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RESEARCH ARTICLE

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An infrared spectroscopic approach to characterise white powders, easily applicable in the context of drug checking, drug prevention and on-site analysis

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Abstract

More and more events, such as the summer music festivals, are considering the possibilities for implementing on-site testing of psychoactive drugs in the context of prevention and harm reduction. Although the on-site identification is already implemented by plenty of drug checking services, the required rapid quantitative dosing of the composition of illicit substances is still a missing aspect for a successful harm reduction strategy at events. In this paper, an approach is presented to identify white powders as amphetamine, cocaine, ketamine or others and to estimate the purity of the amphetamine, cocaine and ketamine samples using spectroscopic techniques hyphenated with partial least squares (PLS) modelling. For identification purposes, it was observed that mid-infrared spectroscopy hyphenated with PLS-discriminant analysis allowed the distinction between amphetamine, cocaine, ketamine and other samples and this with a correct classification rate of 93.1% for an external test set. For quantitative estimation, near-infrared spectroscopy was more performant and allowed the estimation of the dosage/purity of the amphetamine, cocaine and ketamine samples with an error of more or less 10% w/w. An easily applicable, practical and cost-effective approach for on-site characterisation of the majority of the psychoactive samples encountered in Belgian nightlife settings based on IR spectroscopy was proposed.

KEYWORDS

ATR-(N)IR, chemometrics, illicit drugs, mobile detection approaches

1 | INTRODUCTION

In the context of drug prevention and harm reduction, the possibility for implementing on-site drug checking is increasingly being considered by large electronic music events including summer festivals.

The main objective of on-site drug checking is the rapid availability of reliable information regarding the contents of user-provided drug samples and additional consultation with feedback to the potential drug users. Currently, time-consuming analytical procedures hamper the practical implementation. In addition, most drug checking services are developed from a prevention and harm reduction perspective, and have limited funding in comparison with some forensic laboratories, that perform mobile testing for law enforcement purposes. Also, the rather social sciences-related characteristics of the staff, often also including peer-to-peer support, mean that extensive laboratory expertise is lacking in practice as well.

Several approaches in this context already exist. The first approach makes use of classical analytical techniques, including chemical colour reagent testing and thin layer chromatography, whereas a second approach employs spectroscopic techniques such as infrared (IR) or Raman spectroscopy to identify the active components in a user-provided drug sample. In practice, both approaches are frequently complemented by off-site analysis in an accredited laboratory, where gas chromatography hyphenated with mass spectrometry is the gold standard for the analysis of illicit narcotics and party drugs.[1] The first approach is the one most often applied, although in this case different specific sample manipulations are necessary, whereas almost no sample preparation is necessary using the spectroscopic approach. Therefore, spectroscopic techniques appear to be the first choice in this context.

Spectroscopic techniques are now also available in miniaturised version, which even facilitates their use.[2–4] However, the disadvantage of these techniques is that a 'whole sample approach' is utilised. The samples analysed in this context often contain cutting agents (e.g. cocaine samples, which can contain caffeine, levamisole or paracetamol) or are available only as tablets (e.g. ecstasy tablets). This renders data interpretation more difficult. Several commercial applications to solve these problems exist. Often the spectroscopic instrument comes with a library of spectra of reference compounds, and the comparison of the sample spectrum with the library gives a match, which can be recalculated as a probability measure of identity. To solve the problem of several components present, the software comes often with a deconvolution algorithm allowing to 'split' spectra and detect several interfering components with a certain probability. Experience however shows that this approach encounters limitations in the context of drug checking, because here samples are final products used by patients. These products are often of doubtful quality, covering a whole range of purities and cutting agents and/or adulterants. Therefore, chemometric techniques are necessary, which are able to extract the information of interest from the recorded spectra.[5] Some instrument providers also offer a chemometric toolbox in their software especially for identification and clustering purposes.

The limitations of these commercial solutions are also shown by literature, where systematically chemometric softwares are used to deal with the problem of spectral interpretation. Neto et al.[6] described an application based on Fourier transformed IR (FT-IR) and discriminant analysis to identify hallucinogenic NBOMe derivatives and other new psychotropic substances on blotter papers. The majority of the papers however focussed on the characterisation of ecstasy tablets[7–10] and cocaine samples.[11–18] What all these papers have in common is that they only focus on one type of drug samples, have limited sample sets and all make use of chemometric techniques that are not or not yet available through the softwares of IR instrument vendors.

The focus of the approaches, described in literature, on only one drug type, is far from the situation drug checking services encounter at electronic music festivals. On-site, a wide variety of drugs are circulating, in different forms including tablets, powders, liquids and herbs, with a high variety in composition. The most popular active ingredients are MDMA, cocaine, amphetamine and ketamine, but also more 'exotic' substances such as MDE, LSD, mephedrone, synthetic cannabinoids and others can be encountered, in addition to new psychotropic substances. The more when quantification or purity estimation is envisaged in these papers, the more they all make use of reference standards and calibration samples.

As mentioned before, the majority of the drug checking services can only analyse a limited number of samples on-site, due to this diversity, and they still rely on off-site laboratories for a lot of samples. The analysis of all samples encountered to be analysed on-site using only spectroscopic techniques is utopic, though spectroscopy, focussed on the most encountered drug types (MDMA, cocaine, amphetamine and ketamine), could allow the analysis of a higher number of samples, especially the most encountered types, limiting the number of samples sent to the off-site laboratories and so cutting costs. Therefore, to be able to have a reliable first characterisation with spectroscopy on-site, an initial discrimination of samples is necessary, based on both sample form (tablets, powder, etc.) and active ingredients, followed by further characterisation. In this context, our group developed an IR spectroscopic approach combined with chemometrics to discriminate MDMA-containing tablets from other tablets, followed by an estimation of the MDMA dosage in said tablets.[19] This approach was developed using real-life samples seized at different summer festivals in Belgium, without the necessity of reference standards.

This paper extends the IR spectroscopic approach, described above, to the characterisation of white powders seized or found in nightlife settings or summer festivals with as goal to decrease the number of this type of samples, needing off-site analysis. The concept of our approach is that both prior specific operator knowledge and the number of on-site sample manipulations by the operators are minimised. For these reasons, we opted to work only with whole fingerprint regions of the spectra, and not with specific peaks, characteristic for the different compounds targeted. This would also allow easy automatisation of the approach, leaving pretreatment of the spectra, data analysis and interpretation to the computer.

For this purpose, 287 white powder samples were characterised using classical analytical approaches such as GC-MS, GC-FID and UV spectroscopy. In addition, mid-IR and NIR spectra were recorded and modelled using PLS algorithms in order to discriminate between the three most popular drugs in Belgium found as a white powder (cocaine, amphetamine and ketamine) and other powders. The latter need then to be sent to an off-site laboratory. Once identified, quantitative models were built using the recorded spectra to estimate the purity of the powders for the three drugs mentioned above and this without using expensive reference standards.

2 | METHODS AND MATERIALS

2.1 | Standards and samples

Amphetamine sulphate and ketamine HCl reference standards were purchased from Lipomed AG (Arlesheim, Switzerland), whereas

cocaine HCl was obtained from Fagron (Nazareth, Belgium). Methanol absolute HPLC grade came from Biosolve (Valkenswaard, The Netherlands). As internal standards, methyl arachidate (C21) and methyl caprylate (C9), both minimum 99% pure, were used from Sigma-Aldrich (Missouri, USA).

