**Title:** Evaluation and application of gas chromatography - vacuum ultraviolet spectroscopy for drug- and explosive precursors and examination of non-negative matrix factorization for deconvolution

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**Highlights:**

• Vacuum ultraviolet absorption spectroscopy of drug- and explosive precursors  
• deconvolution of co-eluting substances  
• evaluation of non-negative matrix factorization for deconvolution  
• comparison of spectral-based deconvolution and non-negative matrix factorization

**Abstract**

Since the introduction of a benchtop vacuum ultraviolet (VUV) absorption spectroscope with an increased wavelength range towards to the high energetic ultraviolet radiation, gas chromatography coupled to VUV has been proven a powerful tool in several fields of application such as petroleomics, permanent gas analytic, pesticide analytic and many more. In this study, the potential of GC-VUV for investigations was examined, focusing on drug- and explosive precursors as well as chemical warfare simulants. The ability of VUV absorption spectra to differentiate isomers is presented, among others for nitroaromatics. In addition, the limit of detection for target compounds were determined to 0.7 ng absolute on column. Furthermore, non-negative matrix factorization (NMF) was successfully implemented as alternative deconvolution approach and evaluated for the deconvolution of unknown substances. In comparison, the spectral library-based deconvolution was applied to a standard mixture and a simulated case study. The results reveal that the NMF is a useful additional tool for deconvolution because, unlike library-based deconvolution, it allows to investigate unknown substances as well.

**Keywords:** VUV, drugs, precursor, deconvolution, forensic chemistry, isomeric separation

1. Introduction

Drugs, drug precursors, and explosive precursors are prominent target compounds in forensic science. Due to their expanding amount and the wide variety of compound structures, strong analytical techniques and detection systems are required. Commonly, gas chromatography coupled to a flame ionisation detector (GC-FID) or gas chromatography coupled to mass spectrometry (GC-MS) are applied as analytical techniques for analysing volatile representatives of these substance classes [1–3]. While a FID is an almost universal and robust technique with straightforward quantification and a wide linear dynamic range, it lacks specific and identifiable analyte information. In case of chemical warfare agents, flame photometric detectors (FPD) are also utilized because of their specificity for sulphur- and phosphorous compounds [4]. Nevertheless, as with FID, identification of compounds is not possible. MS with electron ionisation provides universal analyte-specific information, but common drawbacks are the need for a more sophisticated quantification and more complex instrumentation. On the one hand, the investigation of complex samples like differentiation of isomeric compounds via GC tandem or high-resolution mass spectrometry (GC-MSn, GC-HRMS) is possible [5]. On the other hand, drawbacks of MS are amplified for GC-MSn and GC-HRMS.

Vacuum ultraviolet (VUV) absorption spectroscopy overcomes the above mentioned drawbacks and combines the selectivity of a spectral detection system with the robustness of an absorption based spectroscopic system. While the early coupling of GC with a far ultraviolet (UV) detection dates back to 1987 [6], and is still in use [10], recent instrumentation improvements led to a growing interest in the use of VUV detectors [7–9]. The advantage of VUV is its quite universal detection behaviour, since nearly every chemical substance absorbs light at wavelengths below 185 nm, and therefore exhibits a higher sensitivity compared to UV as well as the generation of substance-specific absorption spectra. In addition, it benefits from a straightforward and robust quantification applying Beer-Lambert’s Law as known from UV spectroscopy. So far, GC-VUV has been utilized for the investigation of new designer stimulants and cannabinoids [11,12], as well as for identification of thermal decomposition products of nitrate ester explosives [13], demonstratrating its power regarding the detection of specific forensic target compounds. Other substance classes such as drug- and explosive precursors have not yet been investigated. In this study, GC-VUV was applied for the analysis of drug- and explosive precursors as well as chemical warfare agent simulants. Therefore, isomeric differentiation was investigated and the limit of detection was determined. Furthermore, its potential for forensic target compounds was evaluated using an artificially spiked gasoline matrix. For the mathematical separation of co-eluting chromatographic peaks, two different deconvolution approaches were utilized and compared, viz. spectral based deconvolution and non-negative matrix factorization (NMF).

