysis software within Agilent MicroLab Expert software can be used to perform multivariate Principal Component Analysis (MVA-PCA) analysis of the data set.

The PCA analysis successfully separated the spectra of the cocaine, ketamine, MDMA, and caffeine samples, indicating that their spectral characteristics are distinguishable. Also, the analysis identified certain outlier results, which were expected based on the Resolve match data. PCA score plots can highlight trends, which could be used for intelligence gathering.

With suitable standards and further model training, the PCA data reported in this work has shown potential for the quantitative modeling of cocaine, ketamine, MDMA, and caffeine.

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