Forensic Science International 384 (2026) 112923

Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

Profiling the volatile organic compound signature of illicit drugs

Clément Martin [a,c,*], Hélène Soyeurt [a], Natalie Meert [c], Fanny Ruhland [a], Claire Diederich [b], François Verheggen [a]

[a] Terra, Gembloux Agro-Bio Tech, University of Liège, Passage des Déportés 2, Gembloux 5030, Belgium
[b] NARILIS and Dept. of Veterinary Medicine (IVRU), University of Namur, Rue de Bruxelles 61, Namur B-5000, Belgium
[c] Drugs Expertise Center, National Institute of Criminalistic and Criminology (INCC), Chaussée de Vilvoorde,1120 Neder-over-Heembeek, Brussel, Belgium

ARTICLE INFO

Keywords:
Volatolomic
PLS-DA
Drug detection
Forensic chemistry
Drug detection dogs

ABSTRACT

Understanding the intricate chemical profiles of illicit drugs is crucial for combating their unregulated distribution. While gas sensors have been proposed for their detection, dogs remain the primary tool used for law enforcement agencies. However, concerns about their reliability persist due to limited information on the specific odor they detect. To improve both sensor development and dogs training, robust chemical characterisation is needed.

This study aims to characterize the volatile chemical profiles released by illicit drugs seized by the Belgian Police—including amphetamine, cannabis, opium, cocaine, heroin, MDMA, and ketamine—using headspace volatile sampling coupled with gas chromatography and mass spectrometry. In addition to identifying the most abundant compounds for each drug, a partial least square discriminant analysis (PLS-DA) was employed to define their chemical signature. The model achieved a 92% success rate in detecting and differentiating the tested drugs.

These findings highlight the potential for field-deployable gas sensors targeting key signature compounds, and may significantly enhance the detection dog's performance.

1. Introduction

Illicit drugs represent a complex and diverse array of psychoactive substances, each with its own unique origin, mode of preparation, and resulting chemical composition. In the European Union, the quantity of seized drugs increases each year, with cannabinoids being the most seized drugs (69% of seized drugs in 2023) followed by cocaine and amphetamine-type stimulants (ATS) [1]. Among the different detection techniques, drug detection dogs are probably the most widely used method, especially to detect drug presence on people or in hidden locations (*e.g. luggage, parcels)*. From naturally occurring plant-derived narcotics, such as opiates and cannabinoids, to synthetic compounds like methamphetamine and 3,4-methylenedioxy-N-methamphetamine (MDMA), the spectrum of illicit drugs encompasses a wide range of substances with varying chemical structures. In the landscape of substance abuse, illicit drugs may be classified according to their active chemical agents. Cannabinoids (*i.e. cannabis, hashish)*, exemplified by their primary components tetrahydrocannabinol (THC) and cannabidiol (CBD), underscore the diversity of plant-derived substances. Stimulants such as cocaine, (meth)amphetamine, MDMA contrast sharply with opioids like heroin. The diversity in origins and modes of preparation not only underscores the complexity of the illicit drug trade but also significantly influences the chemical composition of these substances [2–5]. Since 2016, there has been growing interest in applying chemometric analyses to illicit substances to extract key information that can help predict the origin of the drugs or even the synthetic methods used in their production [1,6–8].

Deciphering the volatile profile of illicit drugs holds significant promise for the prediction of key information related to drug origin. It has several fields of application, from forensic investigations to public health, offering insights into tracing drug origins and linking evidence to specific criminal activities [2,9,10]. In addition to highlighting marker compounds related to intrinsic characteristic of a seized drug, characterizing volatile biomarkers could also aid drug detection dog handlers to tailor training protocols targeting these specific markers more effectively [2,11–13].

* Correspondence to: Chaussée de Vilvoorde,1120 Neder-over-Heembeek, Brussel, Belgium.
E-mail addresses: Clement.Martin@just.fgov.be (C. Martin), hsoyeurt@uliege.be (H. Soyeurt), Natalie.Meert@just.fgov.be (N. Meert), fanny.ruhland@uliege.be (F. Ruhland), claire.diederich@unamur.be (C. Diederich), fverheggen@uliege.be (F. Verheggen).

https://doi.org/10.1016/j.forsciint.2026.112923

Available online 11 March 2026

Gas chromatography (GC) coupled with mass spectrometry (MS) allows the separation and analysis of complex mixtures of volatile organic compounds (VOCs), while also enabling the identification of their chemical structures [8,10,14,15]. Solid-phase microextraction (SPME) and headspace sampling allow to trap VOCs [16–19]: while SPME enables rapid and efficient sample preparation by trapping VOCs from the headspace of drug samples, headspace collection facilitates VOCs' profile quantification compared to SPME by enriching even trace-level compounds [20]. Less commonly used technics could also bring valuable insight for the detection of drugs' VOCs, such as proton transfer reaction-mass spectrometry (PTR-MS) or electronic nose (E-noses), that both provide real-time detection [12,21]. Thanks to recent technological advances in collection and separation methodologies, we believe dynamic sampling and GC-MS can enable the detection of trace levels of drug-associated VOCs using deep learning analyses as partial least square analyses.

Cannabis, heroin, and cocaine have so far received most of the volatolomic attention, while VOCs from methamphetamine and ecstasy (*e.g.*, MDMA) have received less attention [8,22]. Cannabis is known for its particular aroma, mainly composed of terpenes such as myrcene, limonene and pinene [16]. Various hydrocarbons have been detected from cocaine headspace, linked to the use of petroleum distillates during its extraction from coca leaves [23]. To date, no comprehensive comparison of the volatile profiles of available illicit drugs has been conducted to enhance our understanding of both the intrinsic variability of these substances and the presence of stable compounds. Identifying such stable compounds could benefit air monitoring efforts aimed at detecting drug presence, improve the efficiency of detection dogs through targeted training, and even support the identification of variable compounds that could act as markers for tracking drug batches across specific regions.

Indeed, VOCs released by illicit drugs are impacted by multiple factors, each contributing to the high variability observed in drug odorant profiles during analysis. The chemical composition of the drug itself plays a pivotal role, as each additive, by-product and impurity contribute to its distinct odorant profile [2]. Additionally, factors such as geographical origin [10] and production method [24] can impart unique odorant signatures to these substances. Furthermore, packaging and storage conditions can induce chemical changes that alter the odorant profile over time [10,16].

A comprehensive understanding of the volatile profiles of illicit drugs is highly important for several reasons [25]. First, it is crucial for developing accurate detection methods, thereby reducing the risk of misidentification and ensuring precise law enforcement actions [16]. Moreover, identifying specific chemical signatures could enable differentiation among several variants, and thus help trace origins or distribution networks [2]. A better characterization of drug VOCs would also facilitate the identification of cutting agents, thereby aiding in purity assessment or evaluating potential health risks for consumers [26].

While previous studies have primarily focused on the volatile profile of individual illicit drugs, the present study aims to provide a comprehensive and comparative analysis of volatile organic compounds released by a broad spectrum of illicit substances—including commonly studied drugs such as cannabis, cocaine, and (meth)amphetamine, as well as less-characterized substances like ketamine, opium, and MDMA. By analyzing different seizures using a standardized TD-GC-MS methodology, this work integrates multivariate statistical analyses allowing the identification of both robust and specific chemical signatures. Through this approach, the study offers preliminary insights into the intrinsic chemical variability and stability of drug-emitted volatiles. While based on a limited number of substances, it nevertheless opens promising perspectives for tracing drug origins and improving field detection strategies.

2. Materials and methods

Drug access and purity - Nineteen drugs (Table 1) samples were seized between July 2018 and December 2019 and stored at the headquarters of the Belgium police canine brigade (Neerhespen, Belgium). Each drug seizure was kept individually in a plastic bag placed inside a sealed glass bottle and stored at 10°C in the dark. The samples were never in contact with dogs prior the sampling to avoid any contaminations. The purity of illicit molecules in each sample was provided by the National Institute for Criminalistics and Criminology (Brussels, Belgium) (Table 1).