1. Material and methods
   1. Material and equipment

Safrole, phenylacetone, propofol, 4-hydroxy propofol and piperonyl methyl ketone were obtained from the German Federal Criminal Police Office (BKA, Wiesbaden, Germany). Nitromethane was bought from Carl Roth GmbH + Co. KG (Karlsruhe, Germany) and 2-nitrotoluene from Alfa Aesar (Karlsruhe, Germany). 2-/3-/4-nitrophenol were obtained from Ferak Berlin (Berlin, Germany), 3,4-dinitrotoluene from Dr. Ehrenstofer GmbH (Augsburg, Germany) and 1-adamantylamine from ABCR GmbH & Co. KG, (Karlsruhe, Germany). Methyl salicylate, 2,4/2,6-dinitrotoluene, dimethyl methylphosphonate, trimethyl phosphate, triethyl phosphonate, tributyl phosphate and diisopropyl methylphosphonate were obtained from Sigma Aldrich Chemie GmbH (Steinheim, Germany). Premium grade gasoline (98 octane, DIN EN 228) was bought from TEAM Mineralöle GmbH (Süderbrarup, Germany). All analytes were dissolved in methanol from Carl Roth GmbH + Co. KG (Karlsruhe, Germany).

The VUV detector VGA-100 (VUV Analytics, Inc., Austin, USA) was coupled to an Agilent 7890A gas chromatograph (Agilent Technologies, Palo Alto, USA). The GC separation was achieved by a 30 m Rxi-1ms column (0.32 mm ID, 4 um df; RESTEK GmbH, Bad Homburg, Germany). The VUV detector parameters were chosen as follows: A wavelength range of 125-240 nm, an acquisition rate of 11 ms per spectrum before averaging, 20 micro-spectra averaged, nitrogen with a purity of 5.0 as makeup gas with a pressure of 10.3 kPa and a flow cell temperature of 275 °C. 1 µl analyte was injected in split mode, 1:10 for calibration and 1:200 for the samples. The injection port temperature was set at 200 °C, and a constant He carrier flow of 1.3 ml/min was applied with a purity of 5.0. The oven temperature program consisted of 35 °C start temperature held for 1 minute, subsequently raised with a temperature ramp of 5 °C/min to 320 °C, and held for 1 min. For data processing and evaluation, VUV Model & Analyze (v5.05.194), VUV Spectra LLB (v5.05.194), and VGA 100 Viewer (v5.05.194), from VUV Analytics (Austin, USA) were exploited.

* 1. Deconvolution based on linear combination of spectra

The deconvolution can be based on characteristic compound-specific absorption cross sections. If the absolute cross sections for the applied wavelength range of the investigated substances are unknown, pre-recorded reference spectra can be used. The model spectrum with n analytes included can be calculated by Formula (1).

|  |  |
| --- | --- |
|  | (1) |

is the calculated spectrum, are the weighting factors, and are the basis functions. For every analyte calculated, one term is used in this equation. By linear optimisation of the unknown weighting factors, while considering the base functions, a model spectrum is obtained that appears similarly to the measured one. As demonstrated in previous publications [14,15], this approach can be applied automatically to e.g. fatty acid methyl esters or polychlorinated biphenyls.

* 1. Application of non-negative matrix factorization for deconvolution of spectral information

NMF allows calculating NMF loadings and their contribution on the signal intensity at given datasets [16], e.g. the influence of a substance on a time depending overall absorption spectrum. NMF segments a -matrix M into a -matrix W and a -matrix H. Only the variable and therefore the number of factors is predefined. In this case, is defined as 3, because it is assumed that a co-eluting peak consists of 2 separate peaks and background noise. This results in and for the peaks and for the noise. By multiplying W and H the so called non-negative matrix factorization of M is obtained, as described in Formula (2). NMF itself is an iterative technique and needs an optimisation algorithm for these iterations. Therefore, an alternating least-squares algorithm was used and the iteration starts with random variables of and for W and H. The minimised function

|  |  |
| --- | --- |
|  | (2) |

is verified by adding a boundary condition. Every result that does not fulfil this condition is rejected because these results would not be physically reasonable. This boundary condition states that every deconvoluted signal should only consist of a single chromatographic peak, because deconvolution should lead to a separated signal for each substance. Therefore, every result with two signals for a single substance is rejected. The utilised MATLAB® script can be found in the supplementary material (supplement A).

