Residual solvents in methylenedioxymethamphetamine tablets as a source of strategic information and as a tool for comparative analysis: the development and application of a static headspace gas chromatography/mass spectrometry method*

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ABSTRACT

Various solvents can be used in the synthesis of the illicit synthetic drug methylenedioxymethamphetamine (MDMA, commonly known as Ecstasy). In the crystallization process, traces of those solvents can be trapped inside crystals; during the following tabletting process, the solvent traces remain present in the tablets. The forensic investigation of tablets for solvents may increase knowledge of production methods and contribute to a possible choice of monitoring or regulating certain organic solvents. Further, the identification and quantification of solvents in MDMA tablets may contribute to the chemical characterization of illicit tablets for comparative examination.

The methods of analysis of volatile components in illicit MDMA tablets described so far are often based on solid-phase micro extraction (SPME). To avoid several disadvantages of SPME, a quantitative static headspace method was developed using gas chromatography/mass spectrometry (GC/MS); for quantification, the standard addition method appeared to be advantageous. The residual solvents in 155 MDMA tablets were analysed and 150 of them were quantified.

Keywords: MDMA; Ecstasy; static headspace; residual solvents; volatiles; illicit drugs; tablets

Introduction

The analysis of synthetic drugs in a forensic laboratory can be performed on various levels, the number and depth of which usually depend on the aim of the analysis, as follows:

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(a) Physical description of the material: for powders, often limited to colour and type of material; in the case of tablets and capsules, usually including more descriptors such as shape, dimension, weight and/or imprint (logo) [1];

(b) Qualitative analysis to determine the presence of one or more controlled drugs;

(c) Qualitative analysis of other compounds added to the main drug as so-called "cutting agents" or, in the case of tablets, as "excipients";

(d) Quantitative analysis of the controlled drug;

(e) Quantitative analysis of other controlled drugs, if present, and/or one or more non-controlled drugs;

(f) More in-depth analysis, which may consist of qualitative and quantitative analysis of organic by-products that may be present as a result of the natural origin of compounds or of chemical synthesis or a combination of both. Depending on the type of drug, this will be done on a percentage level or on a trace level [2-12];

(g) "Other" chemical or physical analysis characterizing the material, such as the determination of (trace) elements [13] or isotope-ratio-mass spectroscopy [14].

The number of analyses carried out on a specific item is usually determined by the aim of the analysis. Most often analysis will be related to criminal cases, where the assessment of the identity of the main drug is the main target for court purposes. In many jurisdictions a quantitative analysis is also required, although that requirement may be related to certain (weight) limits being surpassed or to the type of violence involved. Such analyses are not costly, mainly because of their relatively "routine" character; the laboratory time needed for a full qualitative and quantitative analysis of the main drug can be estimated at between 1 and 2 hours per item. More time will be needed if pictures have to be taken or if database registrations are required.

In many forensic laboratories, the types of analysis mentioned under points *(c)-(g)* are not "routine" procedures since they are time-consuming and costly, and not strictly necessary in the majority of cases. However, many laboratories perform (some) comparative analysis in response to requests from police or prosecutors in specific cases. Here, the aim is to link specific samples, cases or suspects to each other.

In some laboratories, extensive analysis is performed with the aim of obtaining strategic information, that is, information that may not be directly used in specific cases but that may be useful in gaining insights into type and scale of production and may reveal possible links between certain seizures that were not previously expected.

In a comparative analysis for casework, a number of characteristics of item A are determined and compared with those of item B. If they match, the samples may have a link. There are no strict rules about how many

characteristics should be compared, while the degree of similarity may also be a point of discussion. Nevertheless, there is a logical approach from which a reasonable strategy can be derived. If item A is very close to item B as regards the determined characteristics, that assessment is of limited value if the characteristics are very common and shared by half of all the samples of that type of drug. On the other hand, if samples A and B are very similar and it can be demonstrated that both are different from many other, non-related samples, then the similarity is of some significance. Since the analysis of a large number of "other" samples is not done at the same time as that of samples A and B, that comparison is done by comparing the data of such samples as have been collected in a database. This is known as "retrospective" analysis [6, 15].

In practice, the casework comparative analysis of tablets of methylenedioxymethamphetamine (MDMA, commonly known as Ecstasy) is usually done by comparing the external characteristics, the MDMA content and the identity of the excipients and often by making an organic impurity profile, that is, a spectrum of the by-products (impurities) that may be present in the MDMA as a result of impurities from the base material and of side reactions during its synthesis.