Volatile collection – All volatile samplings took place in the headquarters of the Belgium police canine brigade (Neerhespen, Belgium) under the supervision of police officers, between February and March 2020 (maximum 18 months after the seizure). Seven categories of drug were collected from the 19 collected drug samples in 5 replicates: cannabinoids (n = 20), cocaine (n = 15), amphetamine (n = 10), ecstasy (n = 25), heroin (n = 15), opium (n = 5), and ketamine (n = 5). Each drug sample came from different seizures (cannabinoid ($n_{seizures}$=4) (*i.e.* marijuana ($n_{seizures}$ =2) and hashish ($n_{seizures}$ =2)), cocaine ($n_{seizures}$ =3), amphetamine ($n_{seizures}$ =2), ecstasy ($n_{seizures}$ =5), heroin ($n_{seizures}$ =3)) except for ketamine and opium which came from one seizure. Replicates were obtained from distinct, unopened packets within the same seizure to preserve intra-seizure heterogeneity. Based on preliminary assays, the drug weight necessary to detect sufficient VOCs was set at 0.1 g for marijuana and hashish; 1.0 g for heroin and ketamine; 5.0 g for opium and 10.0 g for ecstasy (representing approximately 20 pills). Volatile samplings were performed in a sealed polytetrafluoroethylene (PTFE) chamber (cylinder, d = 7 cm, h = 12.5 cm). An empty chamber was sampled as control. Air was pulled at 200 mL.min^{-1} in the chamber to carry the volatile compounds inside a hydrophobic thermal desorption tube (Tenax TA®/Carbograph®; Gerstel, Germany) using an air pump (GilAir plus, Gilian Sensidyne, St Petersburg, Florida, United States). The sampling lasted 10 min and was performed at room temperature (19.5 ± 1.1°C). A charcoal filter was used to filter the air

Table 1
List of the 19 illicit drug seizures, including their concentration in active compounds (%) and the year of seizure, when available. THC: Tetrahydrocannabinol; MDMA: 3,4-methylenedioxy methamphetamine. na is used for unquantified active compound. The concentrations of cocaine, MDMA and ketamine are expressed as the hydrochloride salt form. The concentration of amphetamine is expressed as the sulphate salt form and the concentration of heroin is expressed as the base form.

	Product	Type	Active compound	Year of Seizure
1	Cannabis	Marijuana	16% THC	2019
2	Cannabis	Marijuana	15% THC	
3	Cannabis	Hashish	23% THC	
4	Cannabis	Hashish	1,51% THC	
5	Opium	Resin	na	
6	Cocaine	Powder	76% Cocaine-hydrochloride	2019
7	Cocaine	Powder	80% Cocaine-hydrochloride	2018
8	Cocaine	Powder	92% Cocaine-hydrochloride	2019
9	Heroin	Powder	48% Heroin base	2018
10	Heroin	Powder	55% Heroin base	2018
11	Heroin	Powder	55% Heroin base	2018
12	Amphetamine	Powder	23% Amphetamine sulphate	2018
13	Amphetamine	Powder	96.5% Amphetamine sulphate	2019
14	MDMA	Tablets	95% MDMA-hydrochloride	2018
15	MDMA	Tablets	88% MDMA-hydrochloride	2019
16	MDMA	Tablets	42% MDMA-hydrochloride	2018
17	MDMA	Tablets	29% MDMA-hydrochloride	2018
18	MDMA	Tablets	46% MDMA-hydrochloride	2019
19	Ketamine	Crystals	95% ketamine-hydrochloride	2019

entering the chamber. To allow quantification, an internal standard was then injected on each tube (chlorobenzene, 42.5 ng, Sigma-Aldrich, analytical standard, d=1.106 g.mL^{-1}, p = 100%). After sampling, TD-tubes were sealed and stored at 4 °C until analysis, which was performed within 48 h. To validate the method, ecstasy (synthetic) and cannabis flower (natural) were selected as model drugs. Due to limited access, sampling was restricted to 10 min, prioritizing replicates over duration. Method optimization focused on sample quantity. Breakthrough and carryover were systematically evaluated, and the final protocol was chosen based on their absence. Since the assumptions of normality (p-value = 0.185) and homoscedasticity (p-value = 0.181) were met, repeatability could be reliably assessed and was deemed satisfactory.

Gas chromatography mass spectrometry analyses – Tubes were analysed by thermodesorption gas chromatography coupled with a mass spectrometer (TD30R, QP2020 NX, Shimadzu®, Kyoto, Japan), set in split mode (split ratio = 20). Sampling tubes were first thermo-desorbed at 280°C during 8 min (TD30R, Shimadzu®, Kyoto, Japan) before being cryofocused by the Peltier effect in a Tenax TA trap set at −20°C. The volatiles were then heated at 280°C and separated on the column (5% diphenyl; 30 m×0.25 mm I.D.; 0.5 µmm film thickness, Agilent Technologies). Separation occurred under a constant helium flow set at 1 mL. min^{-1}. The separation started with an initial temperature of 40°C. A first temperature ramp of 8°C min^{-1} was immediately applied up to 210°C. Finally, a second ramp of 25°C min^{-1} was applied up to 300°C. This last temperature was held for 5 min. All compounds were then detected by mass spectrometry (voltage difference = 1 kV, source temperature = 200℃, transfer line temperature = 230℃, scanned mass range: 30–350 *m/z*). They were identified by comparing the recorded mass spectra with spectral libraries (NIST and FFNSC) and by comparing the retention indexes previously calculated based on n-alkanes series. VOCs detected in ≥ 50% of replicates were retained in the final profile as they origin are uncertain due to the exceptional detection. This threshold was applied to reduce the likelihood of including compounds arising from environmental background, matrix-specific artifacts, or experimental contamination.

Statistical analysis – Chromatograms were aligned using GCAligner 1.0 software [27], and VOCs identified in the control samples were removed. Peak areas were adjusted according to the weight of each drug tested. Pie charts were produced for each drug category to highlight the major compounds of their volatile profile using Excel software. To assess potential differences among drug categories (Table 1), volatile profiles were compared using permutational multivariate analyses of variance (permMANOVA) with a Bray distance matrix and 999 permutations ('adonis' command, R-package vegan). P-values were adjusted using Bonferroni's correction to mitigate type I error inflation due to multiple testing. Subsequently, for significant results ($p < 0.05$), multivariate pairwise analyses were conducted to identify differences between drug categories ('pairwise.adonis' command, R-package vegan). Homoscedasticity was assessed using the 'betadisper' function [28]. Finally, we used a partial least squares discriminant analysis (PLS-DA) to construct models that better highlight the key compounds distinguishing the analysed drugs. PLS-DA was chosen as some peaks were correlated to each other. PLS-DA aims to establish a model that segregates observations into classes using the X matrix, comprising linear combinations of volatile composition called factors, and the Y matrix, containing dummy variables describing class membership. This analysis identifies a discriminant plan where the projected observations on the components are effectively separated according to class. From the PLS-DA model, the variable importance in projection (VarImp) coefficients were extracted for each VOC allowing assessment of their importance in the volatile profile of each drug category. A spider chart (Excel software) was then plotted to better assess the number of VOCs driving the differences among each drug category.

3. Results

Illicit drug VOCs profile - A total of 218 volatile compounds was identified from the 95 drug samples and organised per category: amphetamine (n_{VOCs}=84), cocaine (n_{VOCs}=79), cannabinoids (n_{VOCs}=88) [hashish (n_{VOCs}=68) and marijuana (n_{VOCs}=62)], MDMA (n_{VOCs}=54) and heroin (n_{VOCs}=21). No VOC was identified in the headspace of opium and ketamine samples. The total amounts of VOCs (mg of volatile compounds per gram of drug and hour of sampling) were calculated for each drug category (mean ± SD): cannabinoids (252.94 ± 68.71 mg.g^{-1}.h^{-1}, including marijuana (338.53 ± 115.63 mg.g^{-1}.h^{-1}) and hashish (167.35 ± 74.26 mg.g^{-1}.h^{-1})), amphetamine (27.81 ± 10.50 mg.g^{-1}.h^{-1}), cocaine (7.29 ± 3.82 mg.g^{-1}.h^{-1}), heroin (1.42 ± 0.55 mg.g^{-1}.h^{-1}) and MDMA(13.97 ± 4.67 mg.g^{-1}.h^{-1}). Regarding cannabinoids (including marijuana and hashish) four compounds accounted for more than half of the chemical signature, all belonging to the terpene's family (Fig. 1). Similar observations were noted for both heroin and cocaine, where three compounds together accounted for over half of the total amount of the detected VOCs. The odor profile of amphetamine and ecstasy appeared more complex, as the most prevalent compounds only made up 10% of the total VOC amount. Chromatograms are provided in supplemental data 1.

