Introduction

The 2005 UNODC publication, ‘Methods for Impurity Profiling of Heroin and Cocaine’\(^1\) outlines a number of methods for the characterisation and comparison of heroin and cocaine samples for the purposes of establishing origin and/or finding links that help establish trafficking and distribution networks. The methods are categorised into five groups, namely

- major components
- trace organic components
- residual or occluded solvents
- trace elements
- isotopic abundance

The methods contained within this publication are still valid and some, if not all, are in use today. Since the publication of this manual other methods for chemically profiling heroin and cocaine have been reported, additionally some of the principles have been used to investigate other drugs, such as amphetamine type stimulants (ATS). As a result, several groups have produced reviews\(^2\)\(^3\)\(^4\) of the analytical techniques currently available and, in some cases, in use around the world. Analytical methods include capillary gas chromatography (cGC), high-performance liquid chromatography (HPLC), micellar electrokinetic capillary chromatography (MEKCC) and inductively coupled plasma techniques (ICP).

Chemical profiling generates large amounts of quantitative data and the computerisation of comparative analysis has introduced the use of statistical programmes for extensive data

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\(^1\) Methods for Impurity Profiling Heroin and Cocaine, United Nations Office on Drugs and Crime, Vienna, 2005  
\(^3\) Cocaine Profiling Methodology-Recent Advances, J.M.Moore, J.F. Casale, Forensic Science Review, 10:13; (1998)  
handling. Typically, methods used are principal component analysis (PCA) and different types of hierarchical clustering analysis (HCA). These are independent of drug type and the chemical technique used to acquire the data. Some other methods of interpretation are reported here. To make the choice of which interpretation method is most appropriate, a scientist should enlist the expertise of a mathematician (statistician) and information technology (IT) support.

From an investigative point of view sample characterisation/impurity profiling can be carried out for evidential or intelligence purposes and the methods available are the same. The application of any method will produce intelligence to some extent or another but when considering links for evidential reasons the degree of similarity between two samples must pass a threshold whereby a scientist is in no doubt that they share some common history and is prepared to say so. Frequently this may be achieved through the application of multiple tests. Which methods to apply and the extent of chemical profiling undertaken is governed by individual requirements.

**Some basic facts for consideration when choosing a chemical profiling regime.**

- Major components are generally considered to be those present at concentrations in excess of 1% relative to the target compound, e.g. heroin, cocaine, etc. Major component analysis is often of limited value if the drug being analysed is of high purity and/or ‘uncut’. Intelligence value may increase if there are a number of easily determined components in addition to the principle drug. In the case of heroin, for example, these may be alkaloids, such as papaverine and narcotine, derivatised alkaloids, such as acetylcodeine, or adulterants, such as caffeine and paracetamol. Generally, in respect of identifying links, this form of analysis falls short of an evidential standard unless supported by other information (which may or may not be scientific). Major component analysis can be a good screening tool to quickly show where samples are different.

- Crudely made drugs, such as heroin, cocaine and ATS, can contain a large number of organic impurities. These are often referred to as minor components and are generally present in concentrations below 1% relative to the target compound. These minor components may originate from the starting material, be by-products of the production or manufacturing process or arise from materials deliberately added afterwards.

- In most illicit samples of drugs, such as heroin cocaine and ATS, the vast number of organic impurities are at very low concentrations and would not ordinarily be detected by routine evidential methods designed primarily to identify and/or quantify the target controlled drug. The best comparison regime, therefore, would be one that, after routine identification tests, included a method specifically designed for the detection and reproducible measurement of a significant portion of the minor organic components present.
Generally, the larger the number of organic components that can be shown to be the same both qualitatively and quantitatively (either absolutely or in the same relative proportions) the better the comparison and the more weight that can be attached to an interpretation that the samples are linked. Since the 1980’s, methods such as capillary gas chromatography (cGC), liquid chromatography (HPLC, UPLC) and capillary electrophoresis (CE) have been those favoured for the separation and measurement of organic mixtures because they can be relatively simple and inexpensive to run and they can generate a large amount of data. If a single method is to be adopted in an attempt to link samples, minor alkaloid determination by a chromatographic or electrophoretic technique is the method of choice. Of the techniques available, cGC methods are the most common, used widely across the world and viewed by many scientists as the ‘gold standard’ for minor organic component profiling of illicit drugs because of speed, high resolution and cost.

A disadvantage of cGC is that it requires samples to be volatilised but the heating process can result in some compounds decomposing or undergoing chemical transformations in the process. Derivatisation, undertaken during the sample preparation process, can improve the stability and hence the separation and detection of certain compounds. However, the introduction of such a step can introduce problems in respect of the quantitative reproducibility of results. Both underivatized and derivatised cGC methods are reported to be used in Europe and more widely. Some scientists believe that derivatisation methods are best avoided, trading some loss of data for simplicity of sample preparation and improved robustness.

