Profiling of ecstasy tablets

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1 Introduction

The active component in ecstasy tablets is 3,4-methylenedioxymethamphetamine (MDMA, figure 1). MDMA is a derivative of amphetamine. MDMA has two main effects. On one hand it has a stimulating effect. The user gets more energy. The experiences become more intense and the inhibitions disappear. On the other hand MDMA has an entactogenic effect. It raises the empathy for everything and everyone. Therefore ecstasy is also called the love drug. MDMA has little hallucinogenic activity (1). The terms 'Ecstasy' and 'XTC' are used for the first time in the scientific literature in 1982 (2).

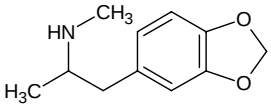

Figure 1: Chemical structure of 3,4-methylenedioxymethamphetamine (MDMA).

Ecstasy tablets are however never pure MDMA. It is not a pharmaceutical product that has been produced in clean rooms by the best chemists. Precursors, intermediary products and reaction by-products will, to a certain degree, always be present. The precursors are, generally, not of pharmaceutical quality. Some raw materials are illegal products or their trade is regulated. When a reaction has not taken place entirely, intermediary products can still be present. With some reactions not only MDMA is produced, but other, undesired, reaction products can be generated. These products are called reaction by-products (3). Before making tablets, sugars are added to the MDMA powder as fillers. These sugars are mainly lactose. Sometimes sorbitol or cellulose and occasionally glucose or mannitol are used as filler. Instead of sugars, talc (magnesium silicate) is sometimes added to the MDMA powder. To bind all this in a nice tablet, phthalates, diethyl phthalate and dibutyl phthalate, and salts of acids, magnesium stearate and palmitine, are added as lubricants. Dyes are often added to the tablets to give them an eye-catching colour and attractive appearance with a matching logo.

Sometimes pills are sold as ecstasy, despite not containing MDMA itself but another of the related phenethylamines such as amphetamine, methamphetamine, MDEA (3,4-methylenedioxyethylamphetamine), MDA (3,4-methylenedioxyamphetamine), 4-MTA (4-methylthioamphetamine), PMA (paramethoxy-amphetamine) and MBDB (N-methyl-1- (3,4-methylenedioxyphenyl) - 2-butamine). These substances have similar effects to MDMA (1;4). Other legal and illegal components which can be present as active ingredients in ecstasy tablets, are ephedrine, caffeine and ketamine. These ecstasy tablets can be dangerous for the user because they produce a different effect, and the user may take more tablets in order to obtain the same effect as MDMA. Additionally, experiencing the desired effect my take longer which might also cause repeat dosing (4).

In Europe ecstasy is the second most used illegal drug, after cannabis, this in contrast to the United States. The popularity of ecstasy in Europe can be explained geographically. Ecstasy is mainly produced in Europe and especially in the Netherlands and Belgium (5;6). The number of illegal laboratories closed down in Belgium has increased in recent years. Between 1999 and 2004 59% of these illegal laboratories produced ecstasy (7).

Nowadays the production of MDMA powder and the production of the tablets from this powder happens less and less in one laboratory. Previously, all the activities where centralised in one laboratory. MDMA powder is produced in a chemical laboratory. In the tablet pressing location several substances, such as fillers, lubricants and dyes, are added to the MDMA powder before pressing the tablets. The type of fillers, lubricants and dyes used and the quantity of these substances added to the MDMA powder as well as the logo are variable within one tablet making location. The consequence of splitting the production procedure between several locations allows powder production in one location which can then be sent to several tablet making sites concurrently. Subsequently MDMA powder produced within one laboratories can have other products added and different

logos or colours depending on where it is pressed into a tablet. Additionally, it is possible that two, externally identical tablets, contain different active components (8).

Illegal ecstasy is prepared according to three different methods. The most popular method for the illegal production of ecstasy is the reductive amination of 1 (3,4-methylenedioxyphenyl) - 2-propanone (PMK) (figure 2). In the clandestine laboratories a diversity of reducing agents is used, but most widespread is reduction with the catalyst PtO_2 (platinum oxide) or reduction with $NaBH_4$ (sodium borohydride) at a low temperature (- 20°C). This last method is called the cold method. In the clandestine laboratories which use this method, there are always a few freezers (3).

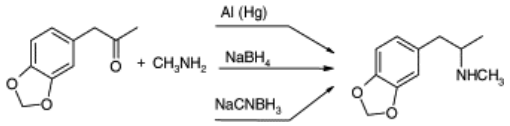

Figure 2: Reductive amination from PMK to MDMA.

The other methods for production of illegal ecstasy are the Leuckart reaction (figure 3) and bromination of safrole (figure 4).