As expected, the multivariate statistical analysis (permMANOVA) indicates significant differences in VOC profiles among the drug categories ($F_{4,57} = 3.43$, $p < 0.001$), with all categories differing from one another (pairwise comparisons, $p < 0.05$).

Identification of key volatiles – To highlight the compounds driving differences among drug categories, we conducted a PLS-DA. This model includes 11 factors (below the threshold of 10 VOCs per factor) and achieves an overall accuracy of 91.8% (Kappa = 0.893). Sensitivity was high for most of the tested drugs (ranging from 0.73 to 1.00), although four heroin samples were misclassified. In terms of specificity, the model demonstrates high specificity for all drugs (specificity = 1.00) except for ecstasy, where seven samples from other drugs were incorrectly classified as ecstasy (Table 2).

Each identified VOC was assigned a VarImp coefficient, indicating its contribution to the model's ability to distinguish among drug profiles. A higher coefficient suggests greater contribution of the compound in discriminating a drug from others. A high VarImp may also be attributed to compounds that should not be present in the drug VOCs profile. Indeed, the absence of specific compounds may serve as a characteristic feature of a given drug. To visualize the key contributors to classification, VarImp coefficients were plotted to provide an overview of the compounds driving the differentiation among the drug categories (Fig. 2).

Specifically, 2,2-dimethyl-decane, 3-methyl-2-undecene, 2-propenoic acid butyl ester, 2,4-di-tert-butylphenol, and pseudococaine exhibited VarImp coefficients exceeding 60% in predicting the **cocaine** volatilome. Their presence therefore provided confidence that the sample contained cocaine. Despite being trace compounds, they significantly contributed to the identification process.

In the case of **MDMA**, 2,5-dimethyl-nonane, lavandulyl 3-methylbutanoate, nonanal, 4-hydroxy-4-methyl-2-pentanone, and 2-ethyl-1-hexanol acetate had VarImp coefficients exceeding 60%. While pentadecane had a relative abundance of 1%, the others were all trace compounds.

Heroin was distinguished by the presence of atrolactic acid, which boasted a confidence coefficient of 100%. Additionally, 3-propyl-2,4-pentadien-1-ol, 1,2-propanediol 1-acetate, and 3-heptanone exhibited high coefficients exceeding 70% in predicting the heroin volatilome. Except for 1,2-propanediol 1-acetate (with a relative abundance of 13.7%), all were trace compounds.

Amphetamine was identifiable by the presence of the following compounds: 1,1-(1-ethenyl-1,3-propanediyl)bis-benzene, 4-piperidin-1-yl-7,8-dihydro-6H-thiazolo[4,5-*c*]azepine, methyl-3,4-methylenedioxy amphetamine, 3-chloro-1-phenyl-1-propanone, and methyl-isopropyl-MDA. Only 1,1-(1-ethenyl-1,3-propanediyl)bis-benzene was

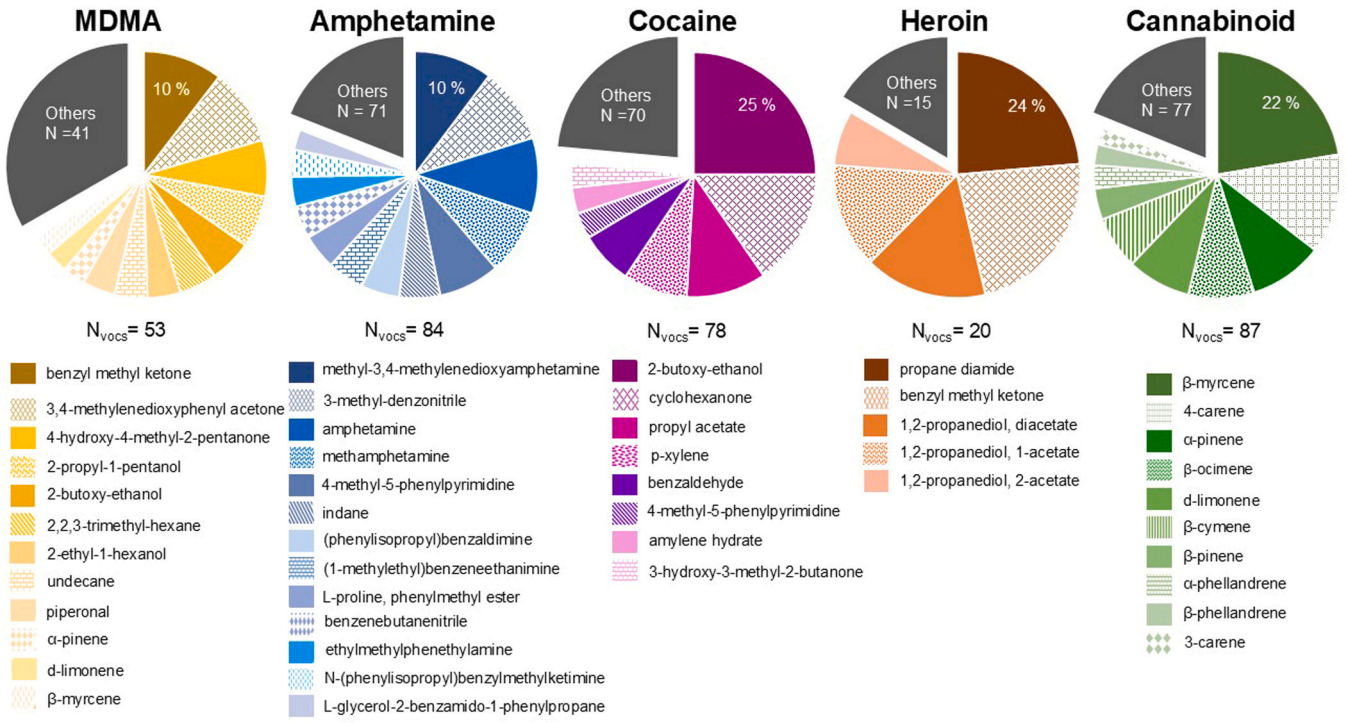


Fig. 1. Pie charts displaying the relative proportions of the VOC contributing to the total detected compounds in each drug category profile. Less abundant compounds are grouped under the label 'Others,' along with their respective numbers for each drug category.

Table 2
Classification performance metrics for the PLS-DA models based on the drug volatilome.

Reference	Amphetamine	Cannabinoid	Cocaine	MDMA	Heroin
Prediction					
Amphetamine	10	-	-	-	-
Cannabinoid	-	19	-	-	-
Cocaine	-	-	13	-	-
MDMA	-	1	2	25	4
Heroin	-	-	-	-	11
Sensitivity	1	0.95	0.86	1	0.73
specificity	1	1	1	0.88	1

consistently detected in all replicates, while the others were present in half of them. These were all trace compounds, each contributing to less than 1% of the total profile, except for methyl-3,4-methylenedioxyamphetamine, considered a major compound with a relative abundance of 10%.

Cannabinoids were identifiable by the presence of linalool, β-selinene, selina-3,7(11)-diene, eremophylene, terpineol and pinocarveol. all were present in over 80% of the replicates, while pinacarveol was less prevalent. However, they were all trace compounds, each accounting for less than 1% of the total VOC profile.

For both amphetamines and cannabinoids, a substantial number of VOCs must be present for confident identification. Considering all VOCs with a confidence coefficient exceeding 40%, 24 VOCs were highlighted for cannabinoid identification and 14 for amphetamine. Among these 24 compounds for cannabinoids, only two were major compounds: 4-carene (relative abundance = 13%) and α-pinene (relative abundance = 9%). Detailed results for each compound and model are provided in Table 3.

4. Discussion

In this study, we successfully characterized the VOC profiles of seven drug categories. Our methodology allowed the identification of VOCs from five of them: cannabinoids, cocaine, MDMA, heroin and amphetamine. The least abundant profile was attributed to heroin, with concentrations reaching 1.5 ng.g^{-1}.h^{-1}. As previously demonstrated, cannabinoids emerged as the most odoriferous of the tested drugs, exhibiting a total concentration of 252.94 ± 68.71 ng.g^{-1}.h^{-1}. Additionally, smell of cannabinoids was the most diversified [29]. However, no VOC was detected for opium and ketamine, likely due to their compounds being below the detection limit or coeluting with environmental VOCs. To our knowledge, the volatile profiles of opium and ketamine have not been previously characterized. However, trained detection dogs appear to be able to detect the presence of low quantities of opium and ketamine in personal luggage (Ellen Van Krunkelsven, advisor biologist in the detection dog team from the Belgium federal police, oral communication). Given the challenges in detecting low-concentration VOC profiles, we recommend using more sensitive sampling techniques such as the HiSorb probe or solid-phase microextraction employing vacuum-assisted headspace and multi capillary trapping [30,31].