Two hundred eighty-seven samples were collected over a period of 2 years. One hundred eighty samples were collected at the music summer festivals in Belgium of seasons 2018 and 2019. These samples originate both from seizures by law enforcement during the festivals and from amnesty bins. From the remaining samples, 80 samples were obtained from Modus Vivendi, a drop-in drug checking facility in Brussels, and so these samples originate directly from the users. Twenty-seven samples were given to us by the National Institute for Criminalistics and Criminology and originate from law enforcement seizures at retail/middle-scale level. Once received, the samples were placed in plastic resealable bags and stored protected from light at ambient temperature.

2.2 | Sample preparation

For each sample, 20 mg (±2% w/w) was weigh in a brown volumetric flask of 20 ml and brought to volume with methanol absolute HPLC grade. Dissolution was facilitated using ultrasonication for 10 min. These solutions were used in all further analysis, and they were used as such for screening purposes using GC-MS. Except for the samples where interfering components were detected, all cocaine and ketamine samples were quantified using UV spectroscopy. Therefore, the solutions prepared for the GC-MS screening were diluted 50 times for the cocaine samples and five times for the ketamine samples, both using absolute HPLC-grade methanol.

All amphetamine samples were contaminated with caffeine, and therefore, these samples were quantified for amphetamine using GC-FID. For this purpose, a reference solution of 1 mg/ml amphetamine was prepared in methanol absolute HPLC grade, as well as a 1 mg/ml methyl caprylate solution, also in methanol absolute HPLC grade, used as internal standard. Reference solution (1 ml) and internal standard solution (0.5 ml) were mixed and used as one-point calibration to quantify amphetamine in the samples. The samples were prepared in the same way: 1 ml of the sample solution used for GC-MS screening was mixed with 0.5 ml of the internal standard solution and used for quantitative analysis.

Exactly the same procedure was followed for cocaine and ketamine samples for which excipients or cutting agents were detected that could interfere with UV spectroscopy. Also here, standard solutions of 1 mg/ml in absolute HPLC-grade methanol were prepared for cocaine and ketamine, respectively, but as internal standard methyl arachidate (1 mg/ml in absolute HPLC-grade methanol) was used. Otherwise, the same steps were followed as for the amphetamine samples.

2.3 | Data acquisition

2.3.1 | FT-mid-IR

Mid-IR spectra were recorded using a Nicolet iS10 FT-IR (Thermo Fisher Scientific, Waltham, USA) equipped with a Smart iTR accessory and a deuterated triglycine sulphate (DTGS) detector. The Smart iTR accessory uses a single bounce diamond crystal and is calibrated once a week using a polystyrene film.

IR spectra were subsequently recorded from 4000 to 400 cm^{-1}, and each spectrum was measured at a spectral resolution of 4 cm^{-1} and consisted of 32 co-added scans. Spectral data were treated using the OMNIC software version 8.3 (Thermo Fisher Scientific, Madison, USA). After each measurement, the crystal was cleaned using a soft tissue soaked with methanol and left to dry in ambient air. Before each sample, a blank measurement was performed to check the crystal for contamination and carry-over using the absorbance limits for contamination defined by the European Directorate for the Quality of Medicines and HealthCare (EDQM).[20] Every hour, a background spectrum against air was measured as well.

2.3.2 | NIR

NIR spectra were recorded using a dispersive handheld device microPHAZIR RX Analyser (Thermo Fisher Scientific, USA). Spectra were recorded for all samples where enough powder was available. As mentioned before, samples were stored in plastic resealable bags. The spectra were recorded immediately through the bags, resulting in a zero loss of sample. Measurements were performed in reflectance diffuse mode with a resolution of 11 nm in the region of 6200–4000 cm^{-1}. An average of five scans was reported. The background was recorded and distracted automatically.

2.3.3 | GC-MS

GC-MS analysis for the identification of the active compounds was performed on an Agilent 7890A GC system (Agilent Technologies, Santa Clara, California, USA) equipped with an Agilent 7683B series injector and hyphenated with an Agilent 5973 Network Mass Selective Detector (Single Quadrupole). Hardware control, data acquisition and data handling were done using the Agilent MSD ChemStation software. Chromatographic separation was achieved using an Agilent J&W HP-5ms capillary column (30 m × 0.25 mm; 0.25 μm) with the following temperature gradient: the gradient started at 80°C and was held for 2 min, followed by a gradient at a rate of 15°C per minute until a temperature of 280°C was reached. This temperature was held for 17 min, resulting in a total runtime of about 32.3 m. Injection volume was set at 1 μl, and helium was used as carrier gas at a constant flow rate of 1 ml/min. The injector was used in split mode (ratio 1:10). The temperatures of the injection port, the ion source, the

quadrupole and the interface were set at 250, 230, 150 and 280°C, respectively. Mass data were recorded in full scan mode.

2.3.4 | GC-flame ionisation detection (GC-FID)

GC-FID analysis was performed on an Agilent 6890N GC system with an FID detector. The analysis was performed under identical chromatographic conditions as for GC-MS (Section 2.3.3). The injection temperature was 250°C, and the flame temperature of the FID, 300°C. Air, hydrogen and nitrogen flows were set at 350, 35 and 30 ml/min, respectively. Again, the Agilent MSD ChemStation software was used for instrument steering, data acquisition and handling.

2.3.5 | UV spectrophotometry

Quantification of the majority of cocaine and ketamine samples was performed on a PerkinElmer Lambda 35 UV/Vis spectrophotometer (PerkinElmer, Waltham, Massachusetts, USA). Spectrophotometric measurements were performed using quartz cuvettes (Quartz Suprasil, 10 × 10 mm, Hellma, Müllheim, Germany) against methanol as blank. The UV spectrum was measured in the range of 200–350 nm at a rate of 480 nm/min. The spectrum is closely inspected as to avoid interference from the presence of adulterants or matrix. Absorption wavelength for the quantification of cocaine was 230 nm, and for the calculation of purity, a specific extinction coefficient for cocaine of 405, *100 ml/gcm*$^{-1}$ was used. For ketamine samples, the quantification wavelength was 277 nm, whereas the specific extinction coefficient used was 19.7, *100 ml/gcm*$^{-1}$.

This procedure was developed and validated by our laboratory in the context of fast drug screening to provide users as quickly as possible with data on their products in the context of harm reduction. Validation under ISO17025 included parallel analysis of samples with UV and GC-FID.

2.4 | Data preprocessing

For the mid-IR spectra, the so-called fingerprint region, defined by the pseudo-absorbance (−log(1/R)) obtained between 2000 and 650 cm^{-1}, was selected and used for further analysis. Figure 1a shows the obtained mid-IR spectra for a cocaine, amphetamine and ketamine sample, respectively. Although some clear differences can be observed, it is clear that visual differentiation is difficult, especially when less pure samples are measured. Therefore, chemometrics will be necessary to extract the information of interest from the spectral data and to discriminate between the three types of samples of interest in this study on one side and between these samples and samples containing other active ingredients on the other side.

For NIR, the whole recorded spectrum, defined by the pseudo-absorbance measured between 6200 and 4000 cm^{-1}, was taken into account. Figure 1b shows the obtained spectra for cocaine, amphetamine and ketamine samples, respectively. Likewise, here it is clear as well that differentiation between the different samples based on the obtained spectra will necessitate the use of chemometrics.