The cGC comparison of samples by comparing multiple organic compounds does not necessarily require the unequivocal identification of those components. In this case a sensitive but low specificity flame ionisation detector (FID) fitted to the instrument will suffice. However, cGC coupled to mass spectrometry (MS) is used increasingly. This technique (cGC-MS) is particularly useful in the chemical profiling of synthetic drugs, such as methylenedioxymethamphetamine (MDMA) because the unequivocal identification of specific compounds can point to the method of synthesis and hence help establish links to the manufacturing source. In recent times even more sophisticated mass spectral detectors have been introduced to cGC methods, e.g. high resolution time-of-flight mass spectrometry (GC-HRTOFMS).

HPLC overcomes a number of the problems associated with cGC, such as heat instability and chemical transformations and in addition there is no need for derivatisation. The method requires that the sample has some degree of solubility and a disadvantage in the past is that no single ultra-violet (UV) detector combined high sensitivity and specificity for all compounds. This latter issue has been overcome with the development of liquid chromatography mass spectrometry (LC-
MS) methods. Ultra performance liquid chromatography (UPLC) with MS/MS detection probably offers the best alternative to derivatised cGC-MS for the comparison of minor organic impurities. Capillary electrophoretic methods are also characterised by low cost, speed and no need for derivatisation. Like HPLC these rely most often on UV detectors, which limits sensitivity and specificity, but laser induced fluorescence detection has found applications for the determination of acidic and neutral impurities in heroin samples.

- Analytical techniques that target major alkaloids are generally of limited value when trying to assign geographical origin. Minor alkaloid analyses coupled with analyses for processing by-products and occluded solvents (solvents used during drug production and refinement and trapped in the solid matrix) can be powerful tools for both establishing links and for determining sample origin. In the latter case there is a dependency of needing to examine samples of known provenance from time to time.

- Some chromatographic methods have been developed to target specific minor organic components rather than a wide range of them. Generally these methods have been devised as part of a wider protocol, such as the US Drug Enforcement Administration (DEA) Cocaine Signature Programme, to help establish country or region of origin. Generally, for comparative work more than one such method should be applied.

- Harmonisation of profiling methods relies upon setting up instruments in an identical way. It is just as important that sample preparations are also standardised and show minimal variation not just between laboratories but also between individual scientists within a laboratory. Simple solvation quickest and easiest form of preparation but may not necessary be feasible or give the best results. Liquid-liquid extractions are common when preparing for chromatographic analysis, both derivatised and underivatized, but potentially can be a source of variability. The use of solid phase extraction techniques such as solid phase microextraction (SPME) can help to limit variability in extraction and the processes can be automated.

- Isotopic abundance and trace element analyses are two additional tools that are applicable to both the determination of sample origin and trafficking links. The isotopic composition of plant-based drugs and their derivatives may be fixed during biosynthesis. Isotope ratios measured in different samples will thus reflect differences in species and, within the same species and variant, differences in environmental conditions. The abundance of stable isotopes, particularly 15N and 13C, measured by isotope ratio mass spectrometry (IRMS) as a means of determining origin and complimenting (but not replacing) other forms of comparative analyses has been widely reported in recent years. Stable isotope analyses can be complicated by synthetic steps in a drug production process, such as the acetylation of morphine to
form heroin, and therefore has most commonly been applied to cocaine. Research in recent years has seen the method extended to other drugs.

- The analysis of trace elements using inductively coupled plasma-mass spectrometry (ICP-MS) has also been reported in sample comparison studies. However, trace elements present in clandestine samples can arise from inadvertent contamination from a myriad of possible sources and therefore interpretation can be difficult. Generally, for intelligence purposes, to link samples, IRMS and ICP-MS methods are seen as additional applications and not the primary or only means of comparison and interpretation of the results must take into consideration whatever known history exists of the samples. However, some recent work (see No.47. below) has shown good correlation ICP-MS and organic impurities results for authentic (high-purity?) samples of heroin.

- Most recently Fourier Transform infra-red (FTIR) has been reported as a tool for comparing illicit drug materials. This may be a good means of rapidly screening powders and tablets. In respect of the target drug, FTIR has the ability to rapidly distinguish between the drug in its salt and base form, e.g. between cocaine hydrochloride and cocaine base.

- Modern X-ray diffraction (XRD) instruments may offer the potential to rapidly compare illicit drug materials, particularly tablets and powders containing inorganic compounds and non-drug related organic compounds, such as sugars. Like FTIR, XRD will allow the differentiation between drug salts and the base form.

