Identification of new psychoactive substances (NPS) by Raman spectroscopy

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Abstract
There is an increasing need of developing methods for fast recognition and identification of new psychoactive substances (NPS). The chemical identification of these new substances produced with the intention of mimicking the effects of controlled drugs is a challenge for forensic and Customs laboratories. In this study, we aim to test the potential of Raman spectroscopy for the identification and classification of seized Customs samples into three NPS families. The performance of two excitation wavelength lasers (785 and 1064 nm) in a benchtop Raman instrument was compared in a set of seized samples that included cathinone, fentanyl, and synthetic cannabinoid derivatives or analogues. The 1064 nm wavelength laser had significant advantages for identifying NPS samples overcoming the intense fluorescence induced when using 785 nm lasers in some substances. Principal component analysis was employed to create a model that successfully discriminates the three NPS families. In order to provide Customs officers with a fast and nondestructive in-field testing method, the same approach used with the benchtop Raman spectrometer was applied using three handheld Raman instruments. The developed identification and classification model allows the discrimination of fentanyl, cathinone, and synthetic cannabinoid analogues or derivatives providing an efficient tool for the rapid identification of three NPS families. The approach presented in this study can facilitate rapid decision-making that could be of high relevance especially in the frame of the fentanyl crisis.

KEYWORDS
chemometrics, fentanyl, handheld Raman spectroscopy, new psychoactive substances (NPS)

1 | INTRODUCTION

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has defined new psychoactive substances (NPS) as “a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by...
substances listed in these conventions."[1] The consumption of these NPS is growing continuously; new molecules appear constantly on the illegal market, hence mimicking controlled and regulated illicit pharmacological substances.[2–5] A continuous increase of NPS on the illicit market is observed. From 2014 to 2015, a 25% increase was reported to the EMCDDA, and since 2016, more than 700 NPS have been reported in about 100 countries.[1,5,6] The threat to public health tends to be more severe because those substances are used for recreational purposes with their toxicity level often unknown and their control is cumbersome.[5] Moreover, they are usually mixtures of drugs, including cutting agents or impurities making their identification or classification more complicated, and they are frequently modified in order to replace the banned ones.[5,7]

In the NPS family, there is a wide diversity of substances, including among others, piperazines, synthetic cannabinoids, opioids, benzofurans, and cathinones.[3,4] Among the compounds monitored by the EMCDDA, the most abundant families of NPS are synthetic cannabinoids and cathinones. Synthetic cannabinoids are the largest group of substances currently monitored in Europe by the EMCDDA (at least 14 chemical families).[1] They are usually sold as smoking herbs that gives the consumer the impression of smoking a natural product.[4] Cathinones appeared on the market at the beginning of 2000, replacing amphetamines and methamphetamines and are usually known as “bath salts.”[4]

The consumption of the opioid related-fentanyl has risen in recent years.[4,8] Fentanyl is the most potent synthetic opioid analgesic drug used by humans and that has a high risk of dependency.[1] It has 100 times the potency of morphine, and a few analogues are approved for human use: sufentanil, alfentanil, and remifentanil. One of its analogues, carfentanil, is estimated to have 10,000 times the potency of morphine and is only used to treat animals.[8] Moreover, the ease of getting ingredients on the Internet, finding videos of manufacturing, and illegal importations have given rise to the current fentanyl crisis.[8]

These three families of substances were selected in this study because there is an urgent need of developing a fast, nondestructive, and cheap analytical method for their detection in the field due to the considerable harms and risks they can produce. Raman spectroscopy has been chosen for this purpose because it has been demonstrated to be a very valuable technique to discriminate NPS.[2,6,7,9–12] Moreover, as mentioned by Zloh et al.[5] it is essential to explore effective ways of identifying and classifying existing and emerging NPS.

Raman spectroscopy has the advantage of noncontact, nondestructive measurements through glass or plastic, enhancing the speed of the analysis and reducing the exposure of operators. Usually, these handheld devices also include spectral identity software to facilitate the “in situ” application. Handheld devices provide the user with many advantages as they can be easily used in the field; the sample can be measured through the container (transparent packaging, plastic bag, amber or clear glass vials, plastic bottles, etc.)[13] that prevents or reduces sample preparation or cross-contamination and can give a fast identification of an unknown compound if it already exists in the library.