Before the application of chemometric techniques, the pseudo-absorbance spectra were pretreated to eliminate or reduce variations introduced in the data by external sources other than the sample itself. Several pretreatment techniques were explored. The first was standard normal variate (SNV), a normalisation procedure eliminating the variation in the data due to the measurement itself, for example, differences in path length, scattering effects and variations in the detector.[21] The second and third pretreatment techniques were SNV followed by the first and second derivatives. The latter techniques remove the background from the spectra and accentuate the spectral framework and therefore highlight the differences between spectra. The first derivative calculates the slope of the spectral curve at each wavenumber, whereas the second derivative calculates the change in slope. Because the slope is not affected by variations in baseline, these derivatives eliminate the effects mentioned earlier.[21] The first or second derivative was calculated using the Savitzky–Golay method[22] with a second-order polynomial and a window size of 17 for the mid-IR spectra and 7 for the NIR spectra. A final approach was the log10 transformation of the spectral data. A log10 transformation is often applied to skewed data in order to get a more normal distribution rendering patterns in the data more interpretable.[21]

A proper validation of chemometric models necessitates the use of an external test set. For this reason, the selected sample sets were split into training and test sets using two different algorithms: Kennard and Stone[23,24] and Duplex.[25]

The first algorithm starts by selecting the sample (S_1) located farthest (or closest) from mean in the multidimensional space defined by the spectral data. The second sample (S_2) is the sample located farthest from S_1 and the third the sample (S_3) located farthest from S_1 and S_2. This process continues until a predefined number of samples is selected for the test set.

The Duplex algorithm is based on a pairwise selection of samples. It starts with the selection of two samples in the data space with the highest Euclidean distance between them for a first set. The next two samples with the highest Euclidean distance between them are selected for a second set. This procedure continues iteratively by selecting sample pairs for the first and second sets, until the predefined number of samples is reached in the second set, the selected test set. The first set and the remaining samples together form the training set.

Both algorithms were applied to each of the spectral data sets used for modelling in this study. From the selected test sets, the best one was selected and used for validation of the obtained model. For qualitative purposes, this was the test set with the best and most equal representation of all four classes considered. For the quantitative models, the test set that best covered the spectral data space, and best represents the entire dosage/purity range in the sample set, was selected. It was decided to select ±20% of the samples in the

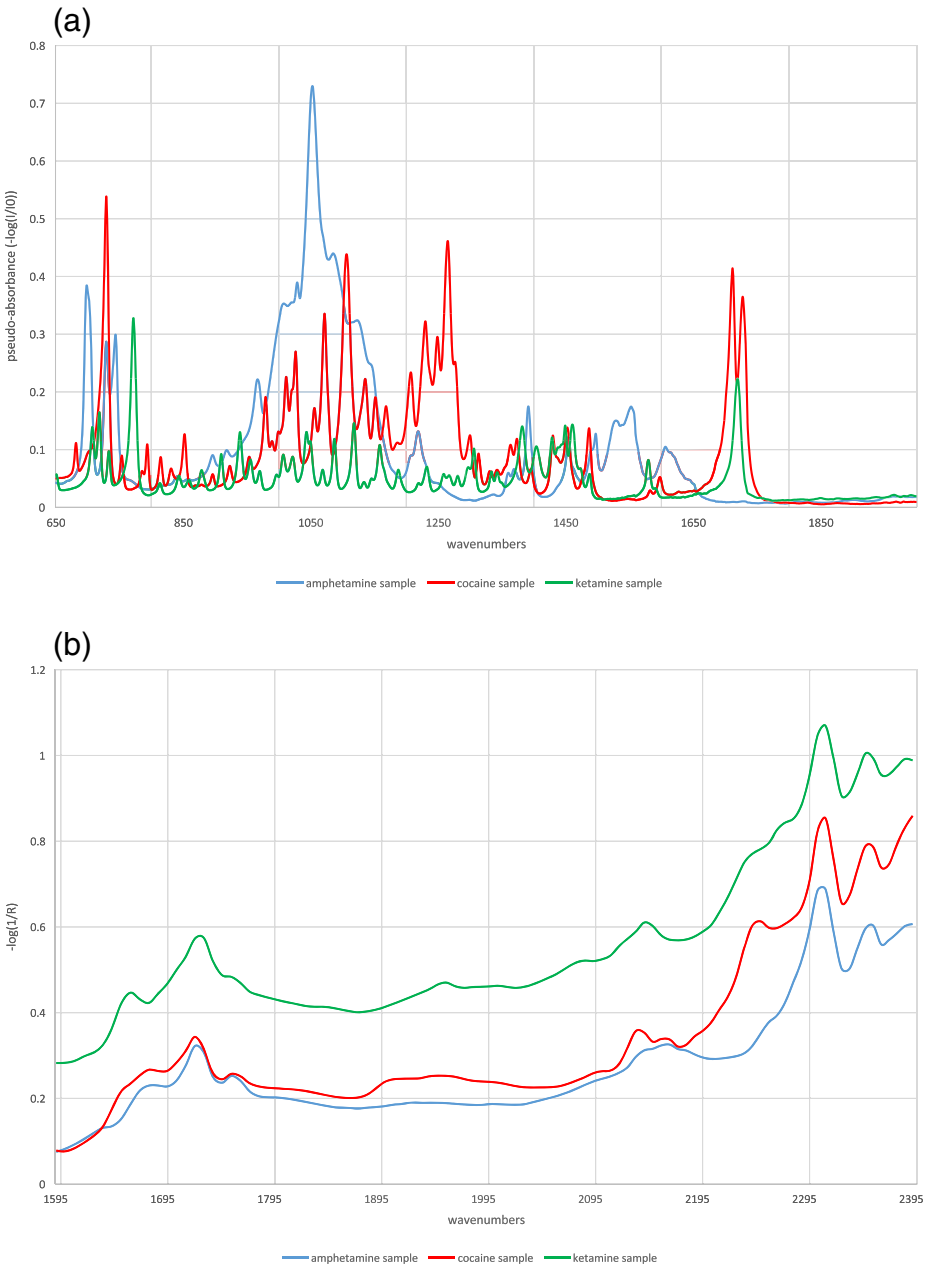

FIGURE 1 (a) Raw mid-IR spectrum for an amphetamine, cocaine and ketamine sample. (b) Raw NIR spectrum for an amphetamine, cocaine and ketamine sample [Colour figure can be viewed at wileyonlinelibrary.com]

sample sets as test set and to perform the test set selection for each spectral data set separately. The latter to avoid that differences in predictive power of the models were due to different variabilities in the spectral data.

2.5 | Principal component analysis

Principal component analysis (PCA) is a projection technique allowing the representation of high-dimensional data in a low-dimensional space defined by new latent variables, which are defined as linear combinations of the manifest variables. These latent variables are called principal components (PC) and are defined in such a way that they represent the highest variance in the data. This means that the first principal component (PC1) is defined to represent the highest variance in the data, whereas the second principal component (PC2) is defined to represent the highest variance around PC1. The third represents then the highest variance around the plane PC1–PC2. This means also that the different PCs are, by definition, orthogonal to each other. The loadings of the variables show their respective contribution to a given PC and the correlation between the different explanatory variables. The projections of the objects on the PCs are called the scores and are a measure for the similarities among objects.[21]

In this study, PCA is used as exploratory technique in order to investigate clustering tendency of the different samples before supervised modelling is applied. PCA was only applied for qualitative purposes.

2.6 | Partial least squares (discriminant analysis)

Partial least squares (PLS) is a supervised projection technique, which is basically based on the same principles as PCA. Also, PLS defines new latent variables, called PLS factors (PLS), as linear combination of the manifest variables, but these combinations are now calculated to represent the highest (PLS1) or remaining (PLS2, PLS3, etc.) covariance between the data and a response. PLS was developed for regression purposes and so for continuous responses like dosages. Though, in an adapted form and by combining PLS with discriminant analysis (PLS-DA), it can also be used for categorical responses and so for classification modelling. In this study, PLS-DA was applied to build discriminatory models for the three active compounds of interest and other samples, and PLS was used for quantitative modelling in order to estimate the dosage/purity of amphetamine, cocaine and ketamine samples, respectively.