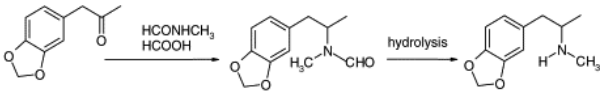

Figure 3: Leuckart reaction production of MDMA from PMK.

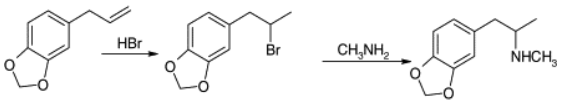

Figure 4: Safrole bromination production of MDMA from safrole.

Chemical profiling of ecstasy is an important process in the control of the international trade in these products. Profiling enables identification of possible reaction pathways being used for the manufacture of drugs. This way the raw materials can be identified and, if necessary, regulated. Tablets of different seizures can be linked and commercial traffic can be identified. Also additives or impurities which are potentially dangerous for the public health, because of their inherent dangers, can be identified.

2 Objectives

Within the framework of this project it was attempted to answer the following three questions:

- Does the chemical analysis of the tablet or of the active substance originating from the synthesis allow to find a link between several drug seizures or between seizures of drugs and the place of production;
- Which are the relevant chemical indicators that will allow this profiling to be used in court;
- Which are the requirements for a database to automate the comparisons?

The aim of the project was chemical profiling of the impurities present in ecstasy tablets. The chemical profiling was done by means of two techniques, RS and GC-MS. The analyses with RS were performed at the Home Office Scientific Development Branch (HOSDB) in London, United Kingdom. GC-MS-analyses were performed at Ghent University. GC-MS is now the preferred method for analyzing of ecstasy tablets. The research project CHAMP (Collaborative Harmonisation of Methods for Profiling of Amphetamine type Stimulants) was set up by the ENFSI (European Network of Forensic Science Institutes) and funded by the European Commission to harmonize the different methods for profiling ecstasy. A disadvantage of the use of GC-MS is that the tablets, for the analysis, need an intensive, time-consuming and destructive preparation. Investigation as to whether RS, a fast and non destructive method, can give analogous or complementary results in comparison with the labour-intensive GC-MS was done.

During the tablet sample collection phase, samples of laboratories and large seizures were taken in order to obtain samples from supposedly different containers/batches. This way the most useful parameters for the intra-batch variation could be examined and a distinction between batches from different laboratories and batches from the same laboratory could be made.

3 Methodology

Samples of different laboratories and large drug seizures (more than 1,000 tablets) were collected.

The external characteristics of the ecstasy tablets were examined: weight, size (diameter and height), form, colour of the tablet, logo (front and back), score, elevation, coating and possible odour. The Europol Ecstasy Logo Catalogue 2005 (9) was used for the identification of the logos.

Chemical profiling was done by means of two techniques, namely RS and GC-MS. After a study of the available literature, contact with research groups of the European project CHAMP and empirical research methods were developed, were validated and were applied for the profiling of ecstasy tablets with RS and GC-MS. Within the CHAMP project the different detection methods for ecstasy were harmonized using GC-MS analysis of the tablets. We analysed all tablets with GC-MS on 46 different impurities.
In order to determine the active components present in the ecstasy tablets, the tablets were also analysed with LC-MS-MS. The quantification of MDMA was done with GC-MS.

The results were introduced in Microsoft Excel, SP3 and SPSS. The different tablets/batches were compared and when possible connections between different seizures were made. Therefore the Pearson correlation was used.

4 Results

4.1 Physical appearance

In table 1 an overview of the external characteristics for the different seizures of which samples were obtained, is given. These external characteristics are the logo, the colour, the score, the mean diameter, the mean height and the mean weight. Some seizures contained several different packages. All these packages are included in this table. The tablets of seizure 7 were with and without score. Both types are shown in the table. The tablets of seizure 8 package 5 (8/5) contained a mixture of external characteristics.

Table 1: Overview of the external characteristics for the different seizures, with exception of package 5 of seizure 8. The external characteristics are the logo, the colour, the score, the mean diameter (in mm), the mean altitude (in mm) and the mean weight (in mg).