In the present article, the focus is on traces from solvents that may be present in tablets. The first aim is of a strategic character. By determining the solvents present, more may be learned from the production process, more information may indicate what solvents were used and a more reliable basis may be gained for decisions as regards possible control or monitoring of those solvents. In that respect, the important role of precursor chemicals in the manufacture of illicit drugs is mentioned, as also the role of the United Nations in trying to limit their misuse for "illicit" purposes.* A second aim is in casework comparative analysis, where the identity—and amount—of a trace solvent can be useful characteristics.

Synthesis of MDMA can be performed via various routes [17], but "reductive amination" is most common. Several organic solvents can be involved in the process. In the first step, MDMA base is formed from piperonyl methyl ketone (PMK), methylamine and a reductive agent; the reaction takes place in an alcoholic solvent such as methanol, ethanol or 2-propanol (IPA). Next, the alcohol and excess of methylamine are removed by distillation. The remaining raw MDMA base is a liquid that is converted into the corresponding hydrochloride salt by dissolving it into an organic solvent, followed by the addition of hydrochloric acid to form a powder. In the illicit drug manufacturing sites found in the Netherlands, the solvent most often used was acetone, but other solvents are occasionally used. During the crystallization process, solvent molecules may be trapped in the MDMA hydrochloride crystals. After its collection, the MDMA hydrochloride is dried, either at room temperature or by heating it in an oven or in some other way. However, the occluded solvent residues are

*See, for example, the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988 [16].

usually not removed in the drying process and stay present, also when the MDMA powder is later (sometimes elsewhere) pressed into a tablet.

Since the residual solvents in MDMA tablets are at a very low concentration level, a sensitive analysis method is required to identify and quantify them. For the analysis of such solvent residues, various methods can be used [18, 19], including the recently developed solid-phase micro extraction (SPME) [20]. SPME is known as an easy and rapid technique with minimal sample handling, small sample volume requirements and high detection sensitivity [21, 22]. However, the application of SPME in the author's laboratory revealed some disadvantages [23]. For instance, the high sensitivity of the SPME fibre resulted in interfering environmental contamination. Although there are many types of fibre material available [24], fibres often fail to absorb all the polar and non-polar components of interest at the same time. Additionally, fibre saturation can affect the linearity of compounds already at the 200 parts per billion (ppb) level [23, 25], which will affect the quantitative determination. In order to obtain proper peak shapes for good quantification, additional cryo-cooling of the injector is advised. The short lifetime of a fibre (50-100 injections) makes the technique rather expensive and less convenient than it first appeared [23]. Static headspace is a well-established technique for the analysis of volatiles and is based on pre-concentration of volatiles in a closed system in an equilibrium between the liquid and the gas phase [26].

In the present research, the latter technique was investigated and validated for the qualitative and quantitative analysis of residual solvents in MDMA tablets. The qualitative results of 155 MDMA tablets are reported, together with the quantitative results of 150 of them.

Analytical procedure

Chemicals

Acetone, toluene and ethanol were purchased from Merck (Darmstadt, Germany). Tris(hydroxymethyl)aminomethane (99+ per cent), isopropanol and sodium chloride (p.a.) were purchased from Acros (Geel, Belgium). 2-butanone (p.a.) was purchased from Fluka (Buchs, Switzerland). Methanol (HPLC grade) and ethanol (glass- distilled grade) were purchased from Rathburn Chemicals Ltd. (Walkerburn, United Kingdom of Great Britain and Northern Ireland). Water was of ultra pure quality, filtered by a MilliQ System (Millipore Corporation, United States of America).

Instrumentation

Gas chromatography/mass spectrometry (GC/MS) analyses were run using Agilent 6890N GC and Agilent 5973 mass spectrometer detector. The ion source temperature was 230 °C, the quadrupole temperature 150 °C and the MS interface temperature 280 °C. The total ion current (TIC) mode was used and the atomic mass unit (amu) range was set at mass 29-200. Helium was used as the carrier gas at a constant flow of 1 millilitre per minute (ml/min). The column

was a ValcoBond VB-1, 30 metre (m), 0.25 mm, 1 μm. Oven temperature programming: 40 °C (held for 1 minute), 10 °C/min to 130 °C, then 40 °C/min to 250 °C. All injections were in split mode (20:1). A straight liner of 1.5 mm diameter was used (Agilent Technologies, Palo Alto, USA). The injector temperature was 275 °C. For the headspace sampling and injections, a Gerstel Multi Purpose Sampler MPS2 was used, equipped with a 2.5 ml gas-tight syringe and an agitator (Gerstel, Mülheim an der Ruhr, Germany). The syringe was kept at 70 °C and the agitator at 60 °C. The agitator speed was set at 500 rpm and the sample was stirred for 60 minutes. The injection volume was 1,200 μl with an injection speed of 370 μl/s. The injection penetration was set at 40 mm. After the injection, the needle was flushed with nitrogen gas for 5 minutes. Alltech (Deerfield, United States) 20 ml headspace vials and magnetic crimp caps were used.