The selection of the optimal number of latent variables to be included in the model was performed using 10-fold cross validation. The validation of the models was based on the root mean squared error of cross validation (RMSECV; internal validation) for the training set and the root mean squared error of prediction (RMSEP; external validation) for the selected test set. For the qualitative models, the RMSECV and RMSEP were expressed as correct classification rates (ccr). In addition, also the accuracy, precision and sensitivity of the models were calculated and evaluated. For the regression models, the coefficients of determination between real and predicted values were calculated as well for both training as test set.

2.7 | Software

Data processing and modelling were performed using Matlab version R2019b (MathWorks, Natick, MA, USA). PCA was performed using the PLS toolbox (Eigenvector Research, Inc., Manson, USA), and the PLS-DA algorithm was part of the ChemoAC toolbox (Freeware, ChemoAC Consortium, Brussels, Belgium, version 4.0).

3 | RESULTS

3.1 | Characterisation of the samples

All collected samples were screened for the presence of illicit drugs using GC-MS. In general, when a sample was found positive for one of the three targeted drugs, the drug content was determined using UV spectroscopy. This was the case for the majority of cocaine and ketamine samples. Some of these samples contained interfering components such as caffeine and were therefore quantified using GC-FID. Because all samples found positive for amphetamine were contaminated with caffeine or other interfering compounds or showed interference of some unknown nature, it was decided to quantify all amphetamine samples using GC-FID.

An overview of the screening results and the obtained dosages/purities in per cent for all 287 samples is given in Table 1. All purities were expressed as weight percentages of the base components. Of the 287 samples, 60 samples were found positive for amphetamine, 87 for cocaine and 47 for ketamine. The remaining 93 samples were identified as containing other illicit drugs, unknown compounds or any drugs (classified as 'negative'). An overview of the screening results for these samples can also be found in Table 1.

For the 60 amphetamine samples, average amphetamine dosage was 30.4% w/w, and the median was 27.5% w/w. The lowest dosage encountered was 2.8% w/w and the highest 86.2% w/w. For the cocaine samples, average cocaine concentration was 75.4% w/w, the median 79.9% w/w and 19.8% w/w and 100% w/w were respectively the lowest and highest purity in the analysed cocaine samples encountered in this sample set, respectively. For the ketamine samples, 75.5% w/w and 81.0% w/w were found as average and median ketamine concentration, respectively, whereas the lowest value in the samples set was 33.9% w/w, and the highest, 92.3% w/w.

3.2 | Qualitative models

Qualitative models were built using the spectra of all samples in the sample set. In first instance, a PCA was performed in order to investigate the possibility of discriminating between the different targeted active compounds on one side and the targeted compounds and other samples on the other side. Discriminative models were consequently built using PLS-DA, and to this end, the sample set was divided into four classes, that is, amphetamine samples (Class 1), cocaine samples (Class 2), ketamine samples (Class 3) and the samples negative for the three targeted compounds (Class 4).

3.2.1 | Mid-IR data

Mid-IR spectra were recorded for all 287 samples. First, a PCA was performed using the different data preprocessing methods proposed in Section 2.4. The best score plot was obtained with the mid-IR spectra, pretreated with SNV. Figure 2 shows the three-dimensional score plots obtained with the mid-IR spectra, and it can be seen that within the plot a differentiation can be made between the samples of Classes 1, 2 and 3, whereas the samples of Class 4 show only a tendency of separation. The latter is probably due to the higher variation present in this class.

From Figure 2, it can clearly be seen that the discrimination between Classes 1 and 2 happens along PC2, whereas the discrimination of Class 3 is defined by PC3. Figure 3 shows the mid-IR spectra of amphetamine sulphate, cocaine HCl and ketamine HCl, together with the loadings of the three first principal components. For the discrimination of Classes 1 and 2 along PC2, it can clearly be seen that the highest absolute values for the loadings of PC2 correspond to specific peaks of the cocaine HCl spectrum, not present in the amphetamine sulphate spectrum. Also for the discrimination of ketamine

TABLE 1 Overview of the analysed samples ordered by class

Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class
1	Amphetamine, caffeine	13.3	1	74	Cocaine	88.3	2	147	Cocaine	78.2	2	220	Chloromethcathinone	-	4
2	Amphetamine, phenacetin	51.4	1	75	Cocaine	90.0	2	148	Ketamine	49.0	3	221	Methylmethcathinone, methamphetamine	-	4
3	Amphetamine	51.2	1	76	Cocaine, phenacetin	82.2	2	149	Ketamine	87.5	3	222	Lidocaine	-	4
4	Amphetamine	41.3	1	77	Cocaine	73.6	2	150	Ketamine	84.0	3	223	4-Chloro-N,N-dimethylcathinone	-	4
5	Amphetamine, caffeine	16.8	1	78	Cocaine	35.4	2	151	Ketamine, MDMA	46.5	3	224	Unknown	-	4
6	Amphetamine, caffeine	34.4	1	79	Cocaine	89.1	2	152	Ketamine	54.1	3	225	Unknown	-	4
7	Amphetamine, caffeine	23.3	1	80	Cocaine, levamisole	87.4	2	153	Ketamine	90.6	3	226	Phenacetin	-	4
8	Amphetamine, caffeine	3.3	1	81	Cocaine, benzoylecgonine	80.8	2	154	Ketamine	90.9	3	227	Unknown	-	4
9	Amphetamine	68.4	1	82	Cocaine	85.6	2	155	Ketamine	53.4	3	228	Dapoxetine	-	4
10	Amphetamine	63.7	1	83	Cocaine	81.2	2	156	Ketamine	68.6	3	229	Unknown	-	4
11	Amphetamine	65.8	1	84	Cocaine, levamisole	82.0	2	157	Ketamine	66.2	3	230	2-Methylmethcathinone, 3-methylmethcathinone, methamphetamine	-	4
12	Amphetamine	46.7	1	85	Cocaine	86.1	2	158	Ketamine	75.0	3	231	Unknown	-	4
13	Amphetamine	67.0	1	86	Coca, levamisole (lidocaine, keta)	83.6	2	159	Ketamine	78.0	3	232	MDMA	-	4
14	Amphetamine	46.9	1	87	Cocaine	37.0	2	160	Ketamine	76.0	3	233	MDMA	-	4
15	Amphetamine	45.6	1	88	Cocaine	84.5	2	161	Ketamine	74.7	3	234	MDMA	-	4
16	Amphetamine	21.9	1	89	Cocaine	81.1	2	162	Ketamine	86.3	3	235	MDMA	-	4
17	Amphetamine	62.9	1	90	Cocaine	80.7	2	163	Ketamine	88.5	3	236	MDMA	-	4
18	Amphetamine, caffeine	17.3	1	91	Cocaine	86.8	2	164	Ketamine	71.7	3	237	MDMA	-	4
19	Amphetamine, caffeine	18.1	1	92	Cocaine	43.0	2	165	Ketamine	89.6	3	238	Mephedrone	-	4
20	Amphetamine, caffeine	49.5	1	93	Cocaine	92.4	2	166	Ketamine	81.0	3	239	Mephedrone	-	4
21	Amphetamine, caffeine	26.9	1	94	Cocaine	64.9	2	167	Ketamine	89.8	3	240	MDMA	-	4

(Continues)

TABLE 1 (Continued)

Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class
22	Amphetamine, caffeine	33.8	1	95	Cocaine	62.8	2	168	Ketamine	86.8	3	241	4-Fluoroam phetamine	-	4
23	Amphetamine, caffeine	14.1	1	96	Cocaine	80.0	2	169	Ketamine	70.9	3	242	Negatif	-	4
24	Amphetamine, caffeine	14.8	1	97	Cocaine	75.1	2	170	Ketamine	86.8	3	243	Negatif	-	4
25	Amphetamine, caffeine	15.1	1	98	Cocaine	71.3	2	171	Ketamine	87.5	3	244	Mephedrone	-	4
26	Amphetamine	37.9	1	99	Cocaine	72.7	2	172	Ketamine	33.9	3	245	AB-FUBINACA	-	4
27	Amphetamine	33.5	1	100	Cocaine	60.8	2	173	Ketamine	74.6	3	246	Lidocaine	-	4
28	Amphetamine, caffeine	6.7	1	101	Cocaine	76.0	2	174	Ketamine	82.9	3	247	Mephedrone	-	4
29	Amphetamine	50.5	1	102	Cocaine	73.2	2	175	Ketamine	69.1	3	248	Lidocaine	-	4
30	Amphetamine, caffeine, metham phetamine	32.6	1	103	Cocaine	42.6	2	176	Ketamine	86.3	3	249	Lidocaine	-	4
31	Amphetamine, caffeine	35.3	1	104	Cocaine	74.9	2	177	Ketamine	83.4	3	250	Diacetylmorphine	-	4
32	Amphetamine	26.3	1	105	Cocaine	86.9	2	178	Ketamine	92.3	3	251	Diacetylmorphine	-	4
33	Amphetamine	25.7	1	106	Cocaine	80.2	2	179	Ketamine	77.8	3	252	Diacetylmorphine	-	4
34	Amphetamine	34.1	1	107	Cocaine	79.5	2	180	Ketamine	87.4	3	253	Negatif	-	4
35	Amphetamine	29.1	1	108	Cocaine	42.3	2	181	Ketamine	77.2	3	254	Negatif	-	4
36	Amphetamine	33.5	1	109	Cocaine	76.2	2	182	Ketamine	87.9	3	255	Cannabidiol	-	4
37	Amphetamine	22.2	1	110	Cocaine	67.5	2	183	Ketamine	84.0	3	256	*N*-Ethyl-2,3-methylenedioxy phenethylamine	-	4
38	Amphetamine	12.2	1	111	Cocaine	55.2	2	184	Ketamine	36.6	3	257	Diacetylmorphine	-	4
39	Amphetamine	40.6	1	112	Cocaine	87.5	2	185	Ketamine	36.7	3	258	Cannabidiol	-	4
40	Amphetamine, MDMA	23.7	1	113	Cocaine	85.9	2	186	Ketamine	61.0	3	259	MDMA	-	4
41	Amphetamine	5.9	1	114	Cocaine	79.7	2	187	Ketamine	77.4	3	260	Negatif	-	4
42	Amphetamine	27.8	1	115	Cocaine	85.9	2	188	Ketamine	80.6	3	261	Diacetylmorphine	-	4
43	Amphetamine	10.3	1	116	Cocaine	81.9	2	189	Ketamine	57.3	3	262	Negatif	-	4
44	Amphetamine, cocaine	11.7	1	117	Cocaine	87.9	2	190	Ketamine	87.3	3	263	MDMA	-	4
45	Amphetamine	15.0	1	118	Cocaine	80.4	2	191	Ketamine	82.4	3	264	Negatif	-	4

(Continues)

TABLE 1 (Continued)

Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class	Sample number	Active compound	Dosage (% w/w)	Class
46	Amphetamine	20.0	1	119	Cocaine	82.2	2	192	Ketamine	85.3	3	265	MDMA	-	4
47	Amphetamine	8.9	1	120	Cocaine	69.2	2	193	Ketamine	85.9	3	266	Negatif	-	4
48	Amphetamine	3.6	1	121	Cocaine	67.4	2	194	Ketamine	87.4	3	267	PCP	-	4
49	Amphetamine	31.5	1	122	Cocaine	79.0	2	195	Mephedrone	-	4	268	Etizolam	-	4
50	Amphetamine	27.2	1	123	Cocaine	70.8	2	196	Mephedrone	-	4	269	4-FA	-	4
51	Amphetamine	2.8	1	124	Cocaine	76.8	2	197	MDMA	-	4	270	MDMA	-	4
52	Amphetamine	3.2	1	125	Cocaine	93.3	2	198	MDMA	-	4	271	Negatif	-	4
53	Amphetamine	86.2	1	126	Cocaine	79.4	2	199	MDMA	-	4	272	Negatif	-	4
54	Amphetamine	14.3	1	127	Cocaine	89.0	2	200	MDMA	-	4	273	THJ 2201	-	4
55	Amphetamine	11.8	1	128	Cocaine	84.2	2	201	MDMA	-	4	274	MDMA	-	4
56	Amphetamine	41.6	1	129	Cocaine	78.9	2	202	MDMA	-	4	275	Negatif	-	4
57	Amphetamine	38.5	1	130	Cocaine	56.2	2	203	MDMA	-	4	276	Negatif	-	4
58	Amphetamine	5.8	1	131	Cocaine	56.2	2	204	MDMA	-	4	277	Negatif	-	4
59	Amphetamine, caffeine	48.8	1	132	Cocaine	79.2	2	205	MDMA	-	4	278	MDMA	-	4
60	Amphetamine, phenacetin	49.2	1	133	Cocaine	82.9	2	206	MDMA	-	4	279	Mephedrone	-	4
61	Cocaine	82.6	2	134	Cocaine	84.6	2	207	MDMA	-	4	280	Mephedrone	-	4
62	Cocaine, levamisole	57.9	2	135	Cocaine	83.0	2	208	MDMA	-	4	281	MDMA	-	4
63	Cocaine, benzoylecgonine	76.4	2	136	Cocaine	83.8	2	209	MDMA	-	4	282	Negatif	-	4
64	Cocaine	84.8	2	137	Cocaine	79.4	2	210	MDMA	-	4	283	MDMA	-	4
65	Cocaine	87.9	2	138	Cocaine	80.9	2	211	Chlorphenamine		4	284	5-MEO-Mipt	-	4
66	Cocaine	79.9	2	139	Cocaine	77.7	2	212	Chlorphenamine		4	285	Negatif	-	4
67	Cocaine, levamisole	56.0	2	140	Cocaine	81.9	2	213	Chlorphenamine		4	286	Negatif	-	4
68	Cocaine, caffeine	20.5	2	141	Cocaine	82.3	2	214	Chlorphenamine		4	287	Mephedrone	-	4
69	Cocaine	77.9	2	142	Cocaine	19.8	2	215	MDMA	-	4				
70	Cocaine, phenacetine, levamisole	75.2	2	143	Cocaine	84.4	2	216	4-Chlorometh cathinone	-	4				
71	Cocaine	86.4	2	144	Cocaine	100.0	2	217	Norbuprenorphine		4				
72	Cocaine	77.1	2	145	Cocaine	86.0	2	218	Unknown	-	4				
73	Cocaine	76.7	2	146	Cocaine	76.3	2	219	Unknown	-	4				

Note: Class 1 = amphetamine; Class 2 = cocaine; Class 3 = ketamine; Class 4 = other active compounds.