	Picture	Logo	Colour	Score	Diameter	Altitude	Weight
Seizure 1		'AJ'	White	–	8.08 ± 0.02	4.27 ± 0,10	259.8 ± 7.1
Seizure 2		'AJ'	White	–	8.09 ± 0.03	4.36 ± 0.06	261.1 ± 3.8
Seizure 3		288-08 (62) Bacardi	Blue	–	7.17 ± 0.05	3.34 ± 0.08	146.2 ± 3.5
Seizure 4		Swallow	Grey-white flecked	+			
– 4/1		"	"	+	8.04 ± 0.01	3.28 ± 0.08	182.2 ± 10.3
– 4/2		"	"	+	8.03 ± 0.02	3.29 ± 0.08	182.8 ± 8.7
– 4/2 b		"	"	+	8.03 ± 0.01	3.27 ± 0.13	180.0 ± 10.6
– 4/3		"	"		8.05 ± 0.02	3.28 ± 0.09	180.5 ± 10.3
Seizure 5							
– 5/1		Armani	Beige-white flecked	+	7.04 ± 0.01	3.27 ± 0.08	171.9 ± 5.5
– 5/2		Armani		+	7.08 ± 0.01	3.30 ± 0.08	172.0 ± 4.2
– 5/3		2 lips	White	–	7.10 ± 0.03	4.33 ± 0.25	190.6 ± 14.0
– 5/4		2 lips	"	–	7.09 ± 0.03	4.21 ± 0.24	185.3 ± 13.3
– 5/5		2 lips	"	–	7.09 ± 0.02	4.38 ± 0.26	190.4 ± 13.2
– 5/6		Kite	White	–	9.13	3.43	252.9
Seizure 6		Dolphin	Red	+	6.08 ± 0.02	4.88 ± 0.11	187.7 ± 8.9
Seizure 7		Bird					
7/1 with		"	Green	+	8.02 ± 0.01	3.79 ± 0.15	245.6 ± 7.0
7/1 without		"	"	–	8.03 ± 0.01	4.01 ± 0.06	249.7 ± 10.1
7/2 with		"	"	+	8.03 ± 0.01	3.79 ± 0.16	245.4 ± 7.9
7/2 without		"	"	–	8.05 ± 0.01	4.02 ± 0.05	247.9 ± 8.7
7/3 with		"	Red	+	8.03 ± 0.01	3.88 ± 0.15	245.5 ± 8.3
7/3 without		"	"	–	8.05 ± 0.01	4.00 ± 0.07	247.2 ± 9.0
7/4 with		"	"	+	8.03 ± 0.01	3.80 ± 0.14	243.1 ± 7.0
7/4 without		"	"	–	8.05 ± 0.01	4.01 ± 0.06	246.0 ± 6.0
7/5 with		"	"	+	8.02 ± 0.01	3.80 ± 0.11	242.4 ± 4.1
7/5 without		"	"	–	8.03 ± 0.01	4.00 ± 0.06	248.1 ± 7.5
7/6 with		"	"	+	8.01 ± 0.01	3.83 ± 0.13	244.4 ± 6.3
7/6 without		"	"	–	8.02 ± 0.01	4.02 ± 0.09	248.3 ± 10.0

	Picture	Logo	Colour	Score	Diameter	Altitude	Weight
7/7 with		“	“	+	8.01 ± 0.01	3.79 ± 0.11	243.1 ± 4.6
7/7 without		“	“	–	8.01 ± 0.01	4.04 ± 0.10	252.9 ± 12.0
7/8 with		“	“	+	8.03 ± 0.01	3.85 ± 0.15	244.3 ± 6.9
7/8 without		“	“	–	8.03 ± 0.01	4.01 ± 0.07	248.6 ± 7.7
7/9 with		“	“	+	8.02 ± 0.01	3.86 ± 0.14	245.0 ± 5.6
7/9 without		“	“	–	8.03 ± 0.01	4.04 ± 0.09	252.4 ± 11.1
Seizure 8							
8/1					7.06 ± 0.01	4.75 ± 0.47	225.3 ± 22.3
– a		Mitsubishi	Brown	–	7.06 ± 0.01	4.51 ± 0.50	218.9 ± 28.6
– b		Euro	“	–	7.05 ± 0.02	4.43 ± 0.29	213.5 ± 16.3
– c		‘LOVE’	“	–	7.05 ± 0.01	5.10 ± 0.33	239.8 ± 16.3
– d		None	“	–	7.06 ± 0.01	5.00 ± 0.32	229.8 ± 15.7
8/2		Euro + Armani Euro	Blue	–	7.06 ± 0.01	6.08 ± 0.10	293.7 ± 3.0
8/3		Euro	White	–	7.07 ± 0.01	4.89 ± 0.26	230.7 ± 19.3
8/4		Mitsubishi	Grey-white flecked	+	8.10 ± 0.01	4.50 ± 0.08	265.3 ± 5.1
8/5	Mixed						

The distribution of the height was larger than that of the diameter. This can logically be explained. Each tablet making machine has a fixed number of positions and each position has a certain diameter. The height of the tablets depends on the quantity of the powder and the pressure. The quantity of the powder is a variable factor. The pressure of the press is generally not changed and therefore this factor is a constant.

4.2 Chemical profiling

Raman spectroscopy (RS)

With RS the active components and the fillers present can be measured. Despite the range of colours, shapes and particle packing of the tablets, these characteristics do not appear to have impeded the collection of Raman spectra.