Interestingly, approximately half of the total volatile profiles of cannabinoids, cocaine, heroin are dominated by three to four major compounds. Cannabinoids are mainly composed of terpenes including β-myrcene, 4-carene and α-pinene with β-myrcene and α-pinene already reported as major compounds in previous studies on cannabis herbs and myrcene on hashish [4,29]. The profile of cocaine exhibits a higher diversity, featuring compounds encompassing ketones, esters, and aromatics, likely stemming from the utilization of solvents during its extraction process. For example, propyl acetate, identified as the third most abundant compound, is a trace of the primary processing solvent commonly associated with the Colombian manufacturing process [32]. Major compounds of heroin mainly include esters [24].

In contrast, MDMA and amphetamine display less chemical diversity among dominant compounds; the most abundant account for only 10% of the total VOCs profile. However, the odor sampling method facilitates the detection of compounds structurally related to amphetamine, such as methyl-3,4-methylenedioxyamphetamine and methamphetamine. Additionally, other compounds serving as markers of synthetic routes

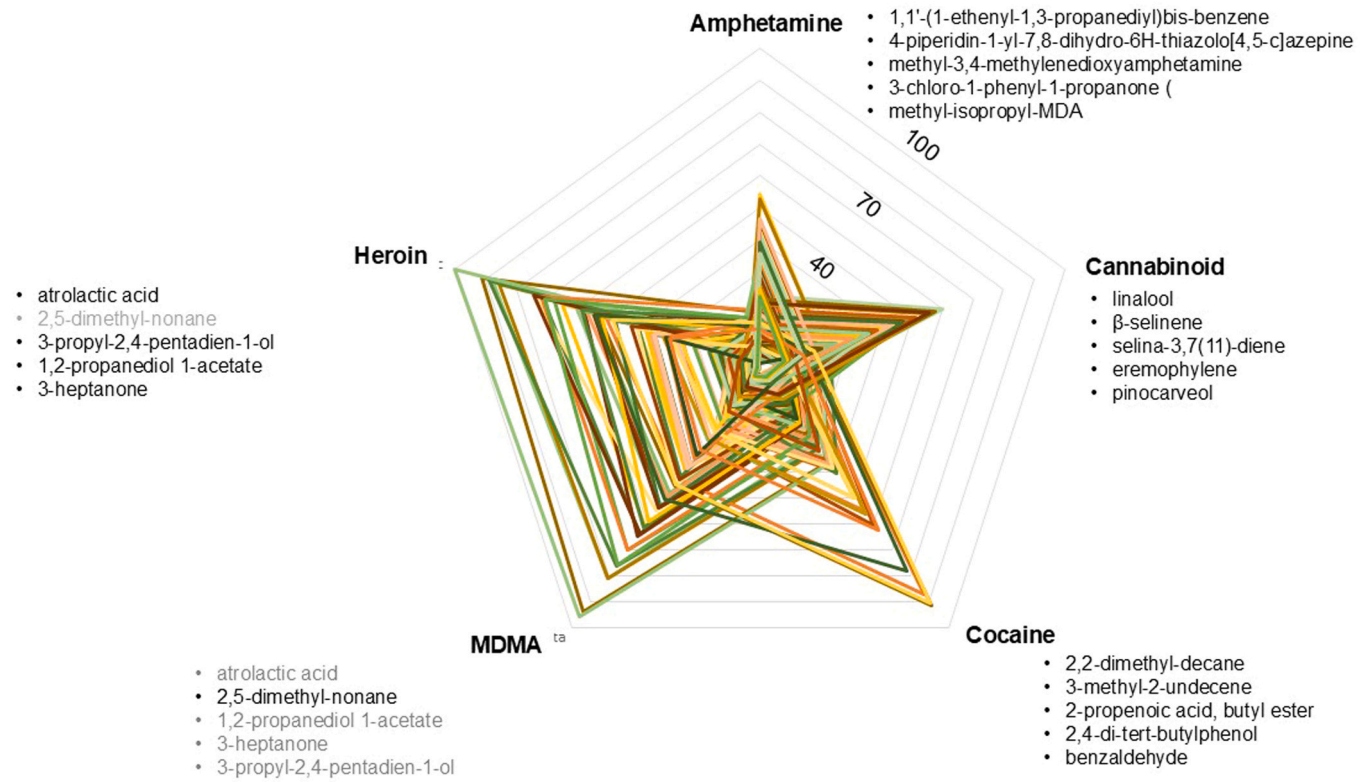


Fig. 2. The spider chart displays all detected compounds represented by each line and their respective contribution in the predicted models generated from the PLSDA analyses. Compounds that do not contribute to the predicted model are centralized on the chart, whereas those extending towards the periphery significantly influence the model predictions. Colours allow to individualize each compound on the chart. The five more important compounds for the model to discriminate each drug are proposed on the spider (grey compounds were not detected on the volatile compounds profile of the drug).

can be identified, such as 4-methyl-5-phenyl pyrimidine, which is indicative of the Leuckart route commonly used in amphetamine production [33,34]. Within the major compounds of MDMA, piperonal has been identified. Piperonal was commonly utilized alongside safrole in the synthesis of MDMA [29,35]. However, these precursors are no longer registered in the European Union for MDMA production [1]. Precursors of other drugs (*i.e.* benzyl methyl ketone, 3,4-methylenedioxyphenyl acetone) have been detected in this work, indicating a potential combination of drugs within the analyzed tablet [36–39].

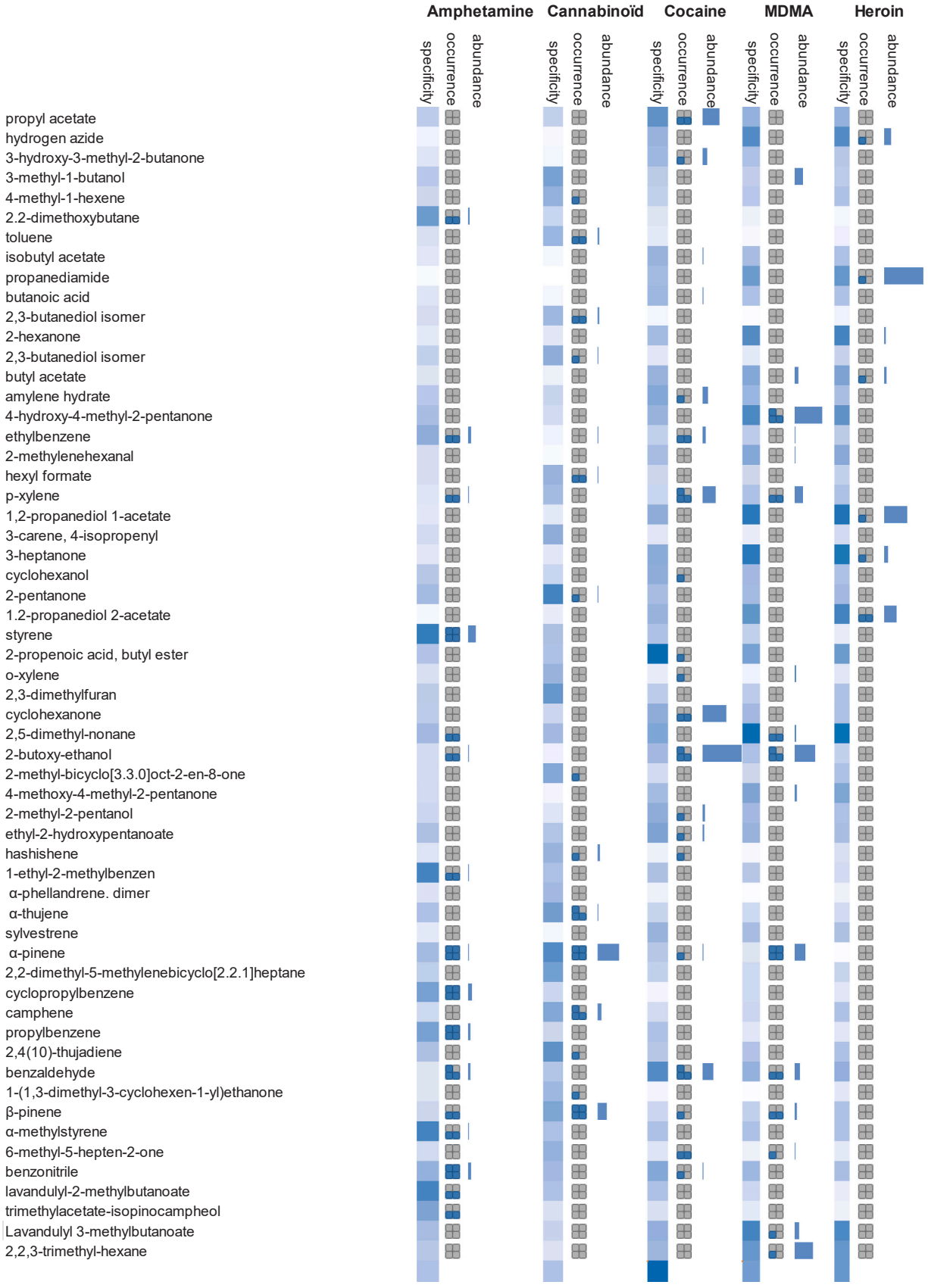
The methods we developed successfully identified unique compounds in specific drugs. For instance, hashishene was found in about half of the cannabinoid samples. It derives from myrcene and is exclusively found in hashish [4]. Pseudococaine has also been detected in one third of the cocaine samples. It is a natural impurity that can contaminate cocaine during the extraction process from coca leaves [40]. In amphetamine samples, the impurities (N-(-phenylisopropyl)benzylmethylketimine) associated with all major synthesis amphetamine routes (*i.e.* Nagai, Emde and Leuckart) was detected [8]. However; in Belgium and Netherlands only Leuckart is used in the production of amphetamine [41]. This compound is also a by-product formed during methamphetamine synthesis [33]. These results indicate that VOCs analysis is a potent method for characterizing both common and novel illicit drugs. By examining drug VOCs, it becomes possible to gather information about the production process, origin, presence of cutting agents, and potentially even information about the distributors involved [2,8,34].