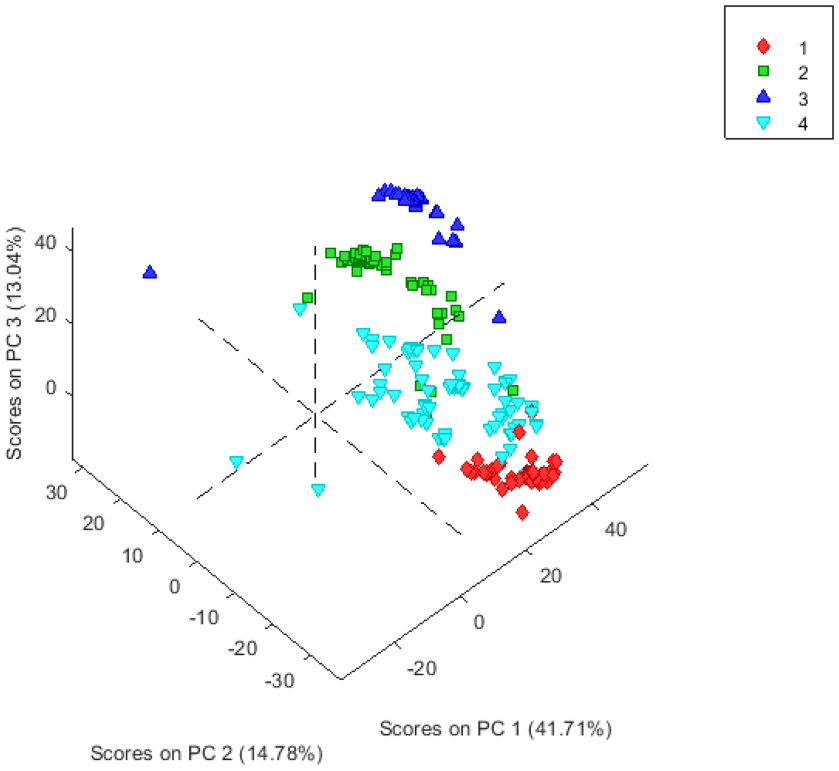

FIGURE 2 PCA score plot obtained with the mid-IR spectra pretreated with SNV [Colour figure can be viewed at wileyonlinelibrary.com]

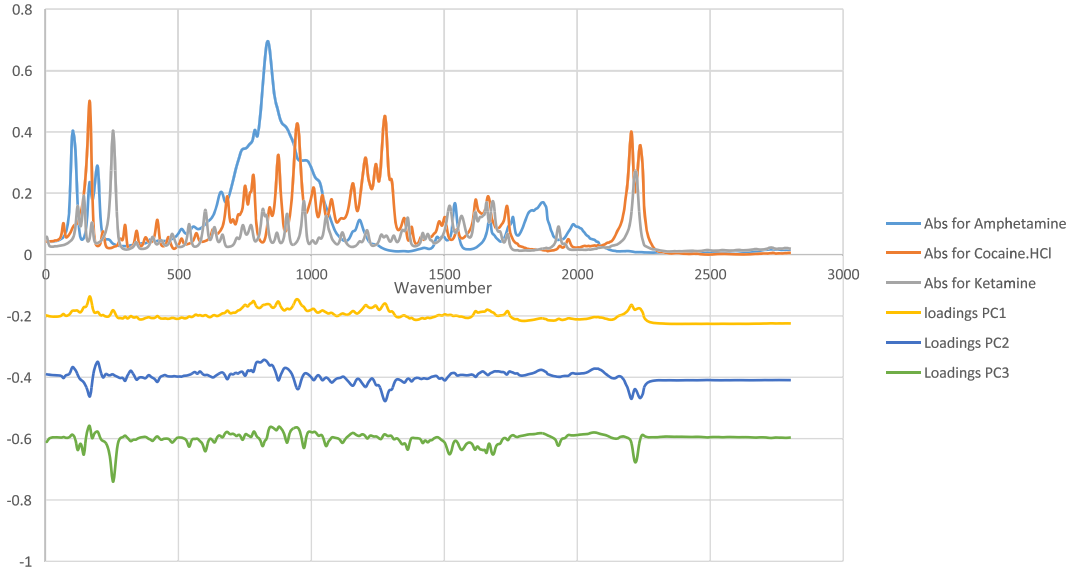

FIGURE 3 The mid-IR spectrum of pure amphetamine, cocaine and ketamine together with the loadings on PC1, PC2 and PC3 obtained during PCA of the mid-IR spectra pretreated with SNV [Colour figure can be viewed at wileyonlinelibrary.com]

samples, the loadings of PC3 clearly follow the spectrum of ketamine HCl, with the highest absolute values of the loadings corresponding to specific peaks in the ketamine spectrum. The loadings therefore show that discrimination of the samples containing the three targeted illicit drugs is based on the presence of the targeted molecules and that they can be discriminated in an unsupervised way based on mid-IR spectroscopy.

Based on the exploratory analysis using PCA, it was concluded that there are clear differences between the spectra of the samples belonging to the different classes and resemblances between the spectra within one class. Because these differences could be obtained in an unsupervised way, supervised modelling with PLS-DA was performed. In first instance, the sample set was split into training and test set using both Kennard and Stone and the Duplex algorithm. Based

on the representation of the different classes, the test set selected with Duplex was preferred. The test set contained 58 samples from which 10 samples belonged to Class 1, 10 to Class 2, 9 to Class 3 and 29 to Class 4. It is normal that these kinds of algorithms select more samples of the class in which more variability is present. PLS-DA models were built after applying all four preprocessing techniques mentioned in Section 2.4. The optimal model was obtained using the mid-IR spectra preprocessed with SNV and was composed of five PLS factors. This model showed a ccr for cross validation of 96.1% or nine of the 229 samples misclassified in the training set. For the test set, a ccr of 93.1% was obtained or four of the 58 selected samples misclassified. A closer look at the misclassifications showed that during cross validation, two samples of Class 1 (amphetamine) and two samples of Class 2 (cocaine) were classified as Class 4, two samples of Class 3 (ketamine) were misclassified as Classes 1 and 2 and one sample of Class 4 was misclassified as Classes 1 and 2, respectively. One of the misclassified samples of Class 1 was a mixture between amphetamine and MDMA, which could explain its classification in Class 4. For the other samples, no logical explanation for misclassification could be found; as a result, they could be attributed to random modelling errors. Table 2 shows the sensitivity, specificity and precision values calculated for each class separately. In general, it can be observed that a good performing model was obtained with a slight lesser performance for Class 4, which can be explained by the higher variability of the spectra and the samples in this class.

In order to compare the performance of the model, the spectra of all samples were also matched against an in-house library of FT-IR spectra, containing the spectra of the targeted narcotics, recorded using the pure standards. If a spectral match of 80% is considered as the limit to obtain a positive identification, it was clear that only 64% of the samples in the data set could be correctly identified and classified according to the four defined classes. The majority of the problems occurred with the samples having low purity or containing cutting agents or adulterants.

3.2.2 | NIR data

Due to the amount of sample available, only for 205 samples the NIR spectra could be recorded. The same procedure as for the mid-IR was followed, though for none of the applied pretreatment techniques a PCA score plot could be obtained that showed clusters of the different classes. Only with SNV followed by the second derivative (results not shown) a slight clustering of the samples of Class 4 from the other classes could be observed. Despite these results, it was decided to continue with PLS-DA modelling. The sample set was split into training and test set and again Duplex gave the best representation of all classes. In total, 41 samples were selected for the test set, of which 10 belonged to Class 1, 8 to Class 2, 3 to Class 3 and 20 to Class 4. After building PLS-DA models with the spectra, pretreated with the different methods, the best model was obtained using SNV followed by the first derivative (dx1) as pretreatment technique. The selected PLS-DA model was based on 14 PLS factors and showed a ccr for cross validation of 94.5% or nine samples of the 164 samples of the training set misclassified. For the test set, a ccr of 78.0% or nine samples of the 41 misclassified was obtained. A closer investigation of the misclassifications showed that for the training set, three samples of Class 1 (amphetamine) were classified as negative (Class 4), one sample of Class 3 (ketamine) was classified as Class 1 and one as Class 4 and one sample of Class 4 was misclassified as Classes 1, 2 and 3. For the test set, two samples of Class 1 as well as one of Class 2 were classified as Class 4, one sample of Class 3 was classified as Class 1 and one and four samples of Class 4 were classified as Classes 1 and 2. Some misclassifications could be explained. One of the misclassified samples of Class 1 contained only 7% of amphetamine and high concentrations of caffeine, which could explain its classification in Class 4. Another misclassification of Class 1 as Class 4 was the same sample as detected with the mid-IR spectra, that is, a sample containing a mixture of amphetamine and MDMA. The same was true for the ketamine sample (Class 3) misclassified as Class 4. In fact, it contains a mixture of ketamine and MDMA. Four samples of the misclassified samples of Class 4 contained chlorpheniramine as active substance. It seems that the model cannot differentiate these samples from the amphetamine and the cocaine samples.