Although there are strong spectral similarities between the compounds (MDMA, MDEA, MDA) there are also sufficient differences to allow them to be distinguishable especially in the fingerprint region of 700-1100cm^{-1}. Figure 5 shows stacked standard spectra of the reference phenylethylamine derivatives. Figure 6 is a spectrum of cellulose one of the four principle excipients identified in the tablets.

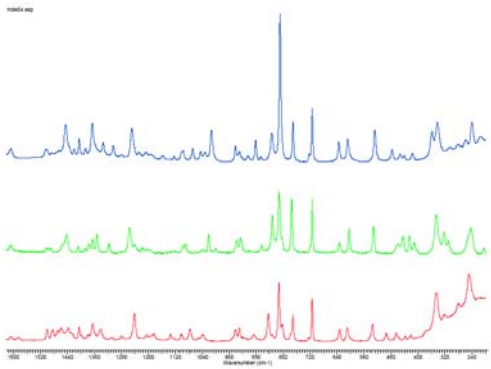

Figure 5: Overlaid reference spectra of the phenylethylamine derivatives MDMA (blue), MDA

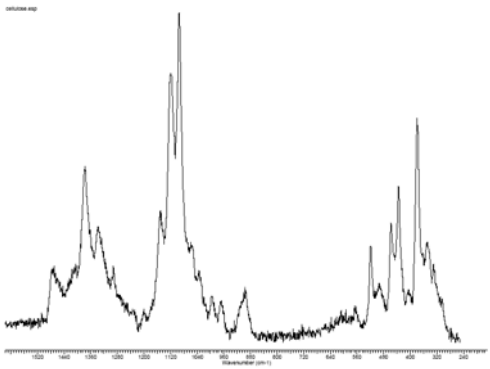

Figure 6: Reference spectra of cellulose.

(green) and MDEA (red).

The spectral similarities between MDMA, MDA and MDEA when they are present as a mixture make it difficult to assign the presence of a particular drug. This difficulty is compounded by the crude methodology used to manufacture the tablets, resulting in the presence of multiple derivatives rather than MDMA itself which is typically sought. Additionally, the smearing effect of the tablet casting machines may amalgamate the particles further, complicating the spectral representation. Additionally, visual comparison of the spectra without consideration of the absolute peak position can result in mis-assignment of the drug components present.

In figure 7 the average excipients peak response for the different fillers (glucose, sucrose, sorbitol and cellulose) for the different seizures is given. In batch 5/1, 5/2, 6 and 7 approximately the same amount of all the different excipients was added. To seizure 1 and 2 only cellulose was added. Whereas to seizure 5 package 3, 4 and 5 mainly sorbitol and to a lesser degree also cellulose and sucrose were added.

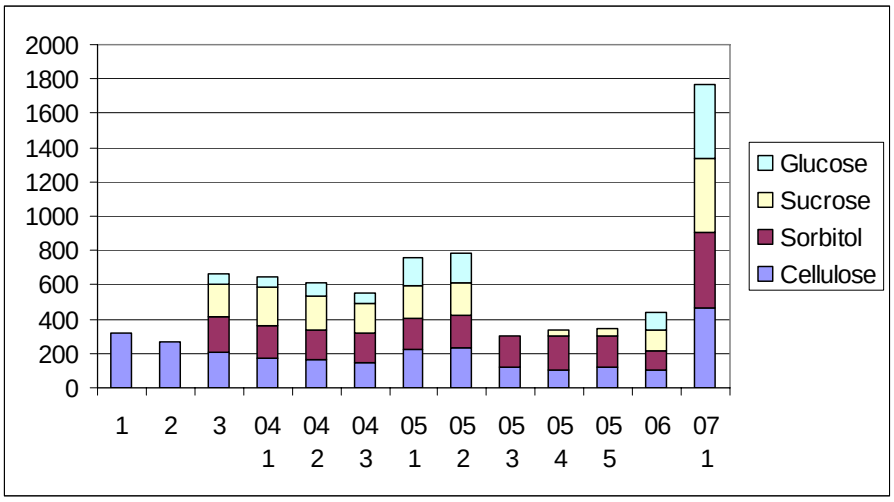

Figure 7: Average excipient(s) peak response tables for the different batches.

In figure 8 the ration of phenylethylamine/cellulose of the different tablets are collected by seizure or by package and plotted in a cluster diagram. The error bars represent the standard deviation of the ratio of phenylethylamine to cellulose. The graphs all support the conclusion that there are differences between the batches but trends within the sub-batches. Interestingly, all of the tablets seem to be grouped within each batch in terms of the ratio of average phenylethylamine derivative to cellulose but in some the intensity of the average phenylethylamine derivative peak intensity is varied. Good examples of this are batches 2 and 3 where the lowest peak intensity is 200 arbitrary units and the highest almost 600 arbitrary units. The errors of uncertainty are also large spanning almost 200 arbitrary units. Batch 2 also has one tablet with the highest ratio of average phenylethylamine derivative to cellulose which could have resulted from a blockage in the press filling machine causing in more drug than filler to be added or the tablet could originate from another batch or laboratory.