The main challenge when analysing NPS samples can be the high fluorescence due to impurities.[2] Previous studies that reported on the use of handheld Raman devices equipped with different laser excitation wavelengths for the identification of a range of commercially available NPS recommended the use of 1064 nm systems or dual laser devices (785 and 1064 nm) to achieve sensitive detection with low/no fluorescence[2,11,12] frequently observed when using 785 nm lasers.

In this study, the application of Raman spectroscopy using 785 and 1064 nm lasers for the identification of a set of seized NPS was evaluated by testing its performance using a Fourier-transform (FT) Raman benchtop spectrometer. The study aims at the differentiation of three NPS families: cathinone, synthetic cannabinoid, and fentanyl derivatives or analogues by the application of multivariate analysis and to transfer the developed discriminatory model to Raman handheld devices. In the specific case of fentanyl, the identification of an unknown sample as belonging to the fentanyl’s family could be of high relevance given the ensuing safety concerns following the fentanyl crisis.

2 | EXPERIMENTAL

2.1 | Samples

An NPS sample set consisting of 8 cathinones (C), 12 fentanylys (F), and 10 synthetic cannabinoids (SC) was obtained from EU and Indonesian Customs Laboratories, the Belgian National focal point, the French Police Scientific Laboratory, and from the National Forensic Institute of Slovenia. A few milligrams (<200 mg) of each sample were received in powder form in glass chromatography vials. The compounds were characterized by nuclear magnetic resonance spectroscopy in our premises following the procedure and experimental conditions described in a previous work.[7] The origin and chemical nature of the NPS samples studied in this work are presented in Table 1. The samples have been grouped in three tables (Table 1a–c) according to the family of substances they belong to. The countries where the samples were seized are indicated with their ISO 3166-2 code. The common names and systematic IUPAC names presented in this
| Sample identifier | Country | EDND name            | Systematic IUPAC name                                 | Molecular structure |
|------------------|---------|----------------------|------------------------------------------------------|---------------------|
| **(a) Cathinones** |         |                      |                                                      |                     |
| S1               | BE      | Alpha-PEP or PV8     | 1-phenyl-2-(1-pyrrolidinyl)heptan-1-one              |                     |
| S2               | BE      | 4-Cl-alpha-PVP       | 1-(4-chlorophenyl)-2-(pyrrolidin-1-yl)pentan-1-one   |                     |
| S3               | BE      | 3-CEC                | 1-(3-chlorophenyl)-2-(ethylamino)propan-1-one        |                     |
| S4               | BE      | Propylone            | 1-(1,3-benzodioxol-5-yl)-2-(propylamino)propan-1-one |                     |
| S5               | BE      | 4-CEC                | 1-(4-chlorophenyl)-2-(ethylamino)propan-1-one        |                     |
| S6               | BE      | N-ethylhexedrone     | 2-(ethylamino)-1-phenylhexan-1-one                   |                     |
| S7               | DE      | 4-chloropentedrone   | 1-(4-chlorophenyl)-2-(methylamino)pentan-1-one       |                     |
| S8               | DE      | Alpha-PPP-MeO        | 3-methoxy-1-phenyl-2-(pyrrolidin-1-yl)propan-1-one   |                     |
| **(b) Fentanyls** |         |                      |                                                      |                     |
| S9               | DE      | Furanylfentanyl      | N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]-furan-2-carboxamide | |
| S10              | BE      | Methoxyacetylfentanyl| 2-methoxy-N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl] acetamide | |
| S11              | BE      | Valerylfentanyl      | N-phenyl-N-[1-(2-phenylethyl)-4-piperidyl]pentanamide |                     |
| S12              | SE      | Tetrahydrofuranylfentanyl or THF-F | N-phenyl-N-[1-(2-phenylethyl)]piperidin-4-yl]tetrahydrofuran-2-carboxamide | |
| S13              | FR      | Despropionyl-2-fluoro fentanyl | N-(2-Fluorophenyl)-1-(2-phenylethyl)piperidin-4-amine |                     |

