The 1995 “Research on Drug Evidence” Report

[From the 11th ICPO / INTERPOL Forensic Science Symposium]

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ABSTRACT: A reprint of the 1995 “Research on Drug Evidence” Report (a review) is provided.

KEYWORDS: INTERPOL, Illicit Drugs, Controlled Substances, Forensic Chemistry.

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Citations in this report from Microgram were (and remain) Law Enforcement Restricted. Most citations listed as “Personal Communications” were unpublished reports from “assisting laboratories” provided to the Laboratory Director of the Special Testing and Research Laboratory upon his request; note that this was the last Symposium where such reports were requested for the “Research on Drug Evidence” review.

Page numbering in the bottom center of the first three pages and the upper corners of all subsequent pages are those in the original document, while those in the footers of each page represent the Microgram Journal numbering.

Although not shown in the document, this review was prepared by the author listed above (Klein), and the summary presentation at the Symposium was provided by Richard S. Frank.

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Microgram Journal 2016, Volume 13; Numbers 1-4
Research On Drug Evidence

June, 1992 - June, 1995

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Drug Enforcement Administration
(Coordinating Laboratory)

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Table of Contents

I) Routine and Improved Analysis of Drug Substances  
II) Novel Syntheses of Illicit Drugs  
III) Reference Drug Standards  
IV) Comparative Analyses  
V) Source Determination of Drugs (Impurity Profiling)  
VI) Analysis of Adulterants and Diluents  
VII) Analytical Artifacts  
VIII) Instrumental Techniques  
IX) Robotics and Computer Programs  
X) Sampling Plans  
XI) Vapor and Particle Detection (Portable Instrumentation)  
XII) Miscellaneous

1  
13  
15  
16  
21  
26  
28  
30  
35  
37  
38  
40
I) Routine and Improved Analysis of Drug Substances

Problem/Issue:

Standard analytical data are required for previously unknown drugs of abuse and analog (i.e., "designer"-type) drugs. Additionally, improved methods of analysis, i.e., faster, more discriminatory, more sensitive, less costly, etc., are needed for all drugs of abuse.

Solution:

Illicit drug seizures are constantly monitored to provide a comprehensive overview of new developments. Case reports providing standard analytical data for new drugs are generated for the forensic and enforcement communities. Ongoing research in the forensic community, as well as the general analytical field, constantly provide new and/or improved methods of analysis for routine analysis of seized drugs.

Recent Developments:

In the United States, use of both heroin and LSD are increasing, while use of cocaine has levelled off and shows some signs of decreasing. "Smoking" heroin has increased, due to both increased purity levels and fear of contracting illnesses (AIDS and Hepatitis B) from use of intravenous needles. Designer drugs are sporadically noted; the most prevalent of the new designer drugs is 4-bromo-2,5-dimethoxyphenethylamine (aka: NEXUS or 2-CB). Use of anabolic steroids is steady, with use of human growth hormones or steroid natural production-stimulating drugs (e.g., gamma-hydroxybutyric acid) showing some increases. Among the amphetamines, use of "ice" methamphetamine continues to be only a regional problem, while use of methcathinone (aka: "CAT") has spread slowly. Abuse of flunitrazepam (Rohypnol) has unexpectedly and dramatically increased and throughout the American southwest.

In Europe, use of amphetamines and heroin remains widespread, while use of cocaine and LSD are both growing; "crack" cocaine use is now evident in many of the larger cities. "Record-level" seizures of bulk cocaine shipments (up to metric ton
quantities) have been reported by several nations. Among the "designer drugs," use of
the methylenedioxyamphetamines has rapidly expanded, with several analogs (notably
N-ethyl) and the corresponding methylenedioxyphenyl-2-butanamines also appearing.

In the Far East, Australia and New Zealand report general across-the-board
increases in drug abuse, while methamphetamine use remains ubiquitous in Japan.
Cocaine use is slowly growing throughout the Far East.