The ratio of the phenylethylamine derivatives to the present filler, cellulose, has a standard normal distribution around the average value for each seizure.

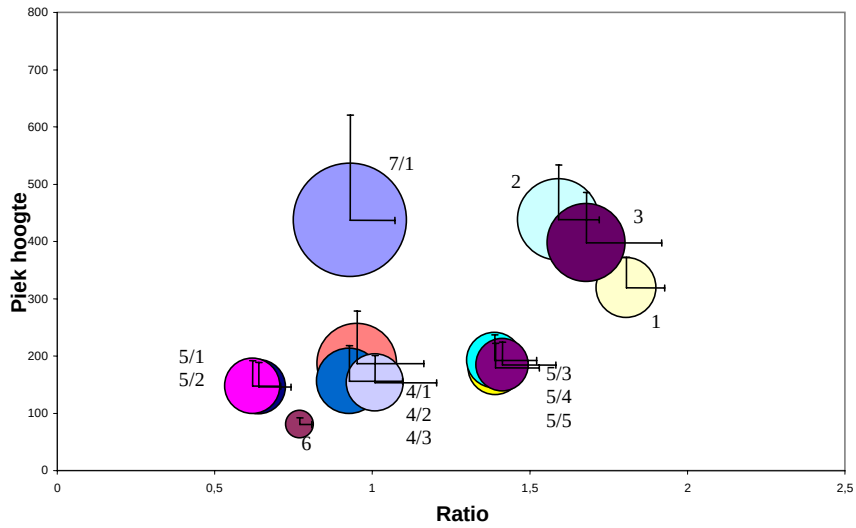

Figure 8: Cluster plot of the ratio of phenylethylamine/cellulose plotted against the average peak intensity for all the analysed tablets. The error bars present the standard deviation of the ratio of phenylethylamine to cellulose (X-as) and the peak height (Y-as).

Comparison of the overall batch average peak positions and peak responses of the phenylethylamine derivatives and excipients shows the variability across the batches for example batch 1 versus batch 3 but also reveals trends within the sub-batches for example sub-batches 4/1, 4/2 and 4/3. However the error bars of the peak responses of the phenylethylamine derivatives overlap across all the batches implying they may not be as discrete as the data shows.

Active components

The active components present in the tablets are listed for all the different seizures in table 2. Some tablets did not only contain MDMA powder but also amphetamine, methamphetamine, cocaine and/or caffeine. Some of these components were deliberately added to the MDMA powder, other components were contaminants.

- MDA and MDEA are possibly present because of the illegal production of MDMA. Table 2 shows that both components are only present in trace amounts. MDA and MDEA were not added to these tablets, but were present as impurities.
- It is customary that caffeine and amphetamine are added to the MDMA tablets.
- The presence of methamphetamine could possibly be explained by the contamination of the precursor PMK (see 1. introduction) with BMK (benzylmethylketone). Because of the contamination of PMK with BMK, methamphetamine was formed during the reaction were PMK is processed to MDMA.
- The presence of cocaine is very exceptional. It is possible that the glassware was contaminated with cocaine. Police information of seizure 6 stated that cocaine was seized together with these ecstasy tablets.
- The amount of MDMA added to the tablets varied from very little, for 5/2 with a mean of 17,72 mg per tablet, to a large amount of MDMA, for 2 with a mean of 150 mg (table 2). The mean concentration of MDMA per tablet was 63.20 mg ± 31.76 mg.

The tablets of seizure 7 had a red or a green colour and there were tablets with or without score, in this table this division is made. The tablets of seizure 8 package 5 had very diverse external characteristics. The division of 8/5a, 8/5b, 8/05e and 8/5f in groups will be explained later.

The batches with no samples over for analysis with LC-MS-MS are not incorporated in this table.

Table 2 will be discussed when the results of the GC-MS analyses are considered. The division of seizure 5 in two groups can be observed. The tablets belonging tot 5/1 and 5/2 show resemblances as do the tablets of 5/3, 5/4 and 5/5.

Table 6: Overview of all the different active components present in the different tablets (in mg).