* 1. Examining NMF capabilities

For examining the capabilities of NMF, artificial convolutions were prepared. This was done by linear addition of known deconvoluted peaks. The resulting convoluted spectrum is based on the examined samples to enable good agreement for practical samples.

1. Results and Discussion
   1. Limit of detection and absorption spectra

The limits of detection (LOD) for a total of 19 substances were determined as given in Table 1. For this purpose, these substances were analysed in a single mixed standard. LOD determination was done by regression analysis according to DIN 32645 [17]. An integration interval from 125 nm to 240 nm was applied for all substances. The detection limits range from 1.4 to 2.4 ng for drug precursors that can be used for drug production, such as safrole or phenylacetone. Explosive precursors, such as 3,4-dinitrotoluene or nitromethane exhibit LODs from 0.7 to 4.2 ng. In addition, chemical warfare agent simulants such as trialkyl-phosphates revealed a LOD of 1.8 to 3.3 ng. For most of the mentioned substances, the LOD is higher compared to other substances published [7]. This can be explained due to differences in the applied integration range and other LOD determination standards. For example, Schug et al. [7] customized the applied integration range. While this yields the best limit of detection, it suffers from the need of manually setting these values. In contrast, in this work, a general method is applied by integration over the full wavelength range. Therefore, the obtained LOD differences are a good indication for the impact of such a difference in approach. In comparison to common detection techniques such as GC-FID, GC-VUV exhibit a ten times higher limit of detection utilizing a signal to noise ratio of S/N > 3 [18]. No correlations could be observed regarding the number of sigma bonds, hetero atoms or pi bonds. A lower LOD was obtained for the investigated analytes with an aromatic structure present. For further information, the relative process standard deviation can be found in the supplementary material (supplement B).

Table1: LOD for different explosive- and drug precursors as well as chemical warfare agent simulants.

|  |  |
| --- | --- |
| Substance Name | Limit of detection / ng on column |
| Nitromethane | 4.2 |
| Dimethyl methylphosphonate | 1.8 |
| Trimethyl phosphate | 3.3 |
| Triethyl phosphate | 2.0 |
| Diisopropyl methanephosphonate | 1.9 |
| Tributyl phosphate | 2.4 |
| Phenylacetone | 2.4 |
| 2-Nitrotoluene | 0.7 |
| Methyl salicylate | 1.5 |
| 1-Adamantylamine | 1.6 |
| Safrole | 1.4 |
| Propofol | 1.6 |
| 4-Hydroxy propofol | 2.1 |
| 2-Nitrophenol | 0.7 |
| 3-Nitrophenol | 1.9 |
| 2,4-Dinitrotoluene | 1.7 |
| 2,6-Dinitrotoluene | 0.8 |
| 3,4-Dinitrotoluene | 0.8 |
| Piperonyl methyl ketone | 1.6 |

Absorption spectra of all investigated substances over the full wavelength range (125 nm to 240 nm) can be found in the supplementary material (supplement C). To the best of the authors’ knowledge, most of these substances have not been investigated yet. The combination of known concentration and absorption at a particular wavelength will enable the calculation of extinction coefficients. Therefore, the used concentration for every attached spectrum is indicated in gram per litre. In addition, existing databases can be extended for identifying unknown compounds, similar to MS fragment spectral databases.

* 1. Isomer discrimination via spectral library comparison

One general advantage of the VGA-100 compared to MS is the ability to differentiate isomeric compounds based on their absorption spectra. Two examples of such an isomeric differentiation can be seen in Figure 1. Part A) exhibits the behaviour for 2-/3-/4-nitrophenol with slight variations between the isomers. The main absorption band at 175 nm reveals a hypsochromic shift for an increasing distance between the phenol- and nitro functional groups. The second absorption band at higher wavelengths also shifts hypsochrom resulting in one broad absorption band for 4-nitrophenol. These differences allow for the differentiation between the isomers. Figure 1 B) demonstrates the isomeric differentiability for the more complex dinitrotoluene isomers. When isomeric discrimination is not sufficient and discrete isomer allocation is required, known absorption spectra of all investigated isomers are necessary. These spectra can be obtained by isomer database hits. Thereby, isomers can be allocated straightforward and fully automatic. If the analyte was not recorded and is not available in a database, isomer allocation is not possible. To overcome this limitation, in silico calculated spectra are under investigation. Few authors have presented calculations of VUV absorption spectra [11,19]. Compared to VUV absorption spectra, calculations of mass spectrometry fragment spectra are also under development, but lacking in predictability [20]. In theory, the calculation of VUV absorption spectra can be useful to gain information about stimulated electronic states and occurring absorption bands to identify target compounds. However, high amounts of calculation power and –time are required, as well as a solid knowledge about proper calculation methods. Therefore, these methods are hardly applicable for daily laboratory usage and more likely reserves for special cases only.