Results from our PLS-DA model are promising for the determination of key VOCs associated with some specific illicit drug categories. Our model based on 11 dimensions, achieved an overall accuracy of 91.8% and successfully classified all investigated drugs ($n_{categories} = 7$, $n_{drug\ samples} = 95$). This model, implemented for the first time on illicit drug samples, shows comparable results with studies dedicated to distinguish other matrix, based on VOCs [42]. The model is also highly specific for all drugs studied except MDMA, for which seven other drugs samples were associated. Impure MDMA contains a high quantity of cutting agents which could explain the difficulty to build a highly specific model for this drug especially regarding the purity of our MDMA samples [2]. On the other hand, the model demonstrates high sensitivity for detecting MDMA and amphetamine, as no misclassifications were observed. Conversely, the lowest sensitivity was observed for heroin, with four samples incorrectly classified by the model as MDMA. This misclassification can be attributed to the shared compounds identified as specific to both drugs, as illustrated in the spider chart. The key difference between the two lies in the unique compounds present in the VOC profiles of heroin that are absent in MDMA, and vice versa.

In addition to identify both major and trace compounds as characteristic features of drugs, the model also ranked compounds based on their significance in distinguishing the various tested illicit drugs. While heroin, MDMA, and cocaine featured key compounds with a confidence coefficient exceeding 90%, amphetamines and cannabinoids relied more on a combination of compounds, each with a lower confidence coefficient, not surpassing 60%. Amphetamines and cannabinoids exhibited a greater diversity of compounds in their profiles, which may account for the absence of high confidence coefficients. Specifically, cannabinoids encompassed both marijuana and hashish, which released different VOCs due to distinct production methodologies: hashish is processed, while marijuana consists of dried flowering buds [4]. The natural variability of these drugs could also explain the observed diversity in their VOCs profiles. Additionally, the two amphetamine samples tested showed different purity levels, suggesting variable amounts of cutting agents, which may lead to diverse VOC emissions and contribute to lower confidence coefficients [2].

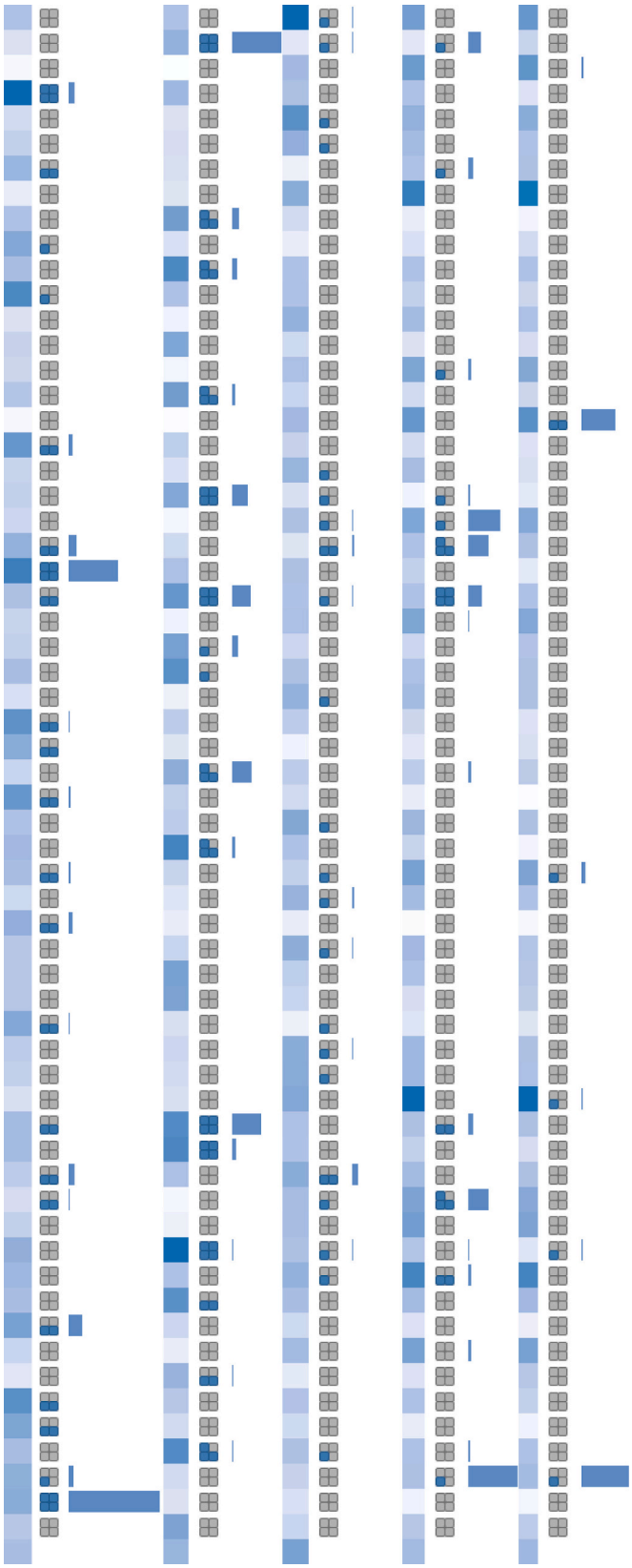
The comparison of these drugs and the generation of predictive VOCs profiles for each of them enhanced our understanding of illicit drug odor profiles. However, it is also important to acknowledge the intrinsic

Table 3
Volatile organic compounds profile of each tested drug. The specificity highlights the importance of the compounds in the predicted profile provided by the Partial Least Square analyses (dark blue: high specificity; light blue: low specificity). The occurrence represented by four squared highlights the number of times the VOCs were identified in the replicates. The relative abundance is represented by bar plot.