Summary:
Since 1992, routine and/or new/improved methods of analysis have been reported
for amphetamines (1-11), Angel Trumpet (12), barbiturates (13-14), benzodiazepines
(15-19) 4-bromo-2,5-dimethoxyphenethylamine (NEXUS) (20), bufotenine (21-24),
cocaine (25-29), dimethpramide (30-31), dimethylaminorex (32), fenetyline (33),
fentanyl (34-35), 4-fluoroamphetamine and 4-fluoromethamphetamine (36), heroin (37-42), gamma-hydroxybutyric acid (GHB) (43), N-(2-hydroxyethyl)amphetamine (44),
N-hydroxy-3,4-methylenedioxyamphetamine (45), inhalants (45-47), Jimson Weed (48),
Khat (49-53), LSD (54-60), marijuana (61-63), methylenedioxyamphetamine and
methylenedioxyphenylbutanamines (64-68), methcathinone and cathinone (69-75),
methylmethaqualone (76), N-methyl-1-phenethylamine (77), opium (78-79), PCP and
PCP analogs (80-82), and steroids (83-91).

References:

Amphetamines:
(1) LeBelle, M.J.; Savard, C.; Dawson, B.A.; Black, D.B.; Katyal, L.K.; Zrcek, F.; By,


Angel Trumpet:

Barbiturates:

Benzodiazepines:
(16) Ripani, L.; Lovera, P.; Muzi, F.; Schiavone, S. "GC/MS Analysis of a Fruit Juice Extract that was Suspected to be a Narcotic Beverage," Microgram 1994, 27, 149.

4-Bromo-2,5-dimethoxyphenethylamine (NEXUS):
Bufotenine:

Cocaine:

Dimethpramide:

Dimethylaminorex:

Fenethylline:

Fentanyls:

4-Fluoroamphetamine/4-Fluoromethamphetamine:

Heroin:


gamma-Hydroxybutyric Acid (GHB):


N-(2-Hydroxyethyl)amphetamine:


N-Hydroxy-3,4-methylenedioxyamphetamine:


Inhalants:


Jimson Weed:

(48) Koverman, G. "Identification of Scopolamine and Hyoscyamine in Jimson Weed (Datura Stramonium)," Microgram 1993, 26, 122.

Khat (Catha Edulis):


LSD:


(58) Morales, R. "Quantitative Analysis of Lysergic Acid Diethylamide by Gas Liquid


Marijuana:


Methylenedioxymphetamines and Methylenedioxyphenylbutanamines:


Methcathinone and Cathinone:


Methylmethaqualone:


N-Methyl-1-phenylethylamine:

(77) Clark, C.C. "The Identification of N-Methyl-1-phenylethylamine," *Microgram*
Opium:

PCP (Phencyclidine) and PCP Analogs:

Steroids:
(89) Morley, M.; Matkovich, C. "Screening of Steroids by Thin Layer


(91) Somsen, G.W.; Gooijer, C.; Brinkman, U.A.T.; Velthorst, N.H.; Visser, T.
II) Novel Syntheses of Illicit Drugs

Problem/Issue:
Forensic chemists must maintain familiarity with current and potential clandestine syntheses of illicit drugs in order to assist enforcement activities, for enhanced safety and effectiveness during enforcement operations and in order to provide expert testimony in Court proceedings.

Solution:
Clandestine laboratory operations are constantly reviewed to provide a comprehensive overview of the field. In cases where new methodologies are in use, case reports are generated for the forensic and enforcement communities.

Recent Developments:
Enforcement efforts and precursor control/monitoring laws have had a fairly dramatic impact on illicit syntheses of amphetamines in the United States, notably on the hydriodic acid/red phosphorus reduction of ephedrine to methamphetamine. Clandestine laboratory operators have responded with new sources of ephedrine and red phosphorus, clandestine syntheses of hydriodic acid and use of alternate phosphorus/iodine reagents. Use of highly reactive active metal reductions of ephedrine (i.e., with lithium or sodium metals in ammonia) is increasing. Use of mobile labs (i.e., motor homes or tractor-trailers) or hotels/short-term rental properties has complicated enforcement efforts; similarly, leaving operating laboratories unattended has become common practice and has increased hazards associated with clandestine laboratory entry. Increasing numbers of "confined space" clandestine laboratories (e.g., buried vehicles, caves, underground chambers or hidden internal compartments in residences, etc.) has necessitated new guidelines for enforcement and forensic personnel entry and disassembly/cleanup. Use of booby-traps in clandestine laboratories and storage sites is increasing.
Summary:

Since 1992, a variety of new methods for synthesis of amphetamine and methamphetamine and their precursors have been reported (1 - 7).