VUV-Figure-1-5Figure 1: A) Normalised absorption spectra of three nitrophenols. B) Normalised absorption spectra of three different dinitrotoluene isomers. C) Normalised absorption spectra of five chemical warfare agent simulants.

* 1. Homologous rows

Similar to the isomeric separations, VUV absorption spectroscopy results in distinct spectra of homologous alkyl phosphates and structurally related substances. In Figure 1 C), VUV absorption spectra of trimethyl-, triethyl-, and tributyl-phosphate as well as dimethyl methylphosphonate (DMMP) and diisopropyl methylphosphonate (DIMP) are shown. Maximum σ🡪σ\* absorption occurs in the low nm range. Utilizing the VGA-100, no absorption was detected from 180 nm to 240 nm. Differences in the relative absorption intensity at around 165 nm can be explained due to the structural disparities. Firstly, shorter alkyl chains yield a higher relative absorption at 165 nm. This can be observed for alkyl phosphates as well as for both phosphonates. Secondly, the relative absorption at 165 nm seems to be higher and the absorption bandwidth is narrower when all substituents are esters, compared to phosphonates with alkyl side chain.

* 1. Deconvolution and simulated realistic case

Co-eluting peaks are frequently encountered with chromatographic separations of complex mixtures. Therefore, either multiple measurements using different chromatographic approaches or deconvolution of the co-eluting peaks can be utilized. For VUV absorption spectroscopy, a supervised method that is based on a linear combination of spectra has been established [7]. It is assumed, that for a known retention time all co-eluting compounds are known and retention indices as well as spectra are deposited in a spectral library. The method is very fast and robust and will indicate if compounds are present, which are not found in a library. For this type of deconvolution, peak profiles are not necessary, however only known co-elutions are handled properly. Therefore, the need for pre-determined library is one of the biggest drawbacks of VUV deconvolution. To extend the abilities of VUV detectors and overcome the mentioned limitations, NMF is a promising technique to survey for overcoming these limitations. It does not require pre-determined retention indices and a spectral library, which allows deconvoluting unknown substances, as in non-targeted studies. For the investigation of two co-eluting substances, NMF works best if the background noise is determined as well. While NMF in general is a well-known mathematical technique and has been adopted to other chromatographic techniques, such as GC-MS and HPLC-MS [21,22], no investigations have been carried out before with respect to a successful application to VUV absorption spectroscopy. In this study, both deconvolution approaches were applied and compared using different co-eluting samples as well as a simulated case study (Figure 2).

In Figure 2 A), the co-elution of cyclandelate and safrole is demonstrated. The spectral similarity based on the sum-squared residual of pairwise-compared spectra is 10.0. This value can be used to describe the similarity between two compared spectra. Further details and values for other compounds measured with VUV have been published previously [19,23]. Both deconvolution approaches exhibit good alignment with the investigated substances. When comparing spectral deconvolution with NMF, a slightly better agreement for cyclandelate was achieved for spectral deconvolution. For safrole a small peak overestimation was observed, compared to a slight peak underestimation for spectral deconvolution. For quantifying the match between measured and calculated spectra, the deviation between both areas was calculated. While spectral based deconvolution reveals an overall area error of 3.2 %, NMF yielded a result with 1.2 % error. Another example with a four times reduced signal intensity is presented for the deconvolution of 3-nitrophenol and 2,6-DNT (Figure 2 B). This comparison features a spectral similarity of 2.9. While the 3-NP signal is correctly deconvoluted for both methods, NMF exhibits noticeable noise for 3-NP. This noise can only be observed with NMF because of a different separation approach. While spectral deconvolution applies noise free spectra from a database, NMF subtracts the noise from the original spectra, resulting in noisy looking spectra. Nevertheless, both methods exhibit good alignment to the measured spectra, as well as good comparability with each other. Similar to the deconvolution of cyclandelate and safrole, the deviation between the areas of 3-NP and 2,6-DNT was determined. While spectral based deconvolution reveals an overall area error of 0.4 %, NMF yielded a result with 5.0 % error. Higher and more differentiated errors are in agreement with the noisier NMF spectra (Figure 2 B). While the signal intensity of B) is only one fourth of A), the overall error increases slightly, but remains in the dimension for both methods. Therefore, it could be assumed that the basic deconvolution error is at the same level for both methods and the measured deviations are random errors.