- There are a number of established statistical methods for finding and interpreting links between samples. Principal component analysis (PCA), Pearson Coefficient and Cosine function are commonly utilised. Large datasets are essential when interpreting results and modern software packages exist that are capable of the rapid statistical analysis of large amounts of data. Depending on the drug in question and the method used to collect data, some statistical approaches can offer certain advantages and disadvantages over others, thus the application of more than one data analysis model might aid interpretation.

The following tables provide a summary of established and recently reported methods for consideration when designing an illicit drug chemical profiling strategy. It is an extension of the content of the UNODC publication cited at the beginning of this report and includes work published since 2005. In some instances, methods may differ because they utilise different analytical techniques, e.g. GC vs CE, in others the difference may be in the manner in which samples are prepared. Many of the methods, where the same technique has been used, are very similar to each other and the relative benefits of one over another must be decided after closer scrutiny than time has allowed here. Advantages and disadvantages are only very
briefly discussed and therefore, for methods of interest, it is recommended that the original papers are consulted.

**Heroin-major alkaloids and adulterants**

1. The quantitation of heroin and selected basic impurities via reversed phase HPLC. 1 The analysis of unadulterated heroin samples

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
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<tbody>
<tr>
<td>S.Lurie and S.M. Carr. <em>Journal of Liquid Chromatography and Related Technologies</em>, vol 9, No.11 (1986) pp 2485-2509 (Summarised in UNODC publication 2005)</td>
<td>A robust liquid chromatographic method providing accurate quantification and precision for heroin and all typical opium alkaloid impurities down to 1% relative to heroin content. A major alkaloid method but in many cases minor alkaloids and adulterants can be quantified at levels as low as 0.1%</td>
</tr>
<tr>
<td>Photo-diode array (PDA) detection</td>
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<tr>
<td>Simple sample preparation – no derivatisation</td>
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</tbody>
</table>

Source: USA

This method is a slightly modified version of the heroin signature 1 method used by the US DEA until it was replaced by a capillary electrophoresis (CE) method in 2003.

The method was also a recommended method in the UNODC manual *Recommended Methods for Testing Opium, Morphine and Heroin, 1998*

2. The routine profiling of forensic heroin samples

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Simple sample preparation – no derivatisation</td>
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</table>

3. Untitled (UNODC – Methods for Impurity Profiling)

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.V.Kemenoe, Forensic Science Service, UK circa 2001. (Summarised in UNODC publication 2005)</td>
<td>Modification of GC method above, for major alkaloids and adulterants, utilising an internal standard. Capillary column and FID detector</td>
</tr>
<tr>
<td>Simple sample preparation with no derivatisation but co-elution issues between diazepam and morphine and sometimes problematic separation of 6-MAM, acetylmethadol and acetylcodeine</td>
<td></td>
</tr>
</tbody>
</table>

Source: UK

Method currently in use in the UK for intelligence purposes
4. Analysis of heroin samples by capillary gas chromatography: comparison of glass capillary and packed columns


A robust method for major alkaloids and adulterants that can be modified in many ways. Sample preparation includes a derivatisation step.
Some known co-elution issues between chloroquine and heroin

**Source:** Germany

This method was the one recommended for major alkaloids in the United Nation manual *Recommended Methods for Testing Opium, Morphine and Heroin*, 1998

5. Untitled (UNODC manual, Methods for Impurity Profiling)

J. Wong, Bureau of Drug Analysis, Health Canada (Summarised in UNODC publication, 2005)

A capillary GC-FID method for major alkaloids and adulterants with a simple derivatisation step.
No internal standard, peaks normalised against heroin
Resolution of 6-MAM and acetylicodeine.
This worker also describes a capillary GC-FID method for minor alkaloids that does not contain a derivatisation step (details summarised in UNODC publication)

**Source:** Canada

6. Component Analysis of Illicit Heroin Samples with GC-MS and Its Application in Source Identification


Capillary GC-MS method used to group heroin samples by measuring ratios of heroin, acetylicodeine and monoacetylmorphine
Applicable to major alkaloids
No derivatisation

**Source:** China

7. A Capillary electrophoresis of illicit drug seizures

B) Use of dynamically coated capillaries for the detection of heroin, basic impurities and adulterants with capillary electrophoresis (CE)

The first paper makes the case for the use of capillary electrophoresis in drugs analysis. With the right detector the technique has better resolution than HPLC and is gentler than GC, not requiring samples to be derivatised. The second paper describes two methods cited by UNODC utilising capillary zone electrophoresis (CZE) and miscellar electrokinetic chromatography (MEKC). Major alkaloids and adulterants allow differentiation of 6-MAM and 3-MAM. Rugged, inexpensive and low cost, allowing high sample throughput.