References:

III) **Reference Drug Standards**

**Problem/Issue:**
Reference drug standards are either commercially unavailable or if available are extremely expensive. No reported procedures existed for cleanup and or authentication of reference standards from either synthesized or seized materials.

**Solution/Summary:**
A systematic procedure for authentication of reference drug standards was developed (1); several reports (2-3) detailed syntheses and/or authentication of specific drug standards.

**References:**

IV) Comparative Analyses

Problem/Issue:

Comparative analysis (i.e., the systematic application of impurity profiling for determination of commonality of origin) is complicated due to both the high complexity of the data and the extremely large numbers of exhibits. Improved methods are needed for data handling and analysis.

Solution:

In-depth analysis helps identify discriminatory components in impurity profiles. Computer databases, sorting programs and pattern recognition/neural networks provide enhanced data handling and analysis. Case reports of new methodologies are generated for the forensic and enforcement communities.

Recent Developments:

In conjunction with impurity profiling, significant advances in comparative analyses were reported for the amphetamines/methylenedioxyamphetamines and cocaine, especially with respect to data handling. Advances in computer speed and capabilities have allowed direct downloading of data from chromatographic systems and rapid analyses. Improved instrumentation, notably capillary electrophoresis, isotope/ratio-mass spectrometry and deuterium nuclear magnetic resonance spectroscopy, offer new methods for more definitive impurity profiling and comparative analysis. New and dramatic improvements in pattern recognition/neural network programs have immensely improved data handling in cocaine comparative analysis and is expected to find similar application for other comparative analysis problems, especially heroin.

Summary:

Since 1991, impurity profiling has been conducted on amphetamines (5-9), cocaine (10-15), heroin (16-18), marijuana (19-22), methamphetamine (23-25), methylenedioxyamphetamines (26), opium (27), and Source Determination (Ballistics) (28-29).
Comparative Analyses has also been addressed in general terms (1-4).

References:

**General Discussions:**

**Amphetamines:**
Cocaine:


Heroin:


Marijuana:

(19) Robertson, J. (Australian Federal Police, Canberra, Australia); Jagadish, V.;

(20) Court, T.M. (Department of Botany, University of Queensland, St. Lucia, Brisbane, Australia) "Characters in Cannabis Indicative of Provenance," Personal Communication, 1995.


Methamphetamine:


Methylenedioxyamphetamines:


Opium:

(27) Remberg, B.; Krenn, L.; Kopp, B.; Buchbauer, G.; Nikiforov, A. "Principal Component Analysis (PCA) of Opium Alkaloid Contents for Origin Determina-
Source Determination (Ballistics):


V) Source Determination of Drugs (Impurity Profiling)

Problem/Issue:
Impurity profiling of drugs is important for comparative analysis protocols. However, although certain drugs have been well characterized with respect to their impurity profiles, most have not been properly investigated.

Solution:
High sensitivity analytical techniques (primarily chromatographic) provide detailed impurity profiles. Identification of individual impurities enhance origin identification and comparative analyses and also aid in development of internal standards for improved accuracy and precision of analysis. Case reports are generated for the forensic and enforcement communities.

Recent Developments:
In contrast to most case reports prior to 1992 (which commonly only reported specific impurities noted in individual seized exhibits), there has been a much more systematic effort to identify impurities and establish signature profiles via in-house syntheses, notably with the amphetamines and methylenedioxyamphetamines. Heroin impurity profiling continues in the United States and Germany, with Australia a recent and fast-growing new research investigator in the field. The United States has made significant advances in cocaine impurity profiling, and several European groups have recently initiated new cocaine signature studies. Impurities in precursor chemicals and occluded trace solvents in finished products (notably cocaine and heroin) were both recognized as being increasingly important in impurity profiling.

Summary:
Since 1992, impurity profiling has been conducted on amphetamine (1-4), cocaine (5-17), heroin (18-20), methamphetamine (21-25), methylenedioxyamphetamines (26-32), occluded solvents in drugs (33-34) and drug precursors (35).
References:

Amphetamine:


Cocaine:


(8) Casale, J.F.; Moore, J.M. "3',4',5'-Trimethoxy-Substituted Analogs of Cocaine, cis/trans-Cinnamoylcocaine and Tropacocaine: Characterization and


Heroin:


(20) [Duplicate Citation] Violante, N.; Quaglia, M.G.; Lopez, A.; Caroli, S.
"Characterization of Cocaine and Heroin samples as a function of their trace