A more complex deconvolution example is given in Figure 2 C) by the detection of drug precursors in a gasoline matrix using GC-VUV, which is a known forensic scenario [24]. To simulate such a sample, gasoline was spiked with 1 ‰ safrole and phenylacetone, which corresponds to a sample with mostly gasoline but relevant residues of drug precursors. Safrole is a precursor for the 3,4-Methyl​enedioxy​methamphetamine (MDMA) synthesis and phenylacetone is utilized for amphetamine and methamphetamine synthesis. The total-intensity GC-VUV chromatogram of the analysed sample exhibits that one of the target compounds co-elutes with the matrix. While safrole (at 43 minutes) is separated from the complex gasoline matrix, phenylacetone (at 38 minutes) co-elutes with 1,2-diethylbenzene. Quantification and identification of phenylacetone would therefore be challenging, especially because both peak maxima cannot be distinguished. To overcome this issue, a deconvolution of phenylacetone and 1,2-diethylbenzene is performed, at first via spectral deconvolution and secondly by NMF. Therefore, spectral information for both substances was added to the library. To verify the obtained results, the deviation between the calculated area of the hidden matrix and the measured area from pure gasoline is calculated.

For spectral deconvolution, the measured area of the non-spiked 1,2-diethylbenzene and the deconvoluted area of the spiked sample results in a deviation of about 7 %. Given that the area of 1,2-diethylbenzene is small compared to the phenylacetone signal (about 4 % area), it is highly probable that this deviation can be tolerated for many cases. This result reveals that spectra based deconvolution can be an alternative to time-consuming, additional measurements when co-elution occurs. This is especially useful for the analysis of complex samples and when full peak separation becomes challenging by one-dimensional gas chromatography. While NMF is capable to separate an approximately 1:1 separation, completely similar signals are known to be not deconvolutable by NMF [25]. While NMF is capable to separate an approximately 1:1 separation, the attempt of deconvoluting phenylacetone spiked gasoline reveals no useful information, because of the non-applicability of the boundary conditions, described in section 2.4. In this case, both deconvoluted peaks reveal no separable maxima and therefore NMF delivers no physically reasonable results. Therefore, the need for separable maxima is a major drawback of the NFM method. However, this drawback can be overcome with spectral deconvolution or by changing the chromatographic setup slightly to generate coleuting peaks with two maxima. An additional drawback, compared to spectral deconvolution, is the need to know how many substances are convoluted in a co-eluting peak, prior to the deconvolution. A solution for only partly deconvoluted peaks could be to alternate the number of presumed compounds for NMF.

VUV-Figure-3-6

Figure 2: A) Deconvolution of cyclandelate and safrole via spectral deconvolution (dotdashed line) and NMF (dotted line) from a deconvolution sample. B) Deconvolution of 3-nitrophenol and 2,6-DNT via spectral deconvolution (dotdashed line) and NMF (dotted line) from the same measurement as A). C) Comparison of the GC chromatograms of the spiked and non-spiked gasoline sample. The enlarged part exhibits the co-eluting peaks at 38 minutes.