	Amphetamine	Methamphetamine	MDA	MDEA	Cocaine	Caffeine	MDMA
1	-	-	0,321	0,0774	-	-	111,32
2	-	-	0,483	0,1521	-	-	150,67
3	-	-	0,179	0,0448	-	-	67,51

	Amphetamine	Methamphetamine	MDA	MDEA	Cocaine	Caffeine	MDMA
4/1	-	0,00477	0,122	-	-	-	54,42
4/2	-	0,00403	0,177	0,0192	-	-	52,83
4/3	-	0,00936	0,164	0,0310	-	-	54,33
5/1	0,502	-	0,152	0,0485	0,0302	31,7	18,07
5/2	0,377	-	0,137	0,0413	0,0437	31,1	17,72
5/3	-	-	0,161	0,0405	-	-	69,01
5/4	-	-	0,201	0,0416	-	-	60,07
5/5	-	-	0,183	0,0344	-	-	65,44
6	-	0,250	0,252	-	0,00874	9,24	35,91
7 green with	-	0,0156	0,299	0,0525	-	-	93,34
7 green without	-	0,0172	0,560	0,0603	-	-	94,67
7 red with	-	0,0372	0,494	0,0817	-	-	93,12
7 red without	-	0,0451	0,547	0,0604	-	-	89,22
8/1	30,96	0,0902	0,170	0,2076	-	+	41,09
8/3	0,0882	-	0,171	0,0226	-	-	32,43
8/4	0,153	0,0219	0,300	0,0449	-	-	66,73
8/5 group 1	31,8	0,249	0,182	0,117	-	+	31,94
8/5 group 2	0,826	1,465	0,119	0,0268	-	1,64	57,90
8/5 group 3	2,2	0,118	0,219	0,0355	-	-	55,27
8/5c + d	0,31	0,0461	0,444	0,0698	-	-	83,93

Gas chromatography – mass spectroscopy (GC-MS)
With GC-MS the impurities typical for the illegal production of MDMA are measured.

To measure the variability of the interpretation of the chromatograms four chromatograms were processed on four successive days by two different persons. The mean Pearson correlation coefficient for the processing by one person was 99.99007. Processing of these data by a second person, gave approximately the same result (mean Pearson correlation coefficient 99.97485).

To examine the variability of the GC-MS the same extract of the same tablet was injected 10 times. The mean Pearson correlation coefficient of these different analyses is 99.99176.

For the mean intra-lot Pearson correlation coefficient the mean Pearson correlation coefficient of the analysed tablets for a seizure or for a package if a seizure contained different packages, was calculated. Every tablet was compared to the other tablets of the same seizure (or the same package) with the Pearson tests. The intra-lot Pearson correlation coefficient is 99.74003. The minimum value for the Pearson correlation coefficient in the same batch is 90.52713 (2 tablets of package 5 of seizure 5). In package 3 of seizure 5 (5/3) the Pearson correlation coefficient is 93.73444. In this batch there was a tablet with a much larger peak area of one component compared to all the other tablets.

In table 3 an overview is given of the mean Pearson correlation coefficients of all the seizures when compared with each other. The high Pearson correlation coefficients (> 99) have been highlighted in red. The tablets with a rather high Pearson correlation coefficient (> 95) are written in bold. The cells of the packages belonging to the same seizure are highlighted in yellow. Of seizure 7 only 4 packages have been incorporated in this table, two packages with green tablets and two packages with red tablets.

Table 3: Mean Pearson correlation coefficient of the analysed tablets with respect to tablets of other seizures.