(Continues)
| Sample identifier | Country | EDND name          | Systematic IUPAC name                                                                                                                                                                                                 | Molecular structure |
|-------------------|---------|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| S16               | ID      | Benzoylfentanyl    | \(N\)-phenyl-\(N\)-[1-(2-phenylethyl)piperidin-4-yl]benzamide                                                                                                                                                    |                    |
| S17               | FR      | Methoxyacetylfentanyl citrate | 2-methoxy-\(N\)-phenyl-\(N\)-[1-(2-phenylethyl)piperidin-4-yl]acetamide citrate                                                                                                                                     |                    |
| S18               | FR      | 4-Fluoro-isobutyr fentanyl or 4F-iBF | \(N\)-(4-fluorophenyl)-2-methyl-\(N\)-[1-(2-phenylethyl)piperidin-4-yl]propanamide                                                                                                                                 |                    |
| S19               | FR      | Cyclopropylfentanyl citrate | \(N\)-phenyl-\(N\)-[1-(2-phenylethyl)piperidin-4-yl]cyclopropanecarboxamide citrate                                                                                                                                  |                    |
|                   |         |                    | (c) Synthetic cannabinoids                                                                                                                                                                                                                                                         |                    |
| S21               | BE      | 5F-AMB or 5F-AMB-PINACA | Methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate                                                                                                                                              |                    |
| S22               | BE      | APP-CHMINACA       | \(N\)-(2-amino-1-benzyl-2-oxo-ethyl)-1-(cyclohexylmethyl)indazole-3-carboxamide                                                                                                                                        |                    |
| S23               | BE      | 5F-APP-PINACA      | \(N\)-(2-amino-1-benzyl-2-oxo-ethyl)-1-(5-fluoropentyl)indazole-3-carboxamide                                                                                                                                         |                    |
| S24               | BE      | NM-2201            | Naphthalen-1-yl 1-(5-fluoropentyl)-1H-indol-3-carboxylate                                                                                                                                                             |                    |
| S25               | BE      | 5F-MDMB-PINACA or 5F-ADB | Methyl[2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate]                                                                                                                                       |                    |
The NPS samples were kept in well-sealed glass chromatography vials and measured through the container; therefore, no sample preparation was required. In the cases in which a sample holder was available, the measurements were carried out through the side of the vial, adjusting the focusing of the laser to get the maximum signal; when a sample holder was not available, measurements were carried out through the base of the vial by optimizing the focusing distance accordingly. As each sample was measured in triplicate, between measurements, the sample was vortexed for 10 s at 2,500 rpm (Reax Control, Heidolph, Germany) to assure homogeneity and a new measurement point. Samples were kept in the refrigerator (+4°C).

### 2.2 Spectroscopic instrumentation and analysis

Raman spectra were collected using four different spectrometers at different wavelengths: a Bruker benchtop spectrometer equipped with 785 and 1064 nm lasers and three handheld instruments (a Progeny from Rigaku, a Bravo from Bruker, and Cora 5600 from Anton Paar [each of the employed instruments is described below]).
The main acquisition parameters for a straightforward comparison among the Raman instruments used can be found in Table 2. The 31 samples were measured in triplicate, and the average spectrum was used for further data analysis. Once the spectra were acquired with the different instruments (benchtop and handheld), they were transferred to a PC for the further processing by multivariate analysis as will be explained later.

### 2.2.1 | Vertex II instrument

Benchtop Raman spectroscopy was performed on a Bruker Vertex 70 spectrometer (Bruker, Belgium) equipped with a RAM II module and two laser channels for Raman analysis: the first channel with an integrated air-cooled diode-pumped Nd:YAG excitation laser running at 1064 nm with a liquid N$_2$ cooled ultrahigh sensitivity Ge detector, and the second channel with an integrated air-cooled diode pumped excitation laser at 785 nm and a Si-avalanche diode TE-controlled detector. Both excitation lasers had a maximum power output of 500 mW. The spectra were collected with a Raman shift scanning range of 0–3600 cm$^{-1}$ for the 1064 nm laser and 0–7735 cm$^{-1}$ for the 785 nm laser with a resolution of 2 cm$^{-1}$; 64 scans were averaged for each spectrum with the OPUS software (OPUS, v.7.5., 2014) being used for data acquisition. A daily check was carried out using a performance qualification “PQ” test.

### 2.2.2 | Progeny handheld instrument

A Progeny (Rigaku Analytical Devices, France) equipped with a 1064 nm excitation laser and a TE-cooled InGaAs 512 pixel detector was employed. The recorded spectral range was 200–2500 cm$^{-1}$, with a spectral resolution of 8 cm$^{-1}$, 450 mW power, and 1000 ms acquisition time. Before each measurement, a background was automatically acquired, and a baseline correction was automatically done. A daily check is required prior to its use and is achieved by acquiring the spectrum of a benzonitrile reference standard.