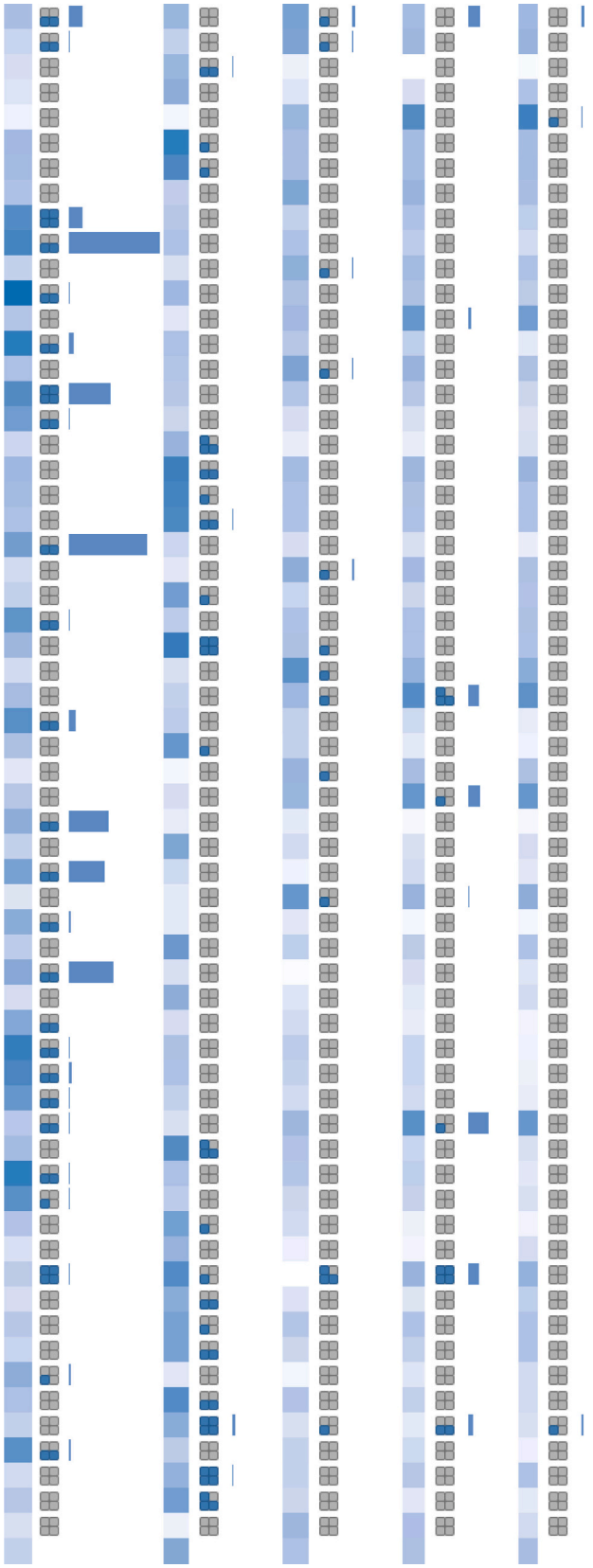
(*continued on next page*)

Table 3 (*continued*)



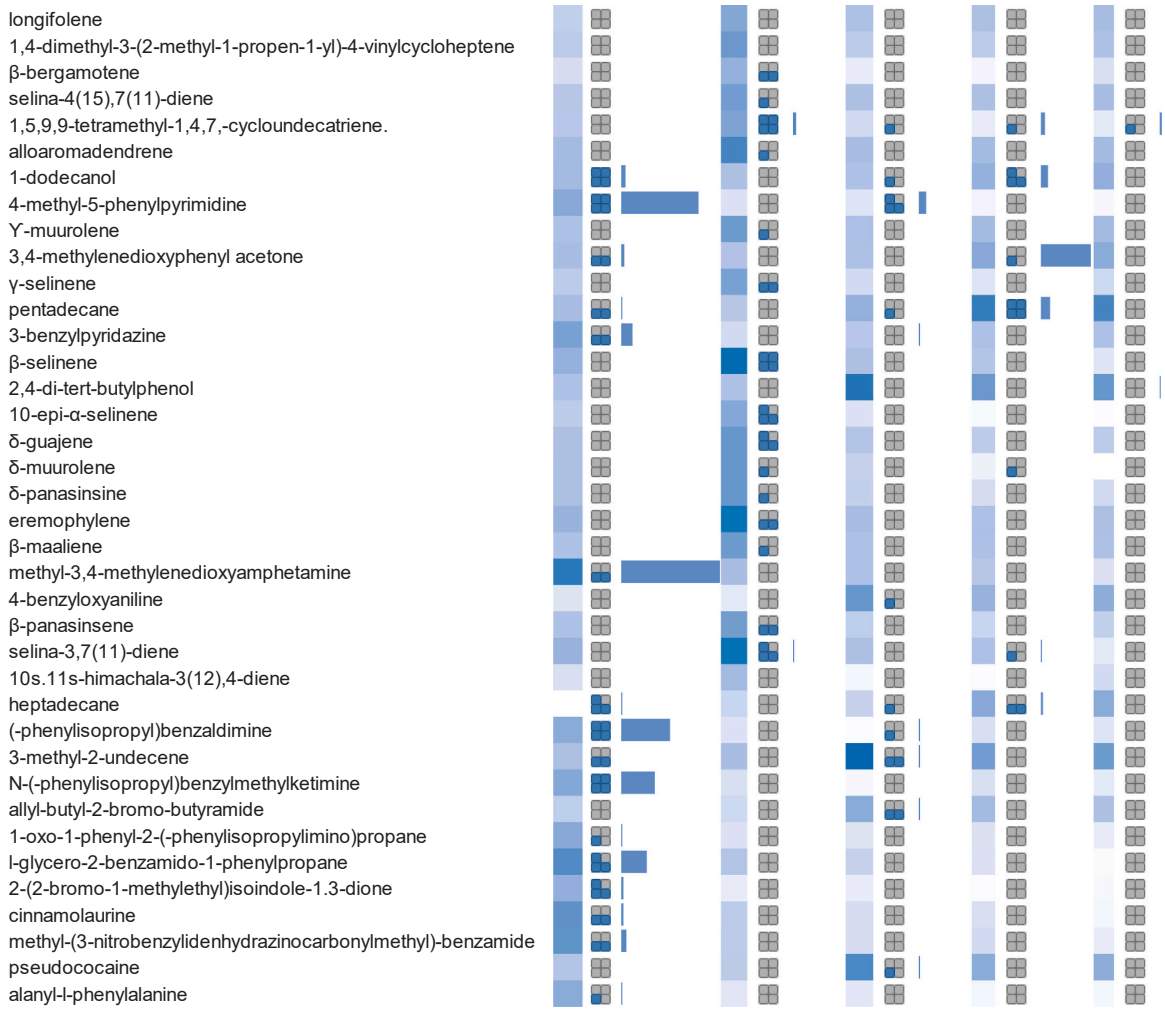
(*continued on next page*)

Table 3 (*continued*)

α-methyl-benzeneethanol	
2-methyl-benzonitrile	
mentha-1,5,8-triene	
3,4-dimethyl-2,4,6-octatriene	
2-ethyl-1-hexanol acetate	
pinocarveol	
3,7,7-Trimethyl-8-(2-methyl-propenyl)-bicyclo[4,2,0]oct-2-ene	
2.3-dihydro-4-methyl-indene	
(2-chloropropyl)-benzene	
3-methyl-benzonitrile	
benzyl acetate	
4-piperidin-1-yl-7,8-dihydro-6H-thiazolo[4,5-c]azepine	
3-methyl-undecane	
3-chloro-1-phenyl-1-propanone	
ethyl benzoate	
L-proline, phenylmethyl ester	
1-chloro-2-(2-propenyl)-benzene	
7-ethylidenebicyclo[3,3,0]octan-3-one	
2-isopropenyl-5-methylhex-4-enal	
4-terpineol	
cimen-8-ol	
methamphetamine	
naphthalene	
3-terpinolenone	
(3-chloroallyl)-benzene.	
α-terpineol	
α-terpinyl acetate	
dodecane	
α-methyl-diphenethylamine	
tridecanal	
methyl benzeneacetate	
3-phenyl-3-buten-2-one	
benzenebutanenitrile	
2-(3'-methyl-2'-butenyl)-3-methylfuran	
ethyl-α-methylphenethylamine	
4-benzyl-4,5-dihydroisoxazole	
2-phenylbutyronitrile	
2-ethylidene-6-methyl-3,5-heptadienal	
α-(1-methylethyl)benzeneethanamine	
2-methyl-3,5-hexadien-2-ol	
(2,3-dimethyldecyl)-benzene	
7-(ethoxysulfonyl)-indene-3-carboxylic acid	
1-phenyl-1-cyclopropanecarbonitrile	
1-phenylpropan-2-one oxime	
piperonal	
ylangene	
methyl-isopropyl-MDA	
methyl-benzamide	
copaene	
β-bourbonene	
tetradecane	
naphthalene	
4,8,8-trimethyl-2-methylene-4-vinylbicyclo[5.2.0]nonane	
trans-α-bergamotene	
dimethyl-benzamide	
α -santalene	
caryophyllene	
1,4-dimethyl-naphthalene	
α-bergamotene	
α-guaiene	
6,10-dimethyl-5,9-undecadien-2-one	