Source: USA
In 2003, capillary electrophoresis replaced gas chromatography as the method used for major alkaloids and adulterants in the US DEA Heroin Signature Programme. This programme is duplicated in Australia.

Heroin-minor organic impurities

8.

A) Profiling of samples by high resolution capillary gas chromatography for forensic services
B) Illicit Heroin Manufacturing By-products: Capillary gas Chromatographic Determination and Structural Elucidation of Narcotine- and Norlaudanosine-Related Compounds.


Describes a capillary GC-FID method for minor alkaloids. Sample preparation includes derivatisation step. Potentially more than 100 compounds detected. Method frequently cited by researchers into illicit heroin profiling. Many slight modifications of this method used around the world. Method used for chemical characterisation of compounds – no statistical analysis.

Source: USA, Germany
This method has been widely used, including in France reported in 1997 (Besacier et al Forensic Science International 86 (1997) 113-125 Comparative chemical analysis of drug samples: general approach and application to heroin) The method, modified by the use of GC-MS, is the basis of the heroin signature 2 method used in the US DEA Heroin Signature Programme and duplicated in Australia. See also Stromber et al at 9. below.

9.

Separation and detection of acidic and neutral impurities in illicit heroin via capillary electrophoresis


Separation and detection of acidic and neutral impurities in illicit heroin. Improved sensitivity in detection using photodiode array UV and laser-induced fluorescence, the latter being 500 times more sensitive than conventional UV for some solutes.

Source: USA
10. Determination of drug-related impurities by capillary electrophoresis

Further makes the case for capillary electrophoresis as an alternative to HPLC and CGC

Source: UK

11. Heroin impurity profiling. A harmonisation study for retrospective comparisons


This capillary GC method for minor alkaloid is based on that described by A.C. Allen and others, above, but with the derivatisation step omitted.
Twenty-four impurities were selected for comparison.
The study involved collaborative work between three forensic institutes in Germany, Sweden and the Netherlands.
Comparisons carried out by the Q-method. It was concluded that the method was good for intra-laboratory comparisons but that a loss of reproducibility was reported when more than one laboratory was involved in the analysis. Centralisation rather than harmonisation is recommended.

Source: Sweden, Germany, The Netherlands
This method is that used for intra-laboratory heroin comparisons in the Turkish Gendarmerie laboratory at Ankara, the National Forensic Centre in Sweden, the National Forensic Institute in the Netherlands. The method is also cited as used in the German Heroin Analysis Programme (HAP) although the method of detection may have changed (see 14. below)

12. Investigation of heroin profiling using trace organic impurities.

(summarised in UNODC publication)

Capillary GC-MS method.
Preparation similar to the capillary GC-FID methods of Wong and Allen et al. Different derivatising agent.
Several versions of this method used worldwide.
Sensitivity of detector makes this method very good for highly refined samples

Source: Australia

13. Signature profiling and classification of illicit heroin by GCMS analysis of acidic and neutral manufacturing impurities


Modification of the method of Allen et al, using cGC-MS to routinely screen for in excess of 30 compounds

Source: USA
This is the basis of the heroin signature 2 method used in the US DEA Heroin Signature
Programme and duplicated in Australia.

### 14.

**Innovative methodology to transfer conventional GC-MS heroin profiling to UPLC-MS/MS**


**UPLC-MS method**

Awaiting full transcript

### 15.

**Classification of illicit heroin by UPLC-Q-TOF analysis of acidic and neutral manufacturing impurities**


**Ultra performance liquid chromatography quadrupole and time of flight mass spectrometry.**

High resolution and does not require derivatisation.

Nineteen compounds detected and included in data analysis

Sample preparation using a modification of method of Morello et all

Partial least squares discriminate analysis (PLS-DA) was performed using SIMCA software (SIMCA P11.0 Umetrics, Sweden) Correlation analysis of Pearson distance was computed by Excel.

**Source:** China

This method probably provides the best alternative to cGC methods for profiling minor organics. Studies have taken place in Europe (Switzerland), but it is not known at this point if any European laboratory is actively using the method for heroin comparisons.

### 16.

**Characterisation of a heroin manufacturing process based on acidic extracts by combining complementary information from two-dimensional gas chromatography and high resolution mass spectrometry**


This very recent method is a collaborative work including the Bundeskriminalamt (Federal Criminal Police Office; BKA) in Germany. The focus was on 44 compounds found in the heroin base and 18 target compounds used within the German Heroin Analysis Program (HAP)

Techniques include two-dimensional gas chromatography-time-of-flight mass spectrometry (GCxGC-TOFMS) and gas chromatography high-resolution time-of-flight mass spectrometry (GC-HRTOFMS).

Data analysis undertaken using commercial software packages.