Buffer solution preparation

The Tris buffer was prepared by dissolving 121.1 grams (g) of Tris(hydroxymethyl)aminomethane in 800 ml ultra pure water. Concentrated hydrochloric acid was added up to pH 8.1 ± 0.05. Then the solution was diluted to 1 l. The shelf life of the buffer solution was set at one month at 5 °C.

Reference standard solution preparation

A reference standard solution of ethanol, acetone, IPA, diethyl ether, methyl ethyl ketone (MEK) and toluene (each 7 g/l) was prepared in methanol by accurate weighing. The solvents were added by pipette into the methanol, and concentrations (weight to weight (w/w)) were calculated from the weights using their densities.

For safest storage, the solution was then poured into a 50 ml glass bottle with a screw cap, filled to the rim to prevent evaporation of the volatiles as much as possible. The solution was freshly made before analysis.

Control sample and samples

The control sample was prepared by homogenizing a seizure of MDMA tablets, containing 25.0 per cent MDMA hydrochloride, 61.0 per cent lactose, talc and magnesium stearate.

The test samples consisted of 155 mostly different MDMA tablets, selected from 140 cases.

Preparation of samples

To a vial was added 3.0 g sodium chloride, 5.0 ml Tris buffer (pH 8.1) and one whole MDMA tablet (not ground). The vial was immediately capped. To another vial was added 3.0 g sodium chloride, 5.0 ml Tris buffer (pH 8.1), one of the same MDMA tablets (not ground) and 3.0 μl of the reference standard solution (at room temperature). The reference standard solution was accurately added using a 10 μl syringe. The vial was immediately capped.

Results and discussion

Method development

Choice of solvent

A buffer was considered necessary to ensure that all tablets released the volatiles under the same conditions. Different buffers and pHs were tested; a Tris buffer at pH 8.1 gave the most consistent results.

Salt addition

The addition of a salt can be used to lower detection limits of the volatiles of interest [27]. The "salting out" effect is responsible for the greater partitioning of the occluded volatiles into the headspace [26]. Since the salt concentration has a pronounced effect on the volatiles in the headspace, the salt was accurately weighed into the vial in order to ensure a saturated solution.

Incubation of the sample

Various headspace parameters were optimized such as incubation temperature, incubation time and mixing speed. The agitator of the autosampler stirs the sample at a maximum speed at 60 °C for 1 hour. Under the chosen conditions, 150 of the 155 (97 per cent) of the tablets disintegrated completely in the buffer releasing the trapped volatiles. The other five tablets (3 per cent) did not fully disintegrate, but a sufficient amount of the organic solvent was released for a qualitative determination. The long stirring time (1 hour) is not a restrictive time factor, since the samples within a sequence are automatically transferred into the agitator during analysis of previous samples.

The "one-point" standard addition method

Initial experiments showed that quantification with an internal standard gave irreproducible results. This is attributed to the fact that each tablet type creates a specific type of matrix, which releases the trapped volatiles to a different extent. Therefore, the use of a standard addition method was considered essential. Thus two MDMA tablets are required for quantification. In the first measurement, the peak area of the volatile in the first tablet is measured. In the second measurement, a standard mixture of volatiles is added and the total peak area is determined. The increment of the peak area of the volatile varies, depending on the type of matrix. The real concentration of the volatile in the sample can be calculated according to formula 1, where W_o is the original concentration (parts per million (ppm)) in the sample, W_a is the added amount of volatile (ppm), A_o is the original peak area and $A(_{o+a})$ is the total peak area.

Formula 1:

$$W_o = \frac{W_a * A_o}{A_{(o+a)} - A_o}$$

In practice, tablets from the same batch show only a minimum variation in weight, so weight correction in comparative cases was seldom necessary. However, between different types of tablet, the amount of organic volatile was expressed per 100 mg of tablet; no normalization on the amount of MDMA hydrochloride was applied.

Method validation

General features of the method

For the release of volatiles from MDMA tablets, the tablets were disintegrated in a solution; for better control, a buffer solution was preferred. The repeatability of the concentrations of acetone and other residual solvents was determined in spiked buffer solutions. Subsequently, a buffer solution was used to determine detection and quantification limits.

Repeatability in buffer solutions

The repeatability of the method was tested by successively analysing 10 sample solutions. The results are summarized in table 1.