Since this is the first report for the application of NMF for VUV deconvolution, supplementary tests were performed. Repeatability, allowed peak ratio and maximum peak overlap were determined. Furthermore, the obtained values were compared to spectral deconvolution. Spectral deconvolution is reported to separate mixed components with a ratio of up to 99:1 [19]. In comparison, calculations with NMF reveal a ratio of down to 10:1 with a maximum relative standard deviation of less than 10%. While the spectral deconvolution is capable of separating fully overlaying chromatographic peaks, NMF operates, for investigated cases, up to an overlap of 33 % with a maximum relative standard deviation of less than 10%. More detailed results are given in Figure 3. Therein, the systematic measurement of repeatability and compliance of NMF deconvolution for different deconvolution issues of two peaks is investigated. For this, the results for every investigated combination of the area ratio between peak 1 and peak 2 and the area overlap of peak 2 with peak 1 are expressed by a coloured pixel. The colour coding is arbitrary and should reflect levels of interest. These levels are green for relative deviations of up to 5 %, yellow for relative deviations between 5 and 10 % and orange for more than 10 % relative deviation. The investigated deconvolutions range from an area ratio between peak 1 and peak 2 from one to ten with only slightly area overlap (Figure 3 A-I) to practically equal peaks with high area overlap (Figure 3 A-III). Figure 3 B illustrates the repeatability of every single investigated combination by measuring the maximum standard deviation based on the thousandfold calculation of the NMF. As a result, the relative maximum standard deviation for most peaks with an area overlap of up to 33 % is less than 5 %. In addition, the peak area ratio only has only little effect on the deviation, while a higher peak overlap above 33 % results in increased deviations. This increase reaches its maximum at 10.9 % with almost complete overlap and would allow separating nearly fully overlapping peaks for all peak ratios. For Figure 3 C, the deconvoluted peaks are summed up again and are compared afterwards with the original spectra. As a result, the relative difference of both areas was plotted. Figure 3 C reveals different maximum standard deviations, especially for a highly overlapping peak area. This is most likely due to the hard colour cut applied for better interpretability. For peaks with an area overlap of up to 33 %, the error is less than 10 % and with a maximum error of 13.8 % all peaks can be separated. In general, these results indicate that NMF is able to separate all investigated combinations of peak ratios and peak overlaps and can reproduce the initial data with minor challenges.

VUV-Figure-4-7Figure 3: Systematic measurement of reproducibility and compliance of NMF deconvolution for different deconvolution issues of two peaks. Therefore, the results are expressed by a coloured pixel for every investigated combination of the area ratio between peak 1 and peak 2 and area overlap of peak 2 with peak 1. The colour coding is arbitrary and should reflect relevant levels. These levels are green for relative deviations of up to 5 %, yellow for relative deviations between 5 and 10 % and orange for over 10 % relative deviation. The measured deconvolutions range from an area ratio between peak 1 and peak 2 from one to ten with only slight overlap (Figure 3 A-I) to practically equal peaks with high area overlap (Figure 3 A-III). Figure 3 B illustrates the reproducibility, by measuring the maximum standard deviation of 1000 measurements for every single investigated combination. Examples of the red marked pixels are drawn at Figure 3 A. For Figure 3 C, the deconvoluted peaks are summed up again and then compared with the original spectra and the resulting relative difference of both areas was plotted.

1. Conclusion

In this study, the capability of GC-VUV is shown for drug- and explosive precursors as well as chemical warfare simulants. Measurements proved that VUV absorption spectroscopy is well suited for these compound classes. The possibility to distinguish different isomers (e.g. common nitroaromatics), regardless of the separation efficiency, is an advantage over other analyser techniques such as mass spectrometric detectors. In addition, the non-destructive characteristic of VUV absorption detection allows coupling to a subsequent detector. Furthermore, the capability to deconvolute co-eluted peaks in a chromatogram was shown using two approaches, which is less time-consuming and eliminates extensive method development. Necessary requirements to conduct spectral deconvolution are the availability of pure substance spectra. In contrast, NMF can be applied to discovery-based approaches when unknown compounds are studied. Therefore, both deconvolution techniques reveal a different scope depending on the availability of pure substance spectra. If pure substance spectra of target compounds are available, spectral deconvolution allows a more flexible application. For scenarios such as the measurement of new synthesised substances or non-target analytics, NMF will be the method of choice. This is especially useful in forensic science because of the ongoing development of new drugs and synthesis routes.