**Source:** Germany

It is currently not known if this methodology has been adopted in the German HAP

### Cocaine – major components
17. A chromatographic impurity signature profile analysis for cocaine using capillary gas chromatography


A capillary GC method with FID detection
Derivatised step in sample preparation
Internal standard method
Near complete picture of major components including adulterants
Authors applied a neural network pattern recognition programme for retrospective database searches.
Modified slightly by Olivier Gueniat in Switzerland (both methods summarised in UNODC publication, 2005)

Source: USA

18.

A) Comparison analysis of illicit cocaine samples
B) Cross matching of cocaine samples: a case study
C) A database for the comparison of illicit cocaine samples

B) K.E. Janzen *Canadian Society of Forensic Science Journal*, vol 20 (1987), pp 77-81

Capillary GC method using a nitrogen-phosphorus detector (NPD)
No extraction or derivatisation
Not most sensitive method but capable of detecting tropococaine, norcodeine and *cis*- and *trans*-cinnamoylcocaines
No internal standard – measures alkaloids relative to cocaine.

Source: Canada

19.

Chemical profiling of cocaine seized by Brazilian Federal Police in 2009-2012: Major components


Simple capillary GC-FID method.
No derivatisation

Source: Brazil (work supported by the US DEA)

Cocaine- minor components

20.

3,4,5 trimethoxy substituted analogues of cocaine, *cis/trans*-cinnamoylcocaine and tropococaine: characterisation of new alkaloids in coca leaf, coca paste and refined illicit
<table>
<thead>
<tr>
<th>Cocaine</th>
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<tbody>
<tr>
<td>A capillary GC method for determination of 14 alkaloids looking particularly at tropacocaine, 3,4,5-trimethoxycocaine and the cinnamoylcocaines. These compounds are useful diagnostic markers for origin. Internal standard method. Relatively complex extraction process using ion-pair chromatography. Method summarised in UNODC publication, 2005</td>
</tr>
<tr>
<td>Source: USA</td>
</tr>
<tr>
<td>This method is included in the US DEA Cocaine Signature Programme and is duplicated in Australia.</td>
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21.

| A) Capillary gas chromatographic-electron capture detection of coca-leaf related impurities in illicit cocaine: 2,4-diphenylcyclobutane-1,3-dicarboxylic acids, 1,4-diphenylcyclonutane-2,3-dicarboxylic acids and their alkaloidal precursors, the truxillines |
| B) Comparative determination of total isomeric truxillines in illicit refined South American cocaine hydrochloride using capillary gas chromatography electro-capture detection. |
| Relatively complex method to target truxilline alkaloids. Method summarised in some detail in UNODC publication, 2005 |
| Source: USA |
| This method is included in the US DEA Cocaine Signature Programme |

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22.

<table>
<thead>
<tr>
<th>Comparison of illicit cocaine by determination of minor components</th>
</tr>
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<tbody>
<tr>
<td>Capillary GC-MS methods with and without derivatisation. Provides a peak rich impurity profile. Good retrospective data searches by comparison of ratios of cinnamoylcocaines to cocaine</td>
</tr>
<tr>
<td>Method summarised in UNODC publication</td>
</tr>
<tr>
<td>Source:</td>
</tr>
</tbody>
</table>

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23.

<table>
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<tr>
<th>Cocaine profiling for strategic intelligence. A cross-border project between France and Switzerland. Part 1. Optimisation and harmonisation of the profiling method and Part 2 Validation of the statistical methodology for the profiling of cocaine</th>
</tr>
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<tbody>
<tr>
<td>A capillary GC method with derivatisation, targeting eight alkaloids. Harmonised process between two laboratories.</td>
</tr>
</tbody>
</table>
Concluded that Cosine or Pearson were the best statistical combinations to discriminate the linked and non-linked samples

**Source: France and Switzerland**

This method currently under development for use in the Turkish Gendarmerie laboratory. Given the authors, it is surmised that this method is in use in France

### 24.

**Fast profiling of cocaine seizures by FTIR spectroscopy and GC-MS analysis of minor alkaloids and residual solvents**


Paper describes a multi-technical approach

Minor alkaloids and residual solvents analysed by GC-MS and headspace (HS)-GC-MS respectively.

Attenuated total reflection (ATR)-FTIR used for comparative analysis of high purity samples

**Source: Italy**

### 25.

**Cocaine classification using alkaloid and residual solvent profiling**


Profiling of eight alkaloids using GC-MS and residual solvents by headspace GC-MS. Sample preparation described in earlier work (referenced *Forensic Science International* vol 264, (2016), pp 56-62)

Comparison of profiles using Pearson Correlation or Cosine Angle.