Table 3 shows the sensitivity, specificity and precision values calculated for each class separately. As can be seen from the table, the performances of the model based on the NIR spectra are clearly inferior to the performance of the model obtained with the mid-IR spectra. This seems logical because mid-IR spectra are generally more specific.

3.3 | Quantitative models

For quantitative modelling, the sample set was split into four groups according to the active compound present. The negative group (Class

TABLE 2 Sensitivity, specificity and precision for the optimal PLS-DA model obtained with the mid-IR spectra pretreated with SNV

Cross validation	Sensitivity (%)	Specificity (%)	Precision (%)	Test set	Sensitivity (%)	Specificity (%)	Precision (%)
Amphetamine (Class 1)	95.7	97.8	91.8	Amphetamine (Class 1)	90.0	97.9	90.0
Cocaine (Class 2)	97.5	99.3	98.7	Cocaine (Class 2)	90.0	97.9	90.0
Ketamine (Class 3)	95.0	100.0	100.0	Ketamine (Class 3)	88.9	100	88.9
Other (Class 4)	95.2	97.6	93.8	Other (Class 4)	96.5	93.1	96.6

TABLE 3 Sensitivity, specificity and precision for the optimal PLS-DA model obtained with the NIR spectra pretreated with dx1

Cross validation	Sensitivity (%)	Specificity (%)	Precision (%)	Test set	Sensitivity (%)	Specificity (%)	Precision (%)
Amphetamine (Class 1)	90.6	98.5	85.3	Amphetamine (Class 1)	80.0	93.5	66.7
Cocaine (Class 2)	100.0	98.1	96.6	Cocaine (Class 2)	87.5	87.9	58.3
Ketamine (Class 3)	93.5	99.2	90.6	Ketamine (Class 3)	66.6	100.0	66.7
Other (Class 4)	90.9	96.7	83.3	Other (Class 4)	75.0	85.0	65.2

4) was discarded, and the other groups (amphetamine, cocaine and ketamine) were modelled separately. The pseudo-absorbances in the spectra were used as manifest variables, whereas the quantitative results in per cent obtained with either UV spectroscopy or GC-FID were used as response variables. Also here, models were built after prereatment with each of the preprocessing methods described in Section 2.4.

3.3.1 | Mid-IR data

Amphetamine

The data set was composed of the mid-IR spectra obtained for the 57 samples, found positive for amphetamine. The sample set was split into a training and a test set based on the spectral data. Twelve samples (±20%) were selected as external test set, and the Duplex algorithm gave the best coverage of both the spectral data space as the concentration range of the sample set.

PLS models were built using the spectra, pretreated with the respective preprocessing techniques. The optimal model was obtained after applying SNV and was composed of eight PLS factors. All validation parameters are given in Table 4. The selected model showed a RMSEC, RMECV and RMSEP of 6.04, 8.64 and 8.48 with determination coefficients of 0.88 for calibration, 0.76 for cross validation and 0.75 for prediction, respectively. These features show that the values of calibration, cross validation and prediction are close together pointing at a robust model without overfitting. When investigating the predictions of both cross validation as external test set in detail, it could be observed that residuals were randomly distributed around the zero axis (see Figure S1a). For cross validation, a mean absolute residual of 6.7% w/w was obtained with residuals higher than 10% w/w for 10 samples with a maximum of 18.5% w/w. For the external test set, a mean absolute residual of 6.6% w/w was obtained with only one sample having a residual of more than 10% w/w (12.3% w/w), which was also the maximal residual obtained for the test set.

Cocaine

For cocaine, the data set was composed of the mid-IR spectra for 89 samples. The best test set of 18 samples (±20%) covering both the spectral data space as the concentration/purity range was obtained with Duplex algorithm. Again, PLS models were built after each of the selected pretreatments. Unfortunately, no acceptable models could be obtained. The best model, obtained after SNV, was composed of two PLS factors with RMSE values around or higher than 10 and R^2 values around 0.6. Table 4 gives the validation parameters more in detail, but based on these values it had to be concluded that no acceptable quantitative model for cocaine could be obtained using the recorded mid-IR spectra.

Ketamine

Forty-seven ketamine samples were analysed using mid-IR spectroscopy. Again, it was Duplex that resulted in the test set of 10 samples, which covered best the data space as well as the dosage range of the ketamine samples.

The best PLS model was obtained using SNV as preprocessing method. The selected model was composed of two PLS factors, and its validation parameters are given in Table 4. It can be seen that the determination coefficients for calibration, cross validation and prediction are nearly identical and that also the RMSE values are very close. This clearly shows that the model is not showing overfitting and that

TABLE 4 Validation parameters for the different selected quantitative models

	Mid-IR			NIR		
	Amphetamine	Cocaine	Ketamine	Amphetamine	Cocaine	Ketamine
Preprocessing	SNV	SNV	SNV	Log10	SNV + dx1	SNV
# PLS factors	8	2	2	7	4	4
RMSEC	6.04	9.53	6.81	5.44	4.61	5.15
R^2_c	0.88	0.62	0.85	0.92	0.86	0.89
RMSECV	8.64	10.12	6.64	5.27	4.94	4.84
R^2_{cv}	0.76	0.57	0.85	0.93	0.83	0.89
RMSEP	8.48	12.4	6.22	2.81	5.78	4.62
R^2_p	0.75	0.54	0.85	0.96	0.89	0.99

the obtained model is quite robust. Closer investigation of the predictions in both cross validation and test set revealed a mean absolute residual for cross validation of 5.9% w/w and a maximum value of 11.7% w/w. For the test set a mean absolute residual of 5.0% w/w was observed and a maximum of 11.3% w/w. For cross validation and test set, three and one samples showed a residual higher than 10% w/w. It could also be observed that a random distribution of the residuals over the zero axis was obtained (see Figure S1c).

3.3.2 | NIR data

Amphetamine

NIR spectra were recorded for 42 of the samples found positive for amphetamine. For this data set, the best coverage of both the spectral data space and the concentration range of the included amphetamine samples was obtained with an external test set selected by applying Kennard and Stone. Nine samples (±20%) were selected, leaving 33 samples for the training set.

Again, PLS models were built after applying the different selected preprocessing methods, and the optimal model was obtained after the log10 transformation of the spectra. The selected model consisted of seven PLS factors, for which the validation parameters can be found in Table 4. RMSEC, RMECV and RMSEP values of 5.44, 5.27 and 2.81 were obtained with determination coefficients of 0.92 for calibration, 0.93 for cross validation and 0.96 for prediction, respectively. A random distribution of the residuals around the zero axis could be observed (see Figure S1d) with a mean absolute residual for cross validation of 4.3% w/w and a maximal residual of 10.4% w/w. Only two samples had residuals above 10% w/w. For the external test set, a mean absolute residual of 2.0% w/w was obtained and a maximal residual of 6.9% w/w. Except of this maximum residual, all other residuals were smaller than 3% w/w.