(*continued on next page*)

Table 3 (*continued*)



variability of each drug. This could be better captured by increasing the number of replicates and considering factors such as production origin or the context of seizure. A valuable direction for future work would be to develop independent models for each drug, accounting for their variability, and then integrate this information into a comprehensive model—a form of database for drug profiling. Such a model would not only be a powerful tool for tracking known substances, but also for classifying newly emerging ones. This progress could be applied in detection dog training, potentially improving canine performances, as dog detection largely depends on the olfactory stimuli used during training [43]. Introducing synthetic stimuli, that include key compounds making up the chemical signature of targeted illicit drugs, could enhance their detection performances. Furthermore, such models could also help chemical manufacturers to put on the market more reliable pseudo narcotic scents for training those biodetectors. However, before developing such training scents, it is crucial to better understand the detection spectrum of drug detection dogs. At present, the specific molecules they target remain largely unknown. Even in other detection contexts, it is still unclear whether dogs rely primarily on major compounds, recurrent compounds, or specific marker compounds. We therefore recommend further investigations to identify the olfactory cues actually used by dogs to recognize illicit substances—for example, through behavioral assays with single molecules. The results of this study could also assist in the identification of new drugs, such as cathiones (*e.i.* flakka, 4-methylmethcathione and 3-methylmethcathione), by comparing specific compounds of the new drug to one already identified volatilome [44]. The identification of by-products and cutting agents could also help forensic scientists trace the origin, manufacturing method, and distribution routes of illicit drugs.

CRediT authorship contribution statement

Clément Martin: Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Hélène Soyeurt:** Writing – review & editing, Formal analysis. **Natalie Meert:** Writing – review & editing. **Fanny Ruhland:** Writing – review & editing. **Claire Diederich:** Writing – review & editing, Supervision, Conceptualization. **François Verheggen:** Writing – review & editing, Validation, Supervision, Conceptualization.

Declaration of Competing Interest

Clément Martin
I have nothing to declare
Héléne Soyeurt
I have nothing to declare
Fanny Ruhland
I have nothing to declare

Natalie meert
I have nothing to declare
Claire Diederich
I have nothing to declare
François Verheggen
I have nothing to declare

Acknowledgement

This project was financially supported by the FNRS through a research credit and a postdoctoral research grant.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.forsciint.2026.112923.