NB: See also by the same authors ‘Variation in chemical profiles within large seizures of cocaine bricks’ *Forensic Science International*, vol 280, (2017), pp 194-199

**Source: Denmark**

Method was in operation at the National Bureau of Investigation -Forensic Laboratory in Finland but is currently not in active use there.

### 26.

**Profiling of cocaine using ratios of GC-MS peaks**


This paper describes an alternative means of classifying samples from GC-MS analysis. Eliminates the influence made by unstable alkaloids when using more traditional statistical methods e.g. Pearson coefficient or cosine angle

**Source: Denmark**

### Comparison of illicit amphetamine and amphetamine-type substances (ATS)

### 27.

Development of a harmonised method for the profiling of amphetamines. III Development of gas chromatographic method, IV Optimisation of sample preparation, V Determination of the
variability of the optimised method, VI Evaluation of methods for comparison of amphetamine.


This body of work is the output of the CHEDDAR and CASE project initiated by a group of European laboratories in the years 1999-2012. CASE (Comprehensive Action against Synthetic Drugs in Europe) was the development of a capillary GC-MS method funded by the Swedish Police Board. The CHEDDAR project which followed was funded by the EU Commission and involved harmonisation of the CASE method across a number of countries and the establishment of a common database to share results. The database was developed in Australia.

This project was followed by further EU funding to establish a harmonised method for methylamphetamine and methylenedioxymethylamphetamine (MDMA) – project name CHAMP (Collaborative Harmonisation of Methods for Profiling of Amphetamine Type stimulants, see No.31 below)

**Source:** European Union

The cGC-MS method is currently in operation in Sweden, Finland and the Netherlands. France has stated that it uses the ‘European’ method which, given that it was EU funded, is also probably this method. This method is most likely in operation in EU countries that participated in the project, notably Belgium and Poland. The current status of the common database is unknown – it is possible that most amphetamine profiling is for ‘within country’ comparison.

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### 28.

**A contribution to the chemical profiling of 3,4-methylenedioxyamphetamine (MDMA) tablets**


A capillary GC-MS method  
Simple sample preparation and extraction, no derivation.  
Paper was primarily to identify new impurities, but some comparison work was undertaken. Good potential shown but conditions not optimised for this type of work. Cosine function used for comparison analysis

**Source:** France

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### 29.

**Organic impurity profiling of 3,4-methylenedioxyamphetamine (MDMA) tablets seized in the Netherlands**


Capillary GC method.  
Building on the work above, extraction and sample preparation conditions optimised for profiling. Simple method developed within the CHAMP project (see 31 below)  
Data analysis techniques such as PCA or neural networks to be applied once body of data sufficiently large

**Source:** The Netherlands
Method used in the Netherlands and very recently introduced into Turkish Gendarmerie laboratory.

<table>
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<th>30.</th>
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<tr>
<td>Impurity profiling of ecstasy tablets seized in Hong Kong by gas chromatography-mass spectrometry</td>
</tr>
<tr>
<td>Capillary GC-MS method, similar to above</td>
</tr>
<tr>
<td>A total of 19 identified impurities were selected as markers for impurity profiling</td>
</tr>
<tr>
<td>Data analysed by hierarchical clustering analysis using commercial software</td>
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<tr>
<td><strong>Source:</strong> Hong Kong</td>
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<th>31.</th>
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<tr>
<td>A) Drug intelligence based on MDMA tablets data 1. Organic impurities profiling</td>
</tr>
<tr>
<td>B) Drug intelligence based on MDMA tablets data 2. Physical characteristics profiling</td>
</tr>
<tr>
<td>Describes further work undertaken within the CHAMP project</td>
</tr>
<tr>
<td>Deal with harmonisation, creation of a common database, methods of statistical analysis and using physical features for intelligence. See 29. above</td>
</tr>
<tr>
<td><strong>Source:</strong> European Union (EU)</td>
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<table>
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<th>32.</th>
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<tbody>
<tr>
<td>Impurity Profiling of Amphetamine and Methamphetamine Using Gas Chromatography Mass Spectrometry (GC-MS) Harmonised Methods</td>
</tr>
<tr>
<td>Investigated the feasibility of using the (CHAMP) work to establish a harmonised GC-MS system</td>
</tr>
<tr>
<td><strong>Source:</strong> Malaysia</td>
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<th>33.</th>
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<tbody>
<tr>
<td>Optimisation of HS-SPME/GC-MS analysis and its use in the profiling of illicit ecstasy tablets</td>
</tr>
<tr>
<td>This describes a solid-phase microextraction procedure (HS-SPME). The extraction optimised using varying conditions.</td>
</tr>
<tr>
<td>Capable of isolating a large number of impurities and can be easily automated</td>
</tr>
<tr>
<td>Presents a viable alternative to liquid-liquid extraction techniques.</td>
</tr>
</tbody>
</table>
Statistical analysis performed to evaluate efficiency, using commercial software (Pearson coefficient)

Source: Switzerland

34.