Table 1. Repeatability data for residual solvents, obtained with 10 sample preparations in buffer solutions

Solvent	*Repeatability in percentage relative standard deviation (n=10)*
Acetone	1.6
2-Propanol (IPA)	3.9
Diethyl ether	1.5
Toluene	1.4
Methyl ethyl ketone (MEK)	1.7
Ethanol	11.3[a]

[a]The high relative standard deviation percentage value of ethanol is a result of low peak area and poor peak shape, due to the polarity of ethanol.

Detection and quantification limits determined in buffer solutions

For this method, the detection and quantification limits for residual solvents in the spiked buffer solutions were determined. The results are summarized in table 2. The detection limit is determined by the smallest concentration measured with GC/MS. The values of the quantification limits fulfil the condition of S/N > 3 and are all within the linear concentration range.

Application to tablet matrices

Repeatability studies on the control sample and on three different types of MDMA tablet were performed and are reported in table 3. The repeatability of

acetone in the control sample was very close to that of the spiked buffer solutions. The somewhat higher relative standard deviation (RSD) values in the tablets compared with the homogeneous control sample may indicate an intra-batch variation. In the same table, the results of the eight-month reproducibility study are reported.

Table 2. Limits of detection and quantification (concentrations in vials), for residual solvents determined in buffer solutions

	Detection limit		*Quantification limit*	
Solvent	*Parts per billion*	*Microgram per vial*	*Parts per billion*	*Microgram per vial*
Acetone	50	0.25	100	0.5
2-Propanol (IPA)	100	0.5	200	1
Diethyl ether	1	0.005	5	0.025
Toluene	0.5	0.003	5	0.025
Methyl ethyl ketone (MEK)	10	0.05	20	0.1
Ethanol	500	2.5	1 000	5
Methanol	nd[a]	nd	5 000	25

[a]nd: not determined.

Table 3. Repeatability and reproducibility data for the acetone concentration in tablet matrices

Sample	*Tablet logo*	*Repeatability acetone (percentage relative standard deviation)*	*Reproducibility acetone (percentage relative standard deviation)*
Control sample		1.7[a]	7.9[b]
Type 1 of MDMA tablets	@	5.2[c]	7.9[d]
Type 2 of MDMA tablets	Mitsubishi	5.8[c]	8.5[e]
Type 3 of MDMA tablets	FF (2nd F upside-down)	3.9[c]	4.9[e]
Type 4 of MDMA tablets	Wooden shoe	nd[f]	10.1[g]
Type 5 of MDMA tablets	Play station/square	nd	3.5[e]

[a]n: 5.
[b]n: 21 in 8 months.
[c]n: 10.
[d]n: 14 in 8 months.
[e]n: 4 in 8 months.
[f]nd: not determined.
[g]n: 6 in 8 months.

Linearity in tablet matrices

The linearity was tested by taking four tablets from one type and adding four different volumes of a reference standard solution (including acetone, IPA, diethyl ether and toluene) resulting in vial concentrations of 5, 10, 15 and 22 ppm

respectively. Since each tablet type creates its own specific type of matrix, the linearity was further tested by analysing three other types of tablet. The resulting buffer solutions thus varied from a kind of gel matrix to a solution with a clear upper layer after sedimentation.

Although all matrices trapped the volatiles to a different extent, linear results in all four matrices were obtained for all compounds (see table 4); in table 4, the linearity maximum is given as the lowest value out of the four types of tablet. The quantification limit in matrices could not be determined, since almost all tablets already contained a certain amount of acetone.

Table 4. Linearity data (concentrations in vials), for residual solvents in methylenedioxymethamphetamine tablets, determined in four different types of tablet (four different matrices)

	Linearity maximum[a]		
Solvent	*Parts per billion*	*Microgram per vial*	*Correlation coefficient*[b]
Acetone	16	80	0.997 to 1.000
2-Propanol (IPA)	15	75	0.996 to 0.999
Diethyl ether	7	35	0.997 to 1.000
Toluene	10	50	0.992 to 0.999

[a]Lowest value of four linearity curves, applicable to all four tablet matrices.
[b]Lowest and highest correlation coefficient of four linearity curves.

It should be noted that when a standard addition of 25 μg acetone per vial is used, with a linearity maximum of 80 μg acetone per vial, a maximum concentration of 55 μg acetone per vial in the sample can be measured. Overall a "one-point" standard addition method can be used in a sufficient linearity range of acetone, IPA, diethyl ether and toluene. Methanol was used as the solvent for the standard addition solution and therefore not included in the linearity tests. Ethanol was not included in this study because of bad peak shapes; MEK was not included in the quantitative study because of its absence in tablets so far.