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1. References

[1] N. Raikos, K. Christopoulou, G. Theodoridis, H. Tsoukali, D. Psaroulis, Determination of amphetamines in human urine by headspace solid-phase microextraction and gas chromatography, J. Chromatogr. B 789 (2003) 59–63. https://doi.org/10.1016/S1570-0232(03)00047-3.

[2] B. Fodor, I. Molnár-Perl, The role of derivatization techniques in the analysis of plant cannabinoids by gas chromatography mass spectrometry, TrAC, Trends Anal. Chem. 95 (2017) 149–158. https://doi.org/10.1016/j.trac.2017.07.022.

[3] J.M. Perr, K.G. Furton, J.R. Almirall, Gas chromatography positive chemical ionization and tandem mass spectrometry for the analysis of organic high explosives, Talanta 67 (2005) 430–436. https://doi.org/10.1016/j.talanta.2005.01.035.

[4] Z. Witkiewicz, E. Sliwka, S. Neffe, Chromatographic analysis of chemical compounds related to the Chemical Weapons Convention, TrAC, Trends Anal. Chem. 85 (2016) 21–33. https://doi.org/10.1016/j.trac.2016.05.006.

[5] K. Zaitsu, H. Miyagawa, Y. Sakamoto, S. Matsuta, K. Tsuboi, H. Nishioka, M. Katagi, T. Sato, M. Tatsuno, H. Tsuchihashi, K. Suzuki, A. Ishii, Mass spectrometric differentiation of the isomers of mono-methoxyethylamphetamines and mono-methoxydimethylamphetamines by GC–EI–MS–MS, Forensic Toxicol. 31 (2013) 292–300. https://doi.org/10.1007/s11419-013-0193-6.

[6] B.S. Middleditch, N.-J. Sung, A. Zlatkis, G. Settembre, Trace analysis of volatile polar organics by direct aqueous injection gas chromatography, Chromatographia 23 (1987) 273–278. https://doi.org/10.1007/BF02311779.

[7] K.A. Schug, I. Sawicki, D.D. Carlton, H. Fan, H.M. McNair, J.P. Nimmo, P. Kroll, J. Smuts, P. Walsh, D. Harrison, Vacuum ultraviolet detector for gas chromatography, Anal. Chem. 86 (2014) 8329–8335. https://doi.org/10.1021/ac5018343.

[8] I.G.M. Anthony, M.R. Brantley, C.A. Gaw, A.R. Floyd, T. Solouki, Vacuum Ultraviolet Spectroscopy and Mass Spectrometry: A Tandem Detection Approach for Improved Identification of Gas Chromatography-Eluting Compounds, Anal. Chem. 90 (2018) 4878–4885. https://doi.org/10.1021/acs.analchem.8b00531.

[9] I.G.M. Anthony, M.R. Brantley, A.R. Floyd, C.A. Gaw, T. Solouki, Improving Accuracy and Confidence of Chemical Identification by Gas Chromatography/Vacuum Ultraviolet Spectroscopy-Mass Spectrometry: Parallel Gas Chromatography, Vacuum Ultraviolet, and Mass Spectrometry Library Searches, Anal. Chem. 90 (2018) 12307–12313. https://doi.org/10.1021/acs.analchem.8b04028.

[10] J. Andrasko, L. Lagesson-Andrasko, J. Dahlén, B.-H. Jonsson, Analysis of Explosives by GC-UV, J. Forensic Sci. 62 (2017) 1022–1027. https://doi.org/10.1111/1556-4029.13364.

[11] L. Skultety, P. Frycak, C. Qiu, J. Smuts, L. Shear-Laude, K. Lemr, J.X. Mao, P. Kroll, K.A. Schug, A. Szewczak, C. Vaught, I. Lurie, V. Havlicek, Resolution of isomeric new designer stimulants using gas chromatography - Vacuum ultraviolet spectroscopy and theoretical computations, Anal. Chim. Acta 971 (2017) 55–67. https://doi.org/10.1016/j.aca.2017.03.023.

[12] A. Leghissa, J. Smuts, C. Qiu, Z.L. Hildenbrand, K.A. Schug, Detection of cannabinoids and cannabinoid metabolites using gas chromatography with vacuum ultraviolet spectroscopy, Sep. Sci. plus 1 (2018) 37–42. https://doi.org/10.1002/sscp.201700005.