	1	2	3	4/1	4/2	4/2b	4/3	5/1	5/2	5/3	5/4	5/5	5/6	6	7/1	7/2	7/8	7/9	8/1	8/2	8/3	8/4	gr 1	gr 2	8/5c	8/5d	8/5g	8/5h	8/5i	8/5j	8/5k	8/5l	8/5m	8/5n
1	100	99	77	86	86	85	86	76	74	69	71	69	82	88	87	87	86	86	76	78	84	91	77	82	68	69	86	87	90	75	69	86	70	74
2		100	75	88	87	87	87	71	69	69	70	68	81	85	88	87	87	87	73	75	84	92	75	83	69	70	86	88	92	75	70	88	71	73
3			100	88	88	87	88	82	81	77	78	77	86	91	86	86	86	86	85	87	88	86	85	80	88	89	85	83	76	73	87	75	88	83
4/1				100	100	97	100	71	70	74	76	74	83	90	92	92	92	92	81	83	89	91	82	83	86	86	86	86	87	73	85	84	85	79
4/2					100	97	100	72	70	75	77	75	84	90	92	92	92	92	82	84	89	91	82	82	87	87	86	86	87	73	86	84	86	80
4/2b						100	98	75	72	81	82	80	91	90	93	92	93	92	85	88	95	95	87	85	91	91	88	90	89	76	92	87	92	86
4/3							100	72	70	76	77	75	84	90	92	92	92	92	82	84	90	92	83	83	87	87	87	87	87	74	86	84	86	80
5/1								100	100	84	85	84	83	92	70	69	70	70	92	92	76	75	92	81	78	78	84	81	75	80	77	76	79	91
5/2									100	84	85	84	81	91	68	67	68	68	92	91	74	72	91	78	75	76	82	78	72	77	74	73	77	90
5/3										100	100	100	84	85	74	73	75	74	87	87	80	75	86	73	80	80	75	76	71	68	81	73	82	88
5/4											100	100	85	86	75	74	76	75	88	88	80	76	87	73	80	81	76	77	72	68	81	74	83	89
5/5												100	83	85	73	73	74	73	86	87	79	75	86	72	79	80	75	75	71	67	80	72	82	87
5/6													100	90	89	88	89	88	85	89	94	94	88	82	87	88	86	91	82	77	89	83	89	88
6														100	87	86	87	87	91	92	89	89	90	84	83	84	89	88	84	78	82	83	84	89
7/1															100	100	100	100	77	81	90	94	79	82	81	81	84	88	87	73	81	84	81	76
7/2																100	100	100	76	81	89	94	78	82	81	81	83	88	86	73	81	84	80	75
7/8																	100	100	78	82	90	94	79	82	82	82	83	88	86	73	82	84	82	77
7/9																		100	78	82	89	94	79	82	81	81	83	88	86	73	81	83	80	76
8/1																			100	99	82	79	99	79	84	85	83	81	77	74	84	78	86	99
8/2																				100	86	84	99	84	88	89	87	86	81	79	88	83	90	99
8/3																					100	97	85	85	89	89	88	91	87	78	90	87	91	85
8/4																						100	83	89	86	86	91	95	93	81	87	91	87	81
gr 1																							100	85	88	89	88	87	82	81	88	84	90	99
gr 2																								100	87	88	99	98	97	98	88	98	87	81
8/5c																									100	100	89	89	82	83	100	84	99	86
8/5d																										100	90	89	83	83	100	85	100	87
8/5g																											100	98	96	96	89	97	89	85
8/5h																												100	97	94	90	97	89	84
8/5i																													100	93	83	99	82	78
8/5j																														100	83	95	83	77
8/5k																															100	86	100	87
8/5l																																100	85	81
8/5m																																	100	89
8/5n																																		100