Analyses results

Application of the method

From different cases in the period 2002-2004, 155 tablets were analysed for solvents. Since five of them did not dissolve well in the buffer, 150 tablets were quantified.

Qualitative results

The qualitative results are summarized in table 5. Acetone was by far the most frequently encountered solvent, which is consistent with the findings in illicit

Table 5. Solvents detected in 155 methylenedioxymethamphetamine tablets

Solvent	*Detected in n tablets*[a]	*Samples (percentage)*
Acetone	146	94
Toluene	46	30
Diethyl ether	16	10
2-Propanol (IPA)	10	6
Dichloromethane	6	4
Ethanol	7	5
Chloroform	1	1
Trichloroethane	1	1
Methyl ethyl ketone (MEK)	0	0
Methanol	0	0
Specification of acetone and one other solvent		
Acetone (only)	78	50
Acetone + toluene	42	27
Acetone + diethyl ether	10	6
Acetone + IPA	9	6
Acetone + ethanol	7	5
Solvent combinations without acetone		
Ethanol + IPA	1	1
Diethyl ether + toluene	4	3
No solvents detected	2	2

[a]The total number is more than 155, because combinations of two or more solvents in some tablets were observed. The number of tablets containing two solvents are specified in the lower section of the table.

laboratories seized in the Netherlands. Thirty per cent of the samples contained toluene. This was not consistent with the author's experience in illicit laboratories, where toluene was almost never encountered. The explanation was found in the extreme sensitivity of the system to toluene; the concentrations found do not point to its use in the process, but to other, so far unidentified, sources. Contamination within the forensic laboratory was excluded by the analysis of a large number of blanks, control samples and excipients, none showing any toluene. In future investigations in illicit laboratories, an attempt will be made to find the source of toluene, which may be the solvents and precursor chemicals used, such as PMK, in which toluene has already been found.

Diethyl ether and IPA were known to be used in the illicit production. MEK was not detected in any of the MDMA tablets analysed. Methanol has a high detection limit because of its polarity and was not detected in any of the tablets analysed. In 48 per cent of the tablets, combinations of two solvents were seen; six tablets had a combination of three solvents and one tablet contained five solvents. Besides the solvents listed in table 5, the aldol-condensation product of two molecules acetone 4-methyl-3-penten-2-one and some acetic acid alkyl ester-like components were observed in the chromatograms. Examples of chromatograms are given in figures I and II.

Figure I. Residual solvents in a methylenedioxymethamphetamine tablet (I)