Cocaine

The sample set for NIR was composed of 65 samples, positive for cocaine. The best coverage of the spectral data space and the concentration range was obtained with an external test set selected using Duplex algorithm. Thirteen samples were selected for this test set.

From the four PLS models built, the best results were obtained with a PLS model composed of four PLS factors calculated based on the NIR spectra, pretreated with SNV followed by the calculation of the first derivative. The calculated validation parameters for this model are summarised in Table 4. With RMSE values between 4.61 and 5.78 and R^2 values between 0.83 and 0.89, it can be concluded that a good model was obtained using the NIR spectra. For what concerns the residuals, a random distribution was obtained (see Figure S1e) for both cross validation as test set with a mean absolute and maximum residual for cross validation of 4.1% w/w and 12.0% w/w and for the test set of 4.4% w/w and 15.5% w/w, respectively. For both cross validation and test set only, one sample had a residual higher than 10% w/w.

Ketamine

NIR spectra for 32 samples were recorded and used for building PLS models. Duplex algorithm resulted in the test set of seven samples covering best the data space and the ketamine dosage range. The best model was obtained by applying PLS to the spectra pretreated with SNV. This model was composed of four PLS factors and showed some promising validation parameters (Table 4). Determination coefficients were minimal 0.89, and the RMSE values were between 4.62 and 5.15, pointing at good predictive abilities of the obtained model. When the residuals are investigated, a random distribution was obtained (see Figure S1f). A mean absolute residual for cross validation of 3.8% w/w was obtained, and only one sample had a residual higher than 10% w/w (12.7% w/w), which was also the sample with the highest residual. For the test set, a mean absolute residual of 3.7% w/w and a maximum residual of 9.1% w/w were observed.

4 | DISCUSSION AND CONCLUSION

In this paper, both qualitative and quantitative models were built using PLS algorithms and two different spectroscopic techniques for the analysis of party drugs presented as white powders.

In the first instance, 287 collected samples were analysed using classical analytical techniques, followed by recording both mid-IR and NIR spectra. The obtained spectral data were consequently modelled using the identity of the active substance (qualitative models) or the purity/dosage values (quantitative models) as response.

When comparing the qualitative models obtained with both mid-IR as NIR spectra, it was observed that the model using mid-IR clearly shows better validation parameters than the model obtained with the NIR spectra (Tables 2 and 3) and therefore is more suited to distinguish the targeted samples (amphetamine, cocaine and ketamine) from samples containing other active substances and to discriminate among them. The reason for this is that mid-IR spectra are more specific than NIR spectra, and therefore chemometrics can better extract the information related to the targeted compounds from the spectral data. This is also illustrated by the loadings obtained during the exploratory PCA (Figure 3). It can clearly be seen that the most important wavenumbers for discriminating the different samples are related to specific ranges in the IR spectra, corresponding to specific bands for the targeted compounds. It was also demonstrated that the chemometric approach resulted in higher correct classification rates, compared with simple spectral match, because according to the latter only 64% of the samples were correctly classified due to samples with low purity or the presence of adulterants. The chemometric approach resulted in 96.1% and 93.1% for training and test set, respectively.

On the other hand, for quantitative purposes, better-performing models were found using the NIR data. For amphetamine and ketamine, mid-IR resulted in acceptable models, but the models built with NIR data were clearly better with higher determination coefficients and lower RMSE values. For cocaine, an acceptable model could be obtained using NIR, although this was not the case when using mid-IR.

In addition, it needs to be mentioned that the NIR analyses in this project were performed with a handheld device. Theoretically, even better models could be obtained when the NIR analysis would be performed using a benchtop instrument because of the higher resolution and an increased spectral range, resulting in more qualitative NIR spectra.

Another point of attention is the relatively small size of sample sets used for quantitative analysis. The small sample set and therefor also the small external test set are probably the reason why for some models better results were obtained with the external test set compared with cross validation.

Based on the results obtained in this paper, we would propose the following strategy for mobile testing of white powders using IR spectroscopy:

1. Measure the mid-IR spectrum and classify the sample according to the PLS-DA model. In case the sample is classified as 'other', the sample should be sent to an accredited laboratory for further analysis.
2. In case the sample is found positive for amphetamine, cocaine or ketamine, the NIR spectrum should be recorded and an estimation of the dosage/purity can be obtained by using the respective PLS models.

The presented approach can be combined with the approach described for MDMA tablets,[19] allowing the on-site analysis of the majority of the samples encountered in nightlife settings encountered in Belgium. When a sample is not part of the big four (MDMA, amphetamine, cocaine and ketamine), the sample should still be sent to a laboratory or, alternatively, be analysed using another 'mobile' technique. First choice here could be a mobile UHPLC equipped with a QDA. The gold standard is clearly GC-MS, though it is difficult for on-site implementation, except if a real mobile laboratory is available. Even if a UHPLC-QDA instrument is available, the spectroscopic analysis of the four major groups would allow to reduce cost, analysis time and workload (sample preparation).

An advantage of the presented approach is that the models are based on the samples themselves, taking into account matrix variations and eliminating the necessity of expensive reference standards. The models can be updated by introducing increasing numbers of samples, increasing the variability taken into account and resulting in better, more robust models, allowing better identification rates and more accurate quantifications. The presented approach is focussed on the four major groups of illicit drugs encountered at the summer festivals, though when enough samples of another illicit drug could be found, spectral data bases and new models including this compound could be added to the approach, allowing a broadening of the scope towards other active compounds.

A limitation of the presented approach is the fact that three different instruments are necessary, a mid-IR instrument, a NIR and a more specific one for samples not belonging to the groups of MDMA, amphetamine, cocaine or ketamine, which could limit practical (mobile) implementation in the field. The problem of the need of both mid-IR and NIR can be solved by the fact that some instruments are on the market, mainly benchtop equipment, that allow to do both. For the more specific analytical techniques, still more investment or an offsite laboratory will be necessary.

Another disadvantage is that quantitative analysis with NIR only estimates the dosage/purity, and this in a range of 5% w/w for MDMA tablets[19] and 10% w/w for amphetamine, cocaine and ketamine samples. The latter could be improved by selecting more specific spectral regions of the NIR spectrum. This should be done for each compound and adds an additional step in the process rendering automatic data interpretation more difficult and reducing the applicability for in-field analysis.

It also has to be said that this approach is to our knowledge the first that allows the characterisation of four different types of party drugs, encountered in the context of drug checking using only spectroscopy. Sure, spectroscopy and chemometrics were already used in this context, but always to characterise a specific type of samples like MDMA tablets[7–10,19] or cocaine.[11–18] Though all these papers focussed on only one type of drug samples and made often use of reference standards or specific calibration samples for quantitative estimations. Also, this approach was developed in the context of drug checking and prevention and not in the context of law enforcement. The approach could be used in this context though off-site confirmation will always be necessary, especially when prosecution will follow.

In general, it can be concluded that a practical and cost-effective approach was presented to increase the number of samples, presented as white powders, that can be analysed on-site in the context of drug checking using only spectroscopy. Combined with the results of Deconinck et al.,[19] our approach allows a first characterisation of the majority of samples encountered at the targeted events and this using purely spectroscopic techniques with minimal sample preparation and analysis time. Increased miniaturisation of both mid-IR and NIR spectrometers in the future provides even more perspectives for the presented approach.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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