Methamphetamine:

Synthesized from Ephedrine by Reduction with HI and Red Phosphorus,"

(22) Noggle, F.T.; Clark, C.R.; DeRuiter, J. "Evaluation of Allylbenzene as a Precursor

(23) Noggle, F.T.; Clark, C.R.; DeRuiter, J. "Characterization of Methamphetamine
and Synthetic By-Products in Clandestine Samples: A Case Report," Microgram

(24) Tanaka, K.; Ohmori, T.; Inoue, T.; Seta, S. "Impurity Profile Analysis of Illicit
Methamphetamine by Capillary Gas Chromatography," J. Forensic Sci. 1994, 39,
500.


Methylenedioxyamphetamines:

(26) Robak, D.R. "Identification of Clandestinely Produced Methylenedioxyiso­

(27) Clark, C.R.; DeRuiter, J.; Andurkar, S.; Noggle, F.T. "Analysis of 3,4-Methylen­
dioxyphenyl-2-propanone and 3,4-Methylenedioxyamphetamine Prepared From

(28) Bohn, M.; Bohn, G.; Blaschke, G. "Synthesis Markers in Illegally Manufactured
3,4-Methylenedioxyamphetamine and 3,4-Methylenedioxymethamphetamine,"

(29) Clark, C.R.; Noggle, F.T. "GC-MS Analysis of Products, Intermediates and By-
Products in the Synthesis of MDA from Isosafrole," Microgram 1994, 27, 188.


Occluded Solvents:


Precursors:
Analysis of Adulterants and Diluents

Problem/Issue:
Most "street-level" drugs are "cut" with various adulterants and diluents. Separation and identification of these extraneous materials can be tedious. In addition, new or unusual adulterants and/or diluents are occasionally identified in drug exhibits; standard analytical data are required for these substances. Finally, improved methods of analysis, i.e., faster, more discriminatory, less costly, etc., are needed for all cutting agents.

Solution:
Illicit drug seizures are constantly monitored to provide a comprehensive overview of adulterants and diluents. Case reports providing standard analytical data for new cutting agents are generated for the forensic and enforcement communities. Ongoing research in forensic community provides new and/or improved methods of analysis for routine identification of all adulterants and diluents.

Recent Developments:
Increased computer speed and enhanced search routines enable simultaneous identification of moderate quantities (i.e., 5 - 20 %) of certain cutting agents in cocaine or heroin by FT-IR spectroscopy. The techniques are based on identification of marker peaks for the adulterant or diluent in available "windows" in the infrared spectra of the controlled substance.

Summary:
Since 1992, four new cutting agents were identified and case reports generated (1-4); in addition, several new methodologies for simultaneous identification of common adulterants and diluents via FT-IR techniques were reported (5-6).
References:

Unusual Adulterants/Diluents:


Simultaneous Analyses of Drugs and Adulterants/Diluents:


Problem/Issue:

Gas chromatographic and tandem gas chromatographic techniques are increasingly the method of choice for routine screening and/or identification of illicit drugs. However, use of high-temperature injectors with GC’s occasionally results in formation of artifacts due to unimolecular rearrangements of the drug substance(s) (or adulterants or diluents) or reaction(s) of the various components in the exhibit with the injection solvent(s). Such artifacts can severely complicate drug analyses, especially when they involve the controlled substance.

Solution:

Case reports providing information of the appearance and reduction/elimination of analytical artifacts are generated for the forensic community.

Recent Developments:

Anabolic Steroids and N-hydroxylated amphetamine/methylenedioxyamphetamine compounds (all fairly recent arrivals in the forensic arena) are all quite prone to artifact formation in heated injection ports. Use of certain solvents, notably chloroform, methanol or ethanol, have been recognized to be problematic for analyses of certain amine drugs at higher injection port temperatures.

Summary:

Since 1992, four case reports on artifact appearance in GC and/or GC/MS analyses of various controlled substances were reported (1-4).

References:


Problem/Issue:

Forensic Chemists must maintain familiarity with updates in current instrumental techniques and become versant in new, improved methods of analysis.

Solution:

Improved/existing and new technologies are reviewed and applied to routine analysis of drugs. In cases where improved performance is observed, case reports are generated for the forensic community.