The seizures containing different bags are discussed below.
Table 3 shows the mean Pearson correlation coefficient of the analysed tablets of the different packages of seizure 4. Because of these high values, as well as the high value for the mean Pearson correlation coefficient (99.07374), there was a presumption that these tablets, in spite of the storage in different packages, were manufactured in the same laboratory. The tablets from the little package, seizure 4/2b, had a lower Pearson correlation coefficient compared to the tablets of the other packages.
Comparison of the mean Pearson correlation coefficient of the different packages of seizure 5 showed large differences (table 3). These tablets were all seized together, but packages 5/1 and 5/2 showed totally different external characteristics and contained different active substances (table 2) then packages 5/3, 5/4 and 5/5. The last tablet, belonging to package 5/6, was again totally different then the previous packages. This was also reflected in the average Pearson correlation coefficient. Packages 5/1 and 5/2 had a high Pearson correlation coefficient when compared with each other. This applied also to the Pearson correlation coefficient of packages 5/3, 5/4 and 5/5. The Pearson correlation coefficient of 5/1 and 5/2 when compared with 5/3, 5/4 and 5/5 and when compared with 5/6 was not so high. Therefore it is possible that the tablets of the first two packages came from the same laboratory. Also the following three packages contained tablets from the same laboratory. The tablet in package 6 was different. This seizure contained tablets from three different laboratories or tablets produced on several days or on another production line.
The mean Pearson correlation coefficient of the tablets with and without score of seizure 7 was 99.95914. It seemed that there was no difference between the tablets with and these without score. The tablets of seizure 7 were divided in nine different packages. The first two packages of these nine packages contained tablets with a green colour. The tablets of the following seven packages had all a red colour. However, it was not possible to distinguish between the mean Pearson correlation coefficient of green tablets when compared with the red tablets and the red or green tablets among themselves. The lowest mean Pearson correlation coefficient between these tablets was 99.5969. These results would tend to support the conclusion that according to GC-MS analyses, these tablets, independent of the colour or the score, are probably manufactured in the same laboratory.
Seizure 8 did not only exist of different packages, but some of these packages also contained tablets with different logos. Package 1 of seizure 8 (8/1) contained tablets with 4 different logos, but the average Pearson correlation coefficient for 8/1 was 99.65114, which could indicate that these tablets were originating from the same laboratory. The tablets of seizure 8/2 had a high average Pearson correlation coefficients in correlation with 8/1. The tablets of package 8/3 and 8/4 had a lower Pearson correlation coefficient when compared with the first two packages (8/1 and 8/2), but had a high Pearson correlation coefficient when compared with each other. This implies that whilst the tablets from packages 8/3 and 8/4 are probably manufactured in the same laboratory, it is likely that this is either a separate laboratory, production line or production day to packages 8/1 and 8/2. Package 8/5 was subdivided according to the external characteristics. The first six packages (8/5a – 8/5f) contained tablets with the same external characteristics in multiple numbers. The last package with samples contained a variety of tablets of which there were only a few tablets in package 8/5 (8/5g – 8/5n). During the preparation for GC-MS analysis, it appeared however that some tablets (8/5a, b, e, f) had a different colour, in spite of the fact that they were considered identical during the sampling. These colour differences were not very distinctive, rather a difference in gradation. It seemed that the colour difference agreed with a classification on the basis of GC-MS analysis, so this group of tablets with the same logo could be subdivided in three different groups. A first group existed of tablet 4, 6, 7, 8, 9 and 10 of 8/5a, tablet 2, 5, 8, 9 and 10 of 8/5b, tablet 3 and 4 of 8/5e and tablet 2, 3 and 5 of 8/05f. These were the tablets with a browner colour. A second group of tablets had a purpler colour: tablet 1, 2, 3 and 5 of 8/5a, tablet 1, 3, 4 and 6 of 8/5b, tablet 1, 2, and 5 of 8/5e and tablet 1 and 4 of 8/5f. Tablet 8/5b/7 was different from all these tablets. This tablet contained only a trace amount of amphetamine and methamphetamine and no caffeine. Tablets of both group 1 and group 2 contained amphetamine, methamphetamine and caffeine (table 2). Tablet 8/5b/5 had a lower Pearson correlation coefficient when compared to the other tablets, but the same added active substances as group 1. The external characteristics of these tablets (8/5a, b, e, f) and these of seizure 8 package 1 (8/1) were very similar. The tablets of group 1 have a high Pearson correlation coefficient (average 98.61615) when compared with the tablets of seizure 8 package 1. Also the active substances (table 2) are the same.
The tablets belonging to 8/5c (logo Mitsubishi) and 8/5d (logo euro) had a different logo, but the other external characteristics were the same. Because of the high Pearson correlation coefficient (table 3), these tablets are probably manufactured in the same laboratory. The tablets 8/5k (Mitsubishi logo) and 8/5m (no logo) had a high Pearson correlation coefficient when compared with each other and with the tablets of 8/5c and 8/5d. It might be stated that these tablets are also manufactured in the same laboratory.

Comparison of the Pearson correlation coefficients of the different seizures shows that the tablets of some seizures are more related than those of other seizures (table 3). Information was given that seizure 1 and seizure 2 were related to each other. The Pearson correlation coefficient of the two seizures is 99.05419. Using the analysis of the impurities a link between these seizures can be identified. The correlation between the tablets of

seizure 6 and those of seizure 3, 4, 5/1 and 5/2, 5/6 and 8/1 and 8/2 is rather good (> 90). But the correlation between these tablets is not so high. The correlation between the tablets of seizure 4, 7 and 8/4 is rather good (> 90). This is also true for tablet 5/6 and the tablets of seizure 8/3 and 8/4. Between these different seizures there is however, except for seizure 1 and 2, no similarity.

The presence of the different impurities depends on the synthesis route and the precursors used. In Belgium and in the Netherlands reductive amination is used for synthesis of MDMA. The components typical for a synthesis route can be found in the literature. The compound, typical for reductive amination, is N-[2-(3,4-methylenedioxyphenyl)-1-methylethymidene]-N-methylamine (17). This compound was found in all the tablets analysed during this project.

5 Conclusion

It was demonstrated that with the aid of the chosen GC-MS method it is possible to appoint tablets to a batch and to determine whether batches are identical. The mean intra-lot Pearson correlation coefficient was determined, 99.74 ± 0.41. Based on these results, the probability is high that tablets belong to a same batch when there Pearson correlation coefficient is higher than 99.74. There was not enough data to set a cut-off for the Pearson correlation coefficient of tablets of different batches belonging to a same laboratory.

The ecstasy tablets were analysed with RS as well and these analyses gave additional, relevant information on the tablets. Where RS gives information on the fillers, GC-MS gives information on the synthesis of the MDMA powder. Both methods are complementary and definitely relevant because the MDMA synthesis and tablet production are being done in separate places. The variability of the RS analysis of one tablet is very high. Because of the high variability it will be difficult to confirm the link between two tablets belonging to the same batch based on RS.
Although a few aspects still need to be investigated, with the used techniques it is possible to profile ecstasy tablets and to show correlations between the different seizures.

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