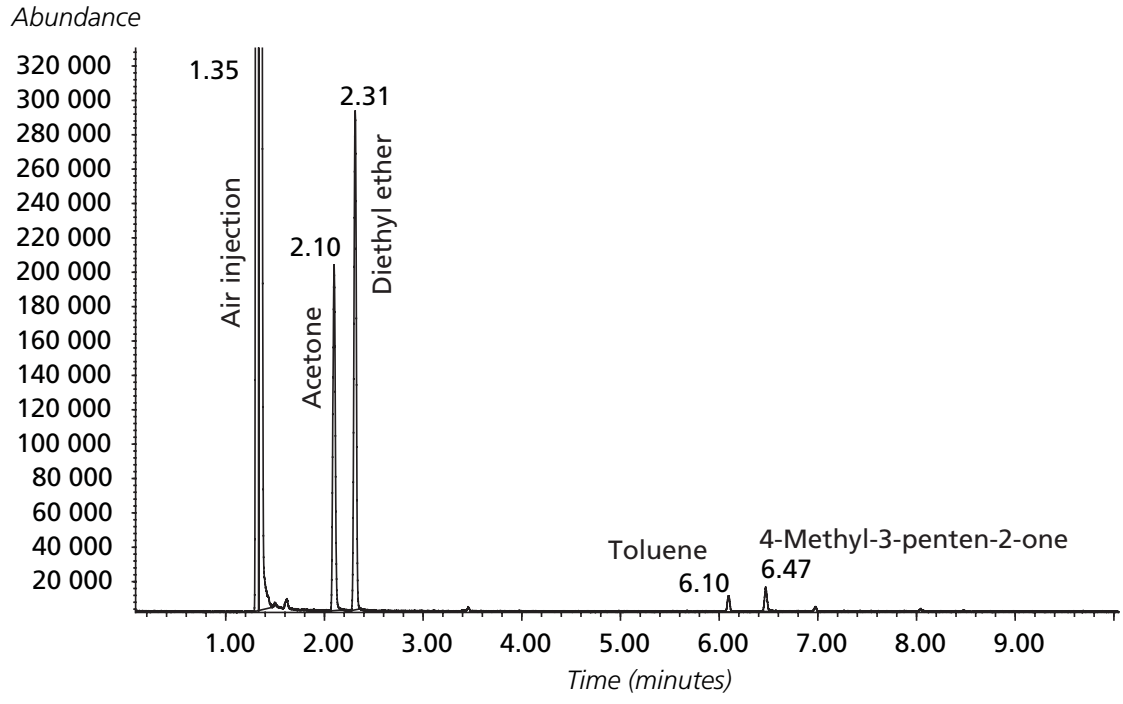
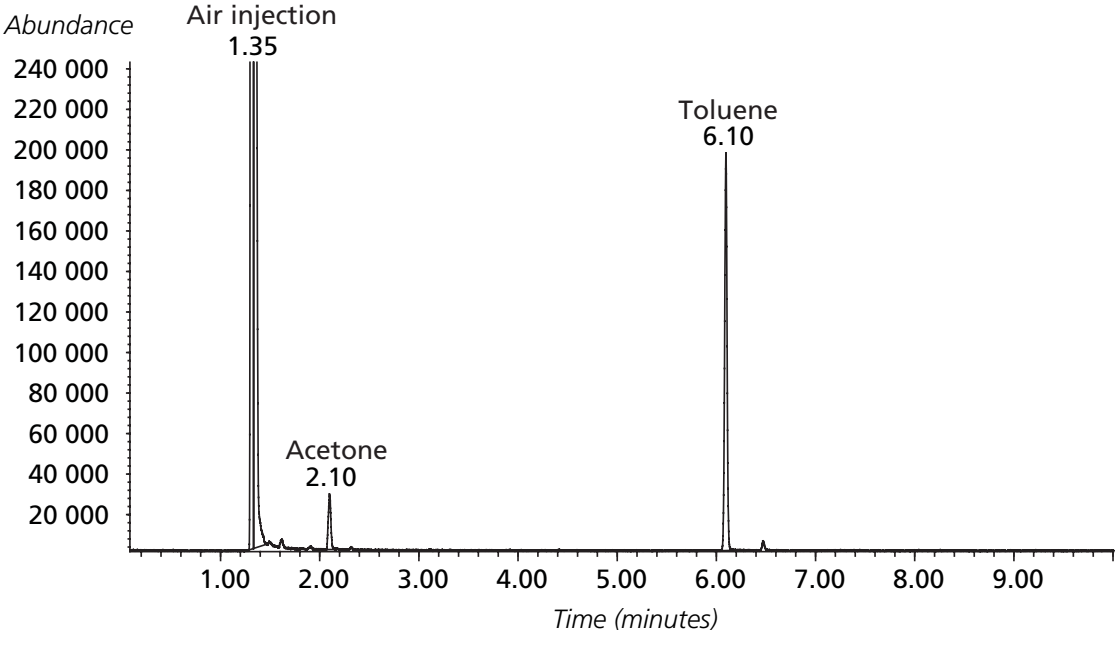


Figure II. Residual solvents in a methylenedioxymethamphetamine tablet (II)



Quantitative results

Figure III shows a chromatogram with the components of the reference standard solution, used for quantification. Figure IV depicts an overview of the acetone concentrations found in the 150 tablets. The highest measured concentration of acetone was 9.4 μg/100 mg tablet. The average concentration of acetone was 2.4 μg/100 mg tablet and the median 2.1 μg/100 mg tablet. The

Figure III. Chromatogram of a headspace analysis showing the components of the reference standard solution