The profiling of MDMA tablets: A study of the combination of physical and organic impurities as sources of information


Evaluates the added value of combining pre-tabletting characteristics and post-tabletting characteristics of seized MDMA tablets.

Utilises the GC-MS method of van Deursen et al (see 29. above).

Physically tablets compared by logo, shape, presence of score, colour, diameter, thickness and weight. Chemical impurity data analysed by hierarchical clustering using commercial software.

Concluded that physical features (except logo and colour) were observed to be persistent in time. Organic impurities demonstrated to be more variable and to have a shorter lifetime. Thus, demonstrates that many batches of powdered drug may be processed through the same tablet machine.

Source: Switzerland

Stable isotopic ratio methods for determining origin

35.

Isotope analysis of C-13 as a tool for comparison


Utilises isotopic ratio-mass spectrometry (IR-MS)

Developed for use on unadulterated samples. Original entry in UNODC publication, 2005. Things have moved on since

Source: France

36.

Geo-location of heroin and cocaine by stable isotope ratios


Utilises IR-MS for unadulterated samples

Developed for use on unadulterated samples. Work ongoing for the application of GC-IRMS to adulterated samples. Original entry in UNODC publication, 2005. See comment above

Source: USA

37.

Tracing the geographical origin of cocaine

Utilises IR-MS to measure abundances of N-15 and C-13
For unadulterated samples

Source: USA

38.
Origin differentiation of a heroin sample and its acetyulating agent with C-13 isotope ratio mass spectrometry.

Describes a gas chromatography-combustion- isotope ratio mass spectrometry (GC-C-IRMS) method for heroin origin determination

Source: China

39.
Isotope ratio mass spectrometry : C-13/C-12 and N-15/N-14 analysis for tracing the origin of illicit
E.M. Galimov, V.S. Sevastyanov, E.V. Kulbachevskaya and A.A. Golyavin, Rapid Communications in Mass Spectrometry, vol 19, (2005), 1213-1216

GC-IRMS analysis of hemp leaves, cocaine and heroin described.

Source: Russia

40.
Geographic Origin Determination of Heroin and Cocaine Using Site-Specific Isotopic Ratio Deuterium NMR

An alternative method to IRMS, capable of yielding further information. However, complex and expensive – difficult to recommended for routine use

Source: France/USA

41.
Bulk and compound specific isotopic characterisation of illicit heroin and clingfilm.

Describes the use of elemental analysis/isotope ratio mass spectrometry (EA/IRMS) and gas chromatography/combustion/isotope ratio mass spectrometry (GC/C/IRMS) for carbon and hydrogen isotopes.
Concluded that EA/IRMS was able to distinguish between most samples of bulk heroin and between clingfilm samples. GC/C/IRMS results gave indication of different geographical sources.

Source: UK

42.
The use of C-13 isotope ratio mass spectrometry for methamphetamine profiling: comparison of ephedrine and pseudoephedrine-based samples to P2P-based samples


Purpose of method to determine route of manufacture. High purity methamphetamine HCl and liquid P2P samples analysed by EA-IRMS. Impure sample mixtures were analysed using GC-C-IRMS

Source: USA

43.

Isotopic profiling of seized benzylpiperazine and trifluoromethylphenylpiperazine tablets using C-13 and N-15 stable isotopes


Demonstrates the increasing use of stable isotope analysis to compare and distinguish between samples

Source: Australia

**Trace inorganic analysis**

44.

Trace element analysis of heroin by ICP-MS


Method used for measuring abundance of sample trace elements in unadulterated samples. A supplement to other comparative methods, not a replacement. Must be aware of potential contamination issues. Best for immediate case by case comparisons. Method reported in UNODC publication, 2005

Source: Australia

45.

Investigation of trace inorganic elements in street doses of heroin.


Use of ICP-MS to measure inorganic elements arising from activities associated with the production process and subsequent actions, e.g. contaminants in water, metallic vessels etc. A good means of providing evidence on a case by case basis – careful interpretation needed if results are input to a larger database.

Source: Malaysia

46.