### 2.2.3 | Cora 5600 portable instrument

A dual-wavelength Cora 5600 instrument (Anton Paar, Austria) equipped with a combination of two excitation lasers: 532 and 1064 nm was used. In this study, only the 1064 nm laser was used together with a 256 pixel InGaAs detector. The recorded spectral range was 100–2300 cm$^{-1}$ with a laser power output of 450 mW; the spectral resolution cannot be chosen; the acquisition or exposure time is automatic, hence it depends on each sample. A dark background was recorded before each measurement; baseline correction was automatically done. The Cora 5600 is not strictly a handheld but a portable device; however, for practical reasons, it is included in the handheld category.

### 2.2.4 | Bravo handheld instrument

The Bravo handheld instrument from Bruker was equipped with a charged coupled device detector and two lasers, one a 785 nm and the other in the range of 1000 nm, but due to confidentiality issues, the exact wavenumber cannot be disclosed. The recorded spectral range is 300–3200 cm$^{-1}$ and with a 50 mW power, 2 cm$^{-1}$ resolution, and two scans of each sample, baseline correction was automatically done.

### 2.3 | Data treatment and chemometrics

Several Raman spectroscopy instruments were used, and therefore, spectra were available in different file extension formats, that is, *.spc for the Progeny and Cora5600 instruments and *.0 for the Vertex and Bravo. As the Vertex instrument has the widest wavenumber range (see Table 2), which facilitates the comparison of all measurements and allows to record and average 64 scans, it was considered as the “master” instrument.$^{[15]}$ Therefore, the spectra from the other instruments were transferred to a single PC and converted to the format used by the Vertex instrument by using the OPUS software (Bruker, version 7.5). Once this was done, a common region of interest (RoI) for all spectra from different instruments, 250–1750 cm$^{-1}$, was selected.

### Table 2 Summary of the acquisition characteristics of each employed Raman instrument

|                          | Wavenumber range (cm$^{-1}$) | Laser (nm) | Scans | Resolution (cm$^{-1}$) | Power (mW) |
|--------------------------|------------------------------|------------|-------|------------------------|------------|
| Vertex                   | 0–3600                       | 1064       | 64    | 2                      | 500        |
| Vertex                   | 0–7735                       | 785        | 64    | 2                      | 500        |
| Progeny                  | 200–2500                     | 1064       | 1     | 8                      | 450        |
| Cora 5600                | 100–2300                     | 1064       | Automatic | Not an option | 450 |
| Bravo                    | 300–3200                     | 785–1000*  | 2     | 2                      | 50         |

*Laser wavelength around 1000 nm. Confidential information not disclosed by Bruker.*
For the statistical analyses, each spectrum (average of three replicates) was considered as an independent measurement.

Spectra were subjected to various multivariate statistics using the software package Unscrambler® X v10.5 (CAMO Software, Trondheim, Norway). When acquiring spectroscopic data, preprocessing of the spectra is one of the most important steps in the analysis to remove undesired systematic variation in the data such as baseline drift and scattering effects and to improve the signal-to-noise ratio. Standard normal variate was employed as a preprocessing step for all the samples. It is a normalization method for correcting the spectra by centring the midpoint of each spectrum and standardizing it with the overall variance.

Principal component analysis (PCA) was used for data exploration. It is an unsupervised method that reduces the dimensionality of the original data matrix into uncorrelated variables containing the maximum information to achieve an accurate differentiation among the different NPS groups. The PCA models were created by mean centring the data, the weights were fixed constant, and they were validated by cross-validation (leave-one-out method, with NIPALS algorithm), the selected RoI for the data of the Vertex was broader than the RoI selected for the handhelds (175–1725 cm\(^{-1}\) and 680–1725 cm\(^{-1}\) respectively). The PCA carried out with each instrument was performed with all the samples analysed and the same wavenumber region (680–1725 cm\(^{-1}\)). PCA score plots were used to visualize patterns in the distribution of the samples, and the loading plots were used to interpret the spectral information corresponding to each drug group.