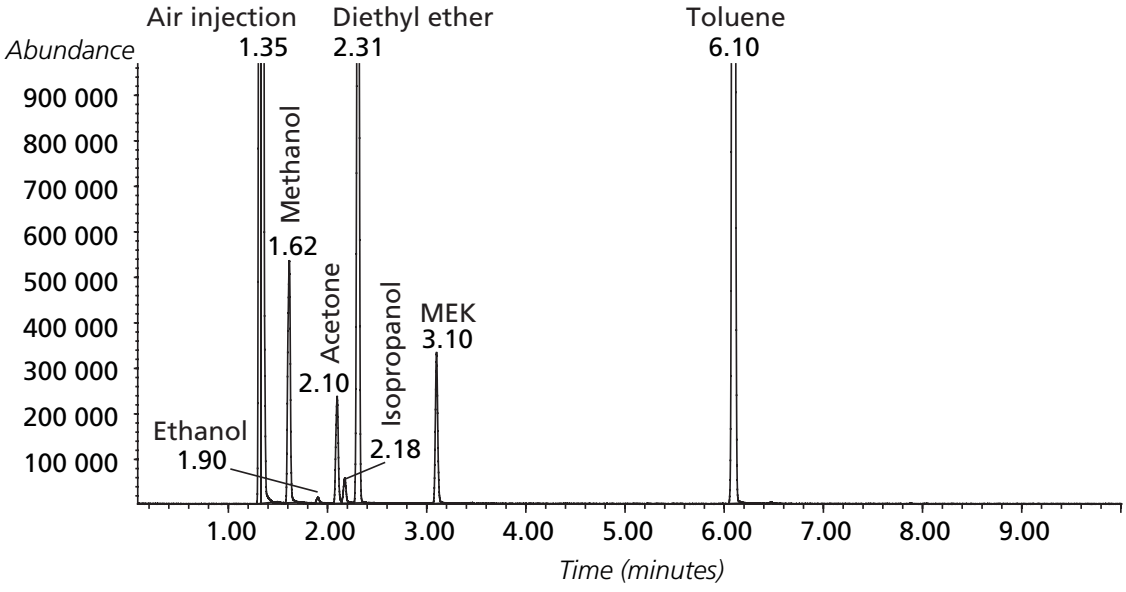
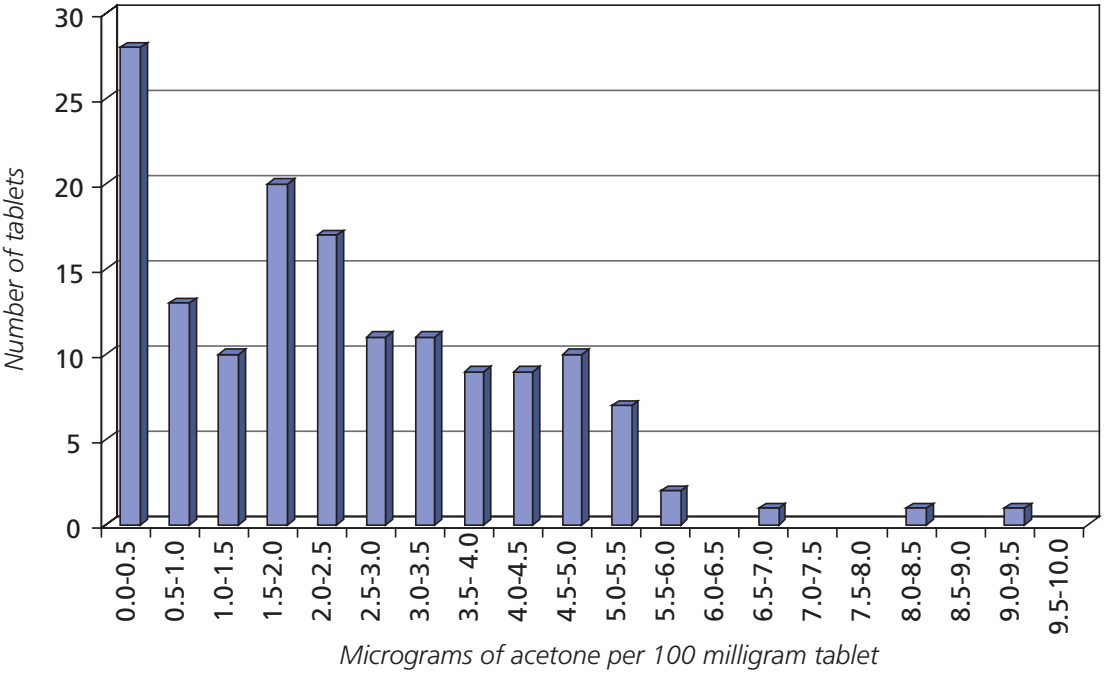


Figure IV. Acetone concentration in 150 quantified methylenedioxymethamphetamine tablets



variation in the acetone concentration makes this analytical method interesting for comparative examinations.

The highest concentration of toluene measured was 7.6 μg/100 mg tablet. In the majority of the toluene-containing tablets, it was present in a concentration of between 0.002 and 0.05 μg/100 mg tablet. Diethyl ether was quantified with a highest measured concentration of 1.9 μg/100 mg tablet. In the majority

of the diethyl ether-containing tablets, concentrations were between 0.01 and 0.2 μg diethyl ether/100 mg tablet. The highest measured concentration of IPA was 5.4 μg/100 mg tablet. The highest measured concentration of ethanol was 4.3 μg/100 mg tablet.[2] Other volatiles were not quantified.