Recent Developments:

Capillary electrophoresis has moved to the forefront in liquid chromatographic analyses of controlled substances. In essence, the technique combines the resolution mechanisms of HPLC and electrophoresis, i.e., a flow system under an electric field, and gives (in many cases) dramatically enhanced resolution and speed of analysis. In particular, use of any of a variety of chiral additives to the run buffer results in chiral differentiation of substrates (a common forensic problem) without use of derivatization or expensive columns. Cleanup time between runs is very fast, and total reagent use and waste materials are far less than in HPLC. Approximately a dozen "routine use" instruments are now commercially offered.

Summary:

Since 1992, a variety of new and/or improved/existing instrumental methods have been utilized for drug analysis, including capillary electrophoresis (and related CE techniques) (1-12), gas chromatography (and tandem GC techniques) (13-18), high performance liquid chromatography (and tandem HPLC techniques) (19-31), thin-layer chromatography (37-39) and several other techniques (32-36).

References:
Capillary Electrophoresis (and Related CE Techniques):


11. Quang, C.; Khaledi, M.G. "Improved Chiral Separation of Basic Compounds in


**Gas Chromatography (and Tandem GC Techniques):**


**High-Performance Liquid Chromatography (and tandem HPLC techniques):**


HPLC Retention Indices:


Other General Analytical Methods:

Thin-Layer Chromatography:
IX) **Robotics and Computer Programs**

**Problem/Issue:**

Repetitive multi-step analyses and/or data entry is tedious, time wasting and can lead to errors due to fatigue and/or boredom.

**Solution:**

Repetitive, multi-step analyses have been automated via use of robotics systems. Repetitive data entry/analyses have been improved via development of enhanced computer programs, macros, search routines, etc. In cases where improved performance is observed, case reports are generated for the forensic community.

**Recent Developments:**

Auto-injectors are now routinely available for virtually all high-quality GC and GC/MS systems, with software already included in the operating systems. Overall capabilities of robotics systems have been greatly enhanced with improved computer support, better "tracking" hardware and software, and new sample-handling protocols (including solid-phase extraction). At least a half-dozen new companies have entered the robotics field.

**Summary:**

Since 1992, several robotics procedures (1-2) and computer programs (3-7) have been reported.

**References:**


Problem/Issue:

Large drug shipments are almost invariably comprised of multiple units of a standard container size, e.g., several thousand 1 kilogram packages of cocaine. Current U.S. sentencing guidelines require accurate assessment of the makeup of an entire shipment; however, comprehensive analyses of such shipments is a daunting and prodigiously labor intensive task.

Solution/Summary:

Representative sampling plans which permit statistical inferences to be drawn with a pre-established, high degree of confidence were developed.

Recent Developments:

Representative sampling plans have survived numerous Courtroom challenges in the United States.

Summary:

Since 1991, several representative sampling plans have been reported (1-3).

References:


XI) **Vapor and Particle Detection (Portable Instrumentation)**

**Problem/Issue:**

New trade agreements and the easing of formally restrictive national and international borders have resulted in dramatic increases in cargo transshipments and personal travel, thereby complicating drug inspection and interdiction efforts at POE's. Discovery and confirmational analysis of suspected drugs in cargo or on individuals is severely hampered by the lack of on-site analytical equipment.

**Solution:**

Development of portable and highly sensitive vapor and/or particle detectors for drug analyses allows forensic chemists to perform screening type analyses on-site. In those cases where new methodologies have proven effective, case reports are generated for the forensic and enforcement communities.

**Recent Developments:**

Use of single ion monitoring instruments (such as the Barringer IONSCAN) have become routine in the United States, and has resulted in numerous seizures of controlled substances (primarily cocaine) at POE's, highway monitoring stations, on board marine vessels (both in port and on the high seas), and at individual buildings (both residential and commercial). Other ongoing efforts involve further miniaturization of various GC or GC/MS-type instruments and development of new technologies based on surface-acoustic-wave (SAW), pulsed neutron or biosensor technologies. This field continues to expand very rapidly.

**Summary:**

Since 1991, a variety of new, portable vapor and/or particle detectors have been reported for drug analyses (1-9).
References:

(1) Sobotka, A.J. (U.S. Drug Enforcement Administration, South Central Laboratory, Dallas, TX, USA) "MAX-2; Field Testing of the Barringer IONSCAN," Personal Communication, 1995.


References (10):