3 | RESULTS AND DISCUSSION

Raman spectroscopy, together with multivariate analysis, has been used for the rapid analysis and identification of three groups of NPS: cathinones, fentanyl, and synthetic cannabinoids. The main advantages of spectroscopic techniques include speed of measurement, which in this case, was a few seconds; it does not require sample preparation, samples were measured directly through the vial; and the fact that it is nondestructive, so the samples can be measured by other techniques and are very relevant in this study due to the health risk of exposure to NPS. The drawback when analysing NPS samples by Raman spectroscopy is the fluorescence resulting from cutting agents that can mask the signal from the active ingredients and which cannot be easily avoided. This study aimed to measure a set of NPS samples with two lasers (785 and 1064 nm) in the benchtop instrument in order to select which wavelength was more appropriate for these types of samples and to transfer the method to handheld instruments for in-field application.

Interference by fluorescence or a very noisy spectrum with the 785 nm laser was observed for 16 out of the 31 samples analysed. This would not allow establishing a routine for classifying or identifying drugs of abuse as it was already mentioned. In some other cases, the spectra obtained with the 785 and 1064 nm laser were in good agreement even though fluorescence resulting from the sample containers (glass vial) in which the measurements were performed was observed (results not shown). The subtraction of the spectrum of the empty vial gave a clear spectrum of the sample of interest, despite requiring an extra step, and contradicts the development of a fast, easy, and nondestructive method.

Therefore, the rest of the study was carried out with the 1064 nm laser, and the method was transferred to handheld instruments operating at the same wavelength. It is well known that the spectral range in the handheld instruments is reduced compared with benchtop instruments. However, the selected range is enough to identify significant bands of the compound of interest. The handheld instruments have a reduced common spectral range (300–2300 cm\(^{-1}\)) and a lower spectral resolution than the benchtop instrument. This implies broadening of bands but with no significant loss of information on the main bands characteristic of a given substance. As expected, the handheld devices give noisier spectra than the benchtop instrument, but they are in good agreement, and important band positions and intensities are well defined.

3.1 | Chemometric data analysis

PCA was carried out with the spectra of the set of NPS collected on the Vertex spectrometer, which was considered as the “master” instrument in this study. As shown in Figure 1, the first two principal components (PCs) explained 37% of the total variance and allowed the discrimination between the three NPS families. Further investigation of the rest of the higher order PCs was therefore not needed. The wavenumber regions that allow the distinction of the NPS groups are also presented: On the bottom left, the loadings of PC1 are shown together with the two main bands characteristic of cathinones, and on the right, the loadings of PC2 with the main band that represents the fentanyl is shown. This explains the grouping of the corresponding PCA model; the cathinones are differentiated along the PC1 and the fentanyl along the PC2.

Moreover, the two N-phenyl-N-[1-(2-phenylethyl)] piperin-4-yl] benzamide (S16 and S17), two N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]-furan-2-carboxamide (S9 and S10), and two 2-methoxy-N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl] acetamide (S11 and S12)
analysed were seized by Customs officers at different locations. The fact that each couple of compounds were projected very close to each other (see the circles in the magnified section of Figure 1) reinforces the robustness of the model and shows that even if the fentanyls had been seized at different locations, the discrimination power of the model is not affected.

As it can be observed in Table 1b, some of the compounds have their citrate form (e.g., S18 is the citrate form of S11 and S12). The PCA model allows also the differentiation between citrate and non-citrate forms even though they differ significantly in the spectra (see Figure 2). Citrate forms of fentanyls (S18 and S20) are plotted together with the rest of the fentanyls but relatively far from the correspondent non-citrate form (see Figure 1).

The Raman spectra of the 12 fentanyls used in this study have been plotted together in Figure 2. As observed from the loadings in Figure 1 and the spectra in Figure 2, the main characteristic of fentanyls is a strong band at 1004 cm$^{-1}$, even though other bands are also significant.
For example, spectra (S9) and (S10) are both furanyl fen-
tanyl but differ in three main regions around (marked
with an arrow at 1030, 1328, and 1750 cm$^{-1}$). Different
Customs officers seized them in different places; thus, it
is highly probable that they contain different impurities
present at minor level and responsible for the observed
differences. However, spectra (S11) and (S12), and (S16)
and (S17) which correspond to 2-methoxy-N-phenyl-N-
[1-(2-phenylethyl)-4-piperidinyl]-acetamide and N-phen-
ynyl-N-[1-(2-phenylethyl)piperidin-4-yl] benzamide,
respectively, show a similar fingerprint.