Excipients

In order to exclude solvents originating from sources other than MDMA hydrochloride, some frequently used excipients were tested, involving various batches of lactose, glucose, starch, talc, microcellulose, caffeine and magnesium stearate, originating from illicit production sites. No residual solvents were detected.

Stability test

The stability of the acetone concentration in the control sample powder and five types of (whole) MDMA tablet were investigated by drying the samples for three hours in an oven at 60 °C. The results are presented in table 6. The control sample and two of the five tablets (types 4 and 5) did not lose acetone; the other tablets (types 1, 2 and 3) lost 60, 80 and 15 per cent, respectively, of their acetone. This supports the general opinion that the occluded acetone may be very stable in the crystals. However, it also suggests that additional acetone in the tablet can—in contrast to the trapped acetone—be removed by heating. At this point, further research needs to be done. The control sample appears to be stable over a period of eight months (see table 3). The preliminary conclusion is that the laboratory must be very careful with the interpretation of quantitative results, especially when there are indications of different sample treatment or long periods of time between the seizures.

Table 6. Stability test: acetone concentration before and after heating for three hours at 60 °C

Sample[a]	*Humidity (percentage)*	*Micrograms of acetone per 100-milligram tablet in original sample*	*Micrograms of acetone per 100-milligram tablet in heated sample*[b]
Control sample (powder)	0.2	2.11	2.18[c]
Type 1 of MDMA tablets	4.3	5.4	2.09
Type 2 of MDMA tablets	2.4	2.72	0.54
Type 3 of MDMA tablets	2.7	2.35	2.00
Type 4 of MDMA tablets	0.3	4.22	4.54[c]
Type 5 of MDMA tablets	2.8	1.65	1.64[c]

[a]See table 3 for the corresponding tablet logos.

[b]Not corrected for humidity.

[c]Values do not mean an increase since they are within the reproducibility of the method.

[2]It should be taken into account that the repeatability of ethanol is high (RSD 11 per cent) because of its polarity, resulting in low peak area and poor peak shape.

Application in casework

The method was applied three times for cases where a comparison between two tablets was requested (see table 7). Both the organic impurities and the volatiles were analysed. In two of the three cases, both the analysis of the volatiles and the organic impurity profile indicated links. In the third case, different acetone concentrations for the "cherry" tablets suggested no batch relation between the tablets. This was consistent with the results of the organic profiling: the conclusion was "not linked".

Table 7. Tablet comparisons

Comparison	*Tablet logo*	*Micrograms of acetone per 100-milligram tablet*	*Conclusion of solvent determination*	*Conclusion of organic profiling*
A1	Crown	2.8	Match	Match
A2	Crown	2.8		
B1	Alien	0.5	Match	Match
B2	Alien	0.5		
C1	Cherry	0.3	No match	No match
C2	Cherry	0.9		

Conclusions

A method was developed for the detection and quantification of solvents in MDMA tablets based on static headspace GC/MS. The different tablet matrices required the use of a standard addition method. From different cases received at the Netherlands Forensic Institute, 155 MDMA tablets were analysed for residual solvents, which were detected in all but two of the tablets. Acetone was found in 94 per cent of the tablets. This is consistent with the findings for illicit production laboratories of MDMA where acetone is widely used at the crystallization stage. The highest measured concentration of acetone was 9.4 μg/100 mg tablet. Toluene was present in 30 per cent of the tablets. In 48 per cent of the tablets, two organic solvents were detected, and in only 5 per cent, three or more solvents.

Regarding toluene, the result was not consistent with the author's experience with illicit laboratories, where toluene was almost never encountered. Since contamination in the Forensic Science Laboratory was excluded, other sources in the illicit production laboratory are suspected to contain traces of toluene, such as the solvents or precursors used. Preliminary tests showed toluene to be present in several samples of PMK, a precursor.

Another crystallization solvent is diethyl ether, which was detected in 10 per cent of the tablets, with a highest measured concentration of 1.9 μg/100 mg tablet.

Alcoholic solvents, which are used in the first synthetic stage in MDMA synthesis, were only occasionally detected in MDMA tablets, most probably because of their high detection limit, a result of their polar character.

The method developed can be used for strategic purposes. The resulting data can be useful since they give insights into the production process and the role of certain solvents. That information can be used as an intelligence tool or as an input for investigations, or as a basis for monitoring and control of precursor chemicals.

Further, it can be used in comparative analysis. It gives information on the solvents used in the synthesis of MDMA, especially on the crystallization stage. The wide variety in the concentration of the solvents may be of value in a comparison. However, it is advisable to be circumspect in drawing conclusions on the quantitative data, since at the present time there is insufficient insight into the stability of those concentrations over time.

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