Street-level classification of illicit heroin using inorganic elements coupled with pattern monitoring


Similar study to above (45.). ICP-MS analysis and data analysis by PCA. Results identified
<table>
<thead>
<tr>
<th>No.</th>
<th>Title</th>
<th>Authors</th>
<th>Details</th>
<th>Source</th>
</tr>
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<tbody>
<tr>
<td>47.</td>
<td>Profiling and classification of illicit heroin by ICP-MS analysis of inorganic elements</td>
<td>Cuimei Liu, Zhendong Hua, Yanping Bai and Yao Liu, <em>Forensic Science International</em>, vol 239, (2014), 37-43</td>
<td>Nineteen inorganic elements measured by ICP-MS. Using PCA to analyse data from 150 authentic samples the results were consistent with the widely used organic profiling method. Savings in time per sample over organic purity method. Commercial data processing software. Pearson distances calculated using SPSS version 17.0. PCA and PLS-DA analysis was performed using SIMCA software.</td>
<td>China</td>
</tr>
<tr>
<td>48.</td>
<td>Profiling of illicit cocaine seized in China by ICP-MS analysis of inorganic elements</td>
<td>Cuimei Liu, Zhendong Hua and Xin Meng, <em>Forensic Science International</em>, vol 276, (2017), pp 77-84</td>
<td>Twenty-six inorganic elements measured by ICP-MS in 183 seized cocaine samples. After hierarchical cluster analysis, 21 groups of linked samples were found, which provided intelligence for case connection and help reveal distribution networks. Data treated statistically using SPSS 12.0 software (SPSS Inc. Chicago) and Matlab R. 2106b (Math Works Inc)</td>
<td>China</td>
</tr>
<tr>
<td>50.</td>
<td>Statistical Assessment using Chemical Profiling of Ecstasy Samples Seized in Turkey</td>
<td>Taner Bora and Huseyin Celikkan, <em>Journal of Analytical Chemistry</em>, vol 73, No.10, (2018), pp1020-1028</td>
<td>In chemical profiling, 17 elements and the main organic constituents were identified in 18 ecstasy samples. Elemental analysis by ICP-MS. Profiles assessed using hierarchical clustering, principal component and correlation analysis. Concluded that some elements can be used to indicate that seizures came from same network – but many more samples need to be analysed and databased before operation use</td>
<td>Turkey</td>
</tr>
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</table>
### Occluded (residual) solvents analysis

51.

<table>
<thead>
<tr>
<th>A) Headspace analysis of solvents in heroin and cocaine samples</th>
<th>B) Occluded Solvent Analysis as a Basis for Heroin and Cocaine Sample Differentiation</th>
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</thead>
<tbody>
<tr>
<td>A simple capillary GC-FID method for the detection of residues of twelve solvents in samples of heroin and cocaine. Detection limits of 2-15ppm in 250-300 milligrams of powder.</td>
<td></td>
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<tr>
<td>Source: Switzerland and UK</td>
<td></td>
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</tbody>
</table>

### Other references concerned with data analysis and interpretation

52.

<table>
<thead>
<tr>
<th>A methodology for illicit heroin seizures comparison in a drug intelligence perspective using large databases</th>
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<tbody>
<tr>
<td>Source: Switzerland</td>
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53.

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<th>Evaluation of links in heroin seizures</th>
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<tbody>
<tr>
<td>Source: Switzerland</td>
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54.

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<tr>
<th>Chemical profiling and classification of illicit heroin by principal component analysis, calculation of inter sample correlation and artificial neural networks</th>
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</thead>
<tbody>
<tr>
<td>Source: Switzerland and Australia</td>
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55.

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<th>Different likelihood ratio approaches to evaluate the strength of evidence of MDMA tablet comparison</th>
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<tr>
<td>Source: The Netherlands, Switzerland and Francez</td>
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</table>
56.

Illicit drug profiling, reflection on statistical comparisons


Source: Switzerland

57.

Study of common database feeding with results coming from different analytical methods in the framework of illicit drugs chemical profiling


Discussion

- This report is dynamic and will be updated as more information about drug profiling in Europe becomes available.

- For the principle drugs, cocaine, heroin and MDMA, methods involving GC-FID and GC-MS of organic impurities methods are the most frequently reported.

- Of the European member states from which information has been obtained to date, GC-FID and GC-MS methods are those used for minor alkaloid profiling (see 8, 11, 16, 23, 25, 27, 29 and 31 above). Methods from this group are currently in operation in the Gendarmerie laboratory in Ankara (see 11, 23 and 29 above)

- Capillary electrophoresis (EC) and HPLC-GC methods (see 1, 7, 9,10, 14 and 15 above) offer viable alternatives to GC-MS but, from contacts to date, there are no records of these being used for organic impurity profiling in Europe.

- Solid phase extraction techniques (see 33 above) may offer an alternative to other sample preparation methods and help reduce variations when harmonising methods

- Stable isotope ratio methods (see 35-43 above) have utility in helping establish geo-location but for complementing other ‘linking’ data is complex and expensive and might not be a cost-effective means of getting additional intelligence.

- Inorganic elemental analysis by ICP-MS (see 44-48 and 50 above) is showing promise as a rapid means of obtaining intelligence, particularly at ‘street level’.

Version 1.0

Steve Reddick