The 1998 “Research on Drug Evidence” Report
[From the 12th ICPO / INTERPOL Forensic Science Symposium]

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ABSTRACT: A reprint of the 1998 “Research on Drug Evidence” Report (a review) is provided.

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

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Research on Drug Evidence

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Table of Contents

I) Routine and Improved Analysis of Drug Substances  1
II) Novel Syntheses of Illicit Drugs, Precursors and Essential Chemicals  22
III) Clandestine Laboratory Appraisals and Safety Issues  26
IV) Reference Drug Standards  29
V) Comparative Analyses  31
VI) Source Determination of Drugs (Impurity Profiling)  34
VII) Analysis of Adulterants and Diluents  41
VIII) Analytical Artifacts  44
IX) New and/or Improved Instrumental Techniques  46
X) Portable Detection and Analytical Instrumentation  54
XI) Miscellaneous  56
I) Routine and Improved Analysis of Drug Substances

Problem/Issue:

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

Solution:

Illicit drug seizures and clandestine laboratory operations are continuously monitored to provide a comprehensive overview of new developments. 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. Case reports providing standard analytical data for new drugs and/or improved analytical protocols for known drugs are generated for the forensic and enforcement communities.

Recent Developments:

In the United States, use of methamphetamine has dramatically increased over the past three years, with concurrent increases in use of amphetamine and other related phenethylamines. Recent increases in both heroin and LSD have leveled off, while use of cocaine has somewhat decreased. Designer drugs - notably the methylenedioxyamphetamines and 4-bromo-2,5-dimethoxyphenethylamine (aka: NEXUS or 2-CB) - are still widely used. Use of anabolic steroids is steady, with use of human growth hormones or steroid natural production-stimulating drugs (e.g., gamma-hydroxybutyrolactone or GHB) continuing to increase. Abuse of flunitrazepam (Rohypnol) as a so-called "date-rape" drug continues. A wide variety of commercial products derived from hemp (cannabis) have been marketed and represent a challenging problem for trace-level analyses of cannabinoids.

In Europe, use of amphetamines, methylenedioxyamphetamines, and heroin
remains widespread, while use of cocaine and LSD continue to grow; "crack" cocaine use is now widespread.

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 growing throughout the Far East.

Use of cocaine, heroin, Mandrax (methaqualone), amphetamine, LSD and methylenedioxyamphetamine all continue to increase in South Africa.

Summary:

Since 1995, routine and/or new/improved methods of analysis have been reported for amphetamines, mono-substituted amphetamines, Amanita Muscaria, Ayahuasca, barbiturates, benzodiazepines, 4-bromo-2,5-dimethoxyphenethylamine (NEXUS) and related compounds, bufotenine, clenbuterol, cocaine, coca tea, dimethypramide, Dragon’s Blood Incense, fenethylline, fenfluramine, fentanyl, flunitrazepam (Rohypnol), heroin, hydrocodone, gamma-hydroxybutyric acid (or lactone) (GHB), N-(2-hydroxyethyl)-amphetamine, imazalil, inhalants, khat (Catha Edulis) and cathinone, LSD and related ergot alkaloids, marijuana and related cannabinoids, mescaline, methamphetamines, methcathinone, methylenedioxyamphetamine and related compounds, morphine and codeine, opium, opium, morphine and heroin (combined studies), 2-phenylethylamine (phenethyamine) and related compounds, poppy tea, psilocybin and psilocin, steroids, and theophylline.

References:

Amphetamines (see also methamphetamines, methylenedioxyamphetamine):


**Mono-Substituted Amphetamines:**


**Amanita Muscaria:**


**Ayahuasca:**


**Barbiturates:**


Benzodiazepines (see also flunitrazepam):


4-Bromo-2,5-dimethoxyphenethylamine (NEXUS) and related compounds:


Bufotenine:


Clenbuterol:

Cocaine:


Coca Tea:


Dimethpramid:


**Dragon's Blood Incense:**


**Fenethylline:**


**Fenfluramine:**


**Fentanyls:**


**Flunitrazepam (Rohypnol) (see also benzodiazepines):**

McKibben, T., "Simple and Rapid Color Screening Tests for Flunitrazepam (Rohypnol)," *J.*


Heroin:


Hydrocodone:


gamma-Hydroxybutyric Acid (or lactone) (GHB):

Wolnik, K.A.; Keitkemper, D.T.; Crowe, J.B.; Barnes, B.S.; Brueggemeyer, T.W., "Application

N-(2-Hydroxyethyl)amphetamine:


Imazalil:


Inhalants:


Khat (Catha Edulis) and Cathinone:


Kalix, P., "Catha edulis, a plant that has amphetamine effects," Pharmacy World and Science, 1996, 18 (2), 69.

LSD and Related Ergot Alkaloids:


Marijuana and related cannabinoids:


Mescaline:


Methamphetamines (see also amphetamines and methylenedioxyamphetamine):


Kuroda, N.; Nomura, R.; Al Dirbashi, O.; Akiyama, S.; Nakashima, K., "Determination of


Methylenedioxyamphetamines and related compounds:

DeRuiter, J.; Holston, P.L.; Clark, C.R.; Noggle, F.T., "Liquid chromatographic and mass
spectral methods of identification for the regioisomeric 2,3- and 3,4-


**Morphine and Codeine:**


**Opium:**


Opium, Morphine and Heroin (Combined