[13] C.A. Cruse, J.V. Goodpaster, Generating highly specific spectra and identifying thermal decomposition products via Gas Chromatography / Vacuum Ultraviolet Spectroscopy (GC/VUV): Application to nitrate ester explosives, Talanta 195 (2019) 580–586. https://doi.org/10.1016/j.talanta.2018.11.060.

[14] H. Fan, J. Smuts, L. Bai, P. Walsh, D.W. Armstrong, K.A. Schug, Gas chromatography-vacuum ultraviolet spectroscopy for analysis of fatty acid methyl esters, Food Chem. 194 (2016) 265–271. https://doi.org/10.1016/j.foodchem.2015.08.004.

[15] C. Qiu, J. Cochran, J. Smuts, P. Walsh, K.A. Schug, Gas chromatography-vacuum ultraviolet detection for classification and speciation of polychlorinated biphenyls in industrial mixtures, J. Chromatogr. A 1490 (2017) 191–200. https://doi.org/10.1016/j.chroma.2017.02.031.

[16] M.W. Berry, M. Browne, A.N. Langville, V.P. Pauca, R.J. Plemmons, Algorithms and applications for approximate nonnegative matrix factorization, Comput. Statist. Data Anal. 52 (2007) 155–173. https://doi.org/10.1016/j.csda.2006.11.006.

[17] Deutsches Institut für Normung, DIN 32645: Chemical analysis - Decision limit, detection limit and determination limit under repeatability conditions - Terms, methods, evaluation, 2008th ed., Beuth, Berlin 71.040.01, 2008.

[18] E. Matisová, S. Škrabáková, Applicability of a novel carbon sorbent for the preconcentration of volatile chlorinated hydrocarbons, Anal. Chim. Acta 309 (1995) 181–188. https://doi.org/10.1016/0003-2670(95)00089-I.

[19] J. Schenk, J.X. Mao, J. Smuts, P. Walsh, P. Kroll, K.A. Schug, Analysis and deconvolution of dimethylnaphthalene isomers using gas chromatography vacuum ultraviolet spectroscopy and theoretical computations, Anal. Chim. Acta 945 (2016) 1–8. https://doi.org/10.1016/j.aca.2016.09.021.

[20] A. Schwarzenberg, J.-C. Tabet, R.B. Cole, X. Machuron-Mandard, H. Dossmann, New insights into dissociation of deprotonated 2,4-dinitrotoluene by combined high-resolution mass spectrometry and density functional theory calculations, Rapid Commun. Mass Spectrom. 29 (2015) 29–34. https://doi.org/10.1002/rcm.7076.

[21] T. Ieda, S. Hashimoto, T. Isobe, T. Kunisue, S. Tanabe, Evaluation of a data-processing method for target and non-target screening using comprehensive two-dimensional gas chromatography coupled with high-resolution time-of-flight mass spectrometry for environmental samples, Talanta 194 (2019) 461–468. https://doi.org/10.1016/j.talanta.2018.10.050.

[22] J. Rapin, A. Souloumiac, J. Bobin, A. Larue, C. Junot, M. Ouethrani, J.-L. Starck, Application of non-negative matrix factorization to LC/MS data, Signal Processing 123 (2016) 75–83. https://doi.org/10.1016/j.sigpro.2015.12.014.

[23] C. Weston, J. Smuts, J.X. Mao, K.A. Schug, Investigation of gas phase absorption spectral similarity for stable-isotopically labeled compounds in the 125-240nm wavelength range, Talanta 177 (2018) 41–46. https://doi.org/10.1016/j.talanta.2017.09.033.

[24] Europol, Largest EVER EUROPEAN HAUL OF AMPHETAMINE PRECURSOR BMK SEIZED, 2015. https://www.europol.europa.eu/newsroom/news/largest-ever-european-haul-of-amphetamine-precursor-bmk-seized (accessed 8 June 2018).

[25] E.J. Karjalainen, U.P. Karjalainen, Component reconstruction in the primary space of spectra and concentrations. Alternating regression and related direct methods, Anal. Chim. Acta 250 (1991) 169–179. https://doi.org/10.1016/0003-2670(91)85070-9.