References

[1] EUDA, Drug supply, production and precursors - the current situation in Europe (European Drug Report 2024), in: 2024. ⟨https://www.euda.europa.eu/publications/european-drug-report/2025/drug-supply-production-and-precursors_en⟩ (accessed June 19, 2025).
[2] A. Żubrycka, A. Kwaśnica, M. Haczkiewicz, K. Sipa, K. Rudnicki, S. Skrzypek, L. Poltorak, Illicit drugs street samples and their cutting agents. The result of the GC-MS based profiling define the guidelines for sensors development, Talanta 237 (2022), https://doi.org/10.1016/j.talanta.2021.122904.
[3] L. Dujourdy, V. Dufey, F. Besacier, N. Miano, R. Marquis, E. Lock, L. Aalberg, S. Dieckmann, F. Zrcek, J.S. Bozenko, Drug intelligence based on organic impurities in illicit MA samples, Forensic Sci. Int. 177 (2008) 153–161, https://doi.org/10.1016/j.forsciint.2007.11.013.
[4] M. Marchini, C. Charvoz, L. Dujourdy, N. Baldovini, J.J. Filippi, Multidimensional analysis of cannabis volatile constituents: identification of 5,5-dimethyl-1-vinyl-bicyclo[2.1.1]hexane as a volatile marker of hashish, the resin of Cannabis sativa L, J. Chromatogr. A. 1370 (2014) 200–215, https://doi.org/10.1016/j.chroma.2014.10.045.
[5] F. Franchina, L. Dubois, J.-F. Focant, High-dimensional analytical strategies for accurate metabolite profiling: application to cannabis. GCxGC Symposium, 2021. ⟨https://orbi.uliege.be/handle/2268/261101⟩.
[6] D. Carby-Robinson, P.W. Dalsgaard, C.B. Mollerup, K. Linnet, B.S. Rasmussen, Cocaine profiling method retrospectively developed with nontargeted discovery of markers using liquid chromatography with time-of-flight mass spectrometry data, Drug Test. Anal. 14 (2022) 462–473, https://doi.org/10.1002/dta.3130.
[7] S. Materazzi, A. Gregori, L. Ripani, A. Apriceno, R. Risoluti, Cocaine profiling: implementation of a predictive model by ATR-FTIR coupled with chemometrics in forensic chemistry, Talanta 166 (2017) 328–335, https://doi.org/10.1016/j.talanta.2017.01.045.
[8] S. Choe, J. Lee, H. Choi, Y. Park, H. Lee, J. Jo, Y. Park, E. Kim, J. Pyo, H.J. Lee, S. Kim, Estimation of the synthetic routes of seized methamphetamines using GC-MS and multivariate analysis, Forensic Sci. Int. 259 (2016) 85–94, https://doi.org/10.1016/j.forsciint.2015.12.018.
[9] S. Giannoukos, A. Agapiou, S. Taylor, Advances in chemical sensing technologies for VOCs in breath for security/threat assessment, illicit drug detection, and human trafficking activity, J. Breath. Res. 12 (2018), https://doi.org/10.1088/1752-7163/aa95dd.
[10] R.Z. Al Bakain, Y.S. Al-Degs, J.V. Cizdziel, M.A. Elsohly, Comprehensive classification of USA cannabis samples based on chemical profiles of major cannabinoids and terpenoids, J. Liq. Chromatogr. Relat. Technol. 43 (2020) 172–184, https://doi.org/10.1080/10826076.2019.1701015.
[11] C. Martin, C. Diederich, F. Verheggen, Cadaver Dogs and the Deathly Hallows — A Survey and literature review on selection and training procedure, Animals 10 (2020) 1–19, https://doi.org/10.3390/ani10071219.
[12] Z. Haddi, A. Amari, H. Alami, N. El Bari, E. Llobet, B. Bouchikhi, A portable electronic nose system for the identification of cannabis-based drugs, Sens. Actuators B Chem. 155 (2011) 456–463, https://doi.org/10.1016/j.snb.2010.12.047.
[13] T. Jezierski, E. Adamkiewicz, M. Walczak, M. Sobczyńska, A. Górecka-Bruzda, J. Ensminger, E. Papet, Efficacy of drug detection by fully-trained police dogs varies by breed, training level, type of drug and search environment, Forensic Sci. Int. 237 (2014) 112–118, https://doi.org/10.1016/j.forsciint.2014.01.013.
[14] L.S. Leite, V. Visani, P.C.F. Marques, M.A.B.L. Seabra, N.C.L. Oliveira, P. Gubert, V. W.C. de Medeiros, J.O. de Albuquerque, J.L. de Lima Filho, Design and implementation of an electronic nose system for real-time detection of marijuana, Instrum. Sci. Technol. 49 (2021) 471–486, https://doi.org/10.1080/10739149.2021.1887213.
[15] S. Rice, J.A. Koziel, Odor impact of volatiles emitted from marijuana, cocaine, heroin and their surrogate scents, Data Br. 5 (2015) 653–706, https://doi.org/10.1016/j.dib.2015.09.053.
[16] N. Wiebelhaus, D. Hamblin, N.M. Kreitals, J.R. Almirall, Differentiation of marijuana headspace volatiles from other plants and hemp products using capillary microextraction of volatiles (CMV) coupled to gas-chromatography–mass spectrometry (GC–MS), Forensic Chem. 2 (2016) 1–8, https://doi.org/10.1016/j.forc.2016.08.004.
[17] M. Chiarotti, R. Marsili, A. Moreda-Piñeiro, Gas chromatographic-mass spectrometric analysis of residual solvent trapped into illicit cocaine exhibits using head-space solid-phase microextraction, J. Chromatogr. B Anal. Technol. Biomed. Life Sci. 772 (2002) 249–256, https://doi.org/10.1016/S1570-0232(02)00109-5.
[18] S. Gura, P. Guerra-Diaz, H. Lai, J.R. Almirall, Enhancement in sample collection for the detection of MDMA using a novel planar SPME (PSPME) device coupled to ionmobility spectrometry (IMS), Drug Test. Anal. 1 (2009) 355–362, https://doi.org/10.1002/dta.81.
[19] M. Dei Cas, S. Arnoldi, L. Monguzzi, E. Casagni, C. Morano, E. Vieira de Manincor, C. Bolchi, M. Pallavicini, V. Gambaro, G. Roda, Characterization of chemotype-dependent terpenoids profile in cannabis by headspace gas-chromatography coupled to time-of-flight mass spectrometry, J. Pharm. Biomed. Anal. 203 (2021) 114180, https://doi.org/10.1016/j.jpba.2021.114180.
[20] J. Vercammen, P. Sandra, E. Baltussen, T. Sandra, F. David, Considerations on static and dynamic sorptive and adsorptive sampling to monitor volatiles emitted by living plants, HRC J. High. Resolut. Chromatogr. 23 (2000) 547–553.
[21] V. Reinstadler, R. Gutmann, F. Pitterl, K. Winkler, H. Oberacher, Gas Chromatography—High-Temperature Proton-Transfer Reaction Mass Spectrometry as a Novel Tool for Forensic Drug Testing, Separations 9 (2022), https://doi.org/10.3390/separations9110328.
[22] B. Mitrevski, B. Veleska, E. Engel, P. Wynne, S.M. Song, P.J. Marriott, Chemical signature of ecstasy volatiles by comprehensive two-dimensional gas chromatography, Forensic Sci. Int. 209 (2011) 11–20, https://doi.org/10.1016/j.forsciint.2010.11.008.
[23] T. Gostič, 2016, Qualitative Determination Residual Solvents Cocaine Samples Static Headspacegcms (Development Cocaine Profiling Methodology)6413.
[24] S. Rice, J.A. Koziel, The relationship between chemical concentration and odor activity value explains the inconsistency in making a comprehensive surrogate scent training tool representative of illicit drugs, Forensic Sci. Int. 257 (2015) 257–270, https://doi.org/10.1016/j.forsciint.2015.08.027.
[25] K.G. Furton, N.I. Caraballo, M.M. Cerreta, H.K. Holness, Advances in the use of odour as forensic evidence through optimizing and standardizing instruments and canines, Philos. Trans. R. Soc. B Biol. Sci. 370 (2015), https://doi.org/10.1098/RSTB.2014.0262.
[26] T.R. Fiorentin, M. Fogarty, R.P. Limberger, B.K. Logan, Determination of cutting agents in seized cocaine samples using GC–MS, GC–TMS and LC–MS/MS, Forensic Sci. Int. 295 (2019) 199–206, https://doi.org/10.1016/j.forsciint.2018.12.016.
[27] S. Dellicour, T. Lecocq, GCALIGNER 1. 0: An alignment program to compute a multiple sample comparison data matrix from large eco-chemical datasets obtained by GC, J. Sep. Sci. 36 (2013) 3206–3209, https://doi.org/10.1002/jssc.201300388.
[28] M.J. Anderson, Distance-based tests for homogeneity of multivariate dispersions, Biometrics 62 (2006) 245–253.
[29] H. Lai, I. Corbin, J.R. Almirall, Headspace sampling and detection of cocaine, MDMA, and marijuana via volatile markers in the presence of potential interferences by solid phase microextraction-ion mobility spectrometry (SPME-IMS), Anal. Bioanal. Chem. 392 (2008) 105–113, https://doi.org/10.1007/s00216-008-2229-z.
[30] S. Mascrez, J. Aspromonte, G. Purcano, Enhance the Performance of Solid-Phase Microextraction by Exploiting Vacuum-Assisted Headspace and Multicumulative Trapping for Olive Oil Characterization, LCGC North Am. (2023) 18–21, https://doi.org/10.56530/LCGC.NA.OC7576I2.
[31] S. Elia, M. Stylianou, A. Agapiou, Advanced micro-extraction techniques (SPME, HiSorb) for the determination of goat cheese whey wastewater VOCs, J. Environ. Manag. 351 (2024) 119934, https://doi.org/10.1016/j.jenvman.2023.119934.
[32] V.L. Colley, J.F. Casale, Differentiation of South American crack and domestic (US) crack cocaine via headspace-gas chromatography/mass spectrometry, Drug Test. Anal. 7 (2015) 241–246, https://doi.org/10.1002/dta.1729.
[33] N. Stojanovska, S. Fu, M. Tahtouh, T. Kelly, A. Beavis, K.P. Kirkbride, A review of impurity profiling and synthetic route of manufacture of methylamphetamine, 3,4-methylenedioxymethylamphetamine, amphetamine, dimethylamphetamine and p-methoxyamphetamine, Forensic Sci. Int. 224 (2013) 8–26, https://doi.org/10.1016/j.forsciint.2012.10.040.
[34] S. El-Akaad, S. De Saeger, N. Beloglazova, Molecularly imprinted polymer based capacitive sensing of a specific Leuckart marker 4-methyl-5-phenylpyrimidine in wastewater, Sens. Actuators B Chem. 343 (2021) 130116, https://doi.org/10.1016/j.snb.2021.130116.
[35] K. Norman, | Austin, L. Ciesielski, J.R. Wagner, Identification and associated hazards of clandestine drug laboratories Drug Compounds Toxicology > Drug Analysis Crime Scene Investigation > Crime Scene Examination, (2020). ⟨https://doi.org/10.1002/wfs2.1393⟩.
[36] N.F. Montiel, M. Parrilla, N. Sleegers, F. Van Durme, A.L.N. Van Nuijs, K. De Wael, Electrochemical sensing of amphetamine-type stimulants (pre)-precursors to fight against the illicit production of synthetic drugs, Electrochim. Acta 436 (2022), https://doi.org/10.1016/j.electacta.2022.141446.
[37] B. Erdélyi, A. Szabó, L. Birincsik, Á. Hoschke, Process development of methylenedioxyphenyl-acetone chiral bioreduction, J. Mol. Catal. B Enzym 29 (2004) 195–199, https://doi.org/10.1016/j.molcatb.2003.10.015.
[38] J.Y.K. Cheng, M.F. Chan, T.W. Chan, M.Y. Hung, Impurity profiling of ecstasy tablets seized in Hong Kong by gas chromatography-mass spectrometry, Forensic Sci. Int. 162 (2006) 87–94, https://doi.org/10.1016/j.forsciint.2006.02.055.

[39] F. Palhol, S. Boyer, N. Naulet, M. Chabrillat, Impurity profiling of seized MDMA tablets by capillary gas chromatography, Anal. Bioanal. Chem. 374 (2002) 274–281, https://doi.org/10.1007/s00216-002-1477-6.
[40] J.M. Poupko, W.L. Hearn, F. Rossano, Drug contamination of U.S. paper currency and forensic relevance of canine alert to paper currency: a critical review of the scientific literature, J. Forensic Sci. 63 (2018) 1340–1345, https://doi.org/10.1111/1556-4029.13755.
[41] F.M. Hauser, J.W. Hulshof, T. Rößler, R. Zimmermann, M. Pütz, Characterisation of aqueous waste produced during the clandestine production of amphetamine following the Leuckart route utilising solid-phase extraction gas chromatography–mass spectrometry and capillary electrophoresis with contactless conductivity dete, Drug Test. Anal. 10 (2018) 1368–1382, https://doi.org/10.1002/dta.2394.
[42] L. Cecchi, M. Migliorini, E. Giambanelli, A. Cane, B. Zanoni, V. Canuti, N. Mulinacci, F. Melani, Is the volatile compounds profile a suitable tool for authentication of virgin olive oils (Olea europaea L.) according to cultivars? A study by using HS-SPME-GC-MS and chemometrics, Food Control 139 (2022) 109092, https://doi.org/10.1016/j.foodcont.2022.109092.
[43] C. Martin, M. Malević, C. Diederich, F. Verheggen, Copycatting the smell of death: deciphering the role of cadaveric scent components used by detection dogs to locate human remains, J. Forensic Sci. (2023), https://doi.org/10.1111/1556-4029.15277.
[44] E. Göl, I. Çok, New psychoactive substances in Turkey: Narcotics cases assessed by the Council of Forensic Medicine between 2016 and 2017 in Ankara, Turkey, (2018). ⟨https://doi.org/10.1016/j.forsciint.2018.11.003⟩.