3.2 | Transferability to the handheld
instrument

Once the PCA model was created with the benchtop
Raman spectrometer, the same approach was used with
the Progeny to study the feasibility of transferring the
approach to handheld instruments. The samples were
measured with the handheld device, and then the mea-
surements were transferred for further multivariate anal-
ysis to a laptop computer for further processing. One
sample out of the 31 gave a very noisy spectrum due to
the small amount of sample present in the vial; thus,
the other 30 samples were used to create the PCA model.
In this case, the first two PCs explained 54% of the total
variance and the samples could be differentiated into
three groups (Figure 3, top). Again, the band of
1,004 cm$^{-1}$ as the main characteristic contributed to the
separation of the fentanyls along the PC1 and the
cathinones along PC2, as it can be observed in the corre-
sponding loadings plotted in Figure 3 (bottom).

To substantiate the transferability of the statistical
model, two other handheld instruments, a Bravo and a
Cora 5600, were used to analyse some of the samples of
each of the described groups. The measurements carried
out with these instruments were also transferred to a lap-
top for further data treatment. The PCA of the obtained
spectra (results not shown) produced the same clusters
of NPS, which demonstrated the possibility of using com-
mercially available handheld Raman instruments to iden-
tify and classify NPS.

3.3 | Chemometrics supporting identity
(ID) software from handheld instruments

The two main aims of the Customs officers, when faced
with a suspicious sample, are (a) to identify the different
cases of suspicious samples and/or (b) to verify the Cus-
toms declarations. When a suspicious sample gets a posi-
tive confirmation, it is important to know which of the
NPS type they face. For safety and enforcement reasons,
classifying each sample in the corresponding NPS family
is crucial. This is why handheld instruments, with an
integrated library and software that allows for accurate identification, are essential. These types of handheld instruments have an integrated library with thousands of Raman spectra from different substances, and the algorithm integrated into the handheld device tries to match the acquired spectrum with the spectra in the library. On the basis of the correlation between the unknown and the known library spectra, the software will then suggest the identity of the analysed substance. Depending on the handheld instrument/software, it can also indicate a mixture of ingredients. For further chemometric analysis, the measurements can be transferred to a laptop via Wi-Fi or a USB.

Moreover, handheld instruments allow for a straightforward analysis through certain containers, which greatly facilitates the analysis. To avoid the contribution of the container to the spectra, an important aspect is to optimize the focusing of the handheld before analysing the samples. Moreover, there are still many other challenges, on the one hand, creating libraries for handheld instruments and keeping them updated, and on the other hand, dealing with the fact that in most cases, the seized NPS are mixtures of the active ingredient and cutting agents. The Progeny instrument used in this study has ID software installed and 95% of the times, the match obtained is a mixture, which may suggest that the analysed sample may have some impurities present. The fact of getting an accuracy of 95% shows that when the libraries are properly fed with the right information, spectrum, CAS number, systematic name, etc., they can be beneficial for rapid identification to Customs officers. The statistical models developed can be very helpful to assign an unknown substance to an NPS family but not to the extent that the exact nature of the compound can be revealed.

4 | CONCLUSIONS

This is the first study that combines Raman spectroscopy and chemometrics for the identification and classification of NPS and presents a model capable of distinguishing fentanyl, cathinone, and synthetic cannabinoid analogues or derivatives. This work also shows the transferability of the developed model to commercially available handheld devices, which makes the method fit for purpose for field applications.
Even if the spectra of a suspect substance cannot be found in the library of a handheld device, which is often the case due to the fast development of the NPS, this screening method can provide a first indication whether the suspicious NPS is fentanyl, cathinone, or synthetic cannabinoid. This study demonstrates the feasibility of this approach that once validated would require the uploading of the prediction model on board the instrument's platform in order to provide the Customs officials with a fast screening tool. However, the relevance of the quality of the spectra becomes essential to feed these libraries. Therefore, the way the sample is presented to the Raman spectrometer, the purity of the NPS, the number of replicate measurements to overcome heterogeneity of the sample, and so forth have to be considered.

This can be useful for safety reasons in Customs laboratories and as a support tool to facilitate the implementation of the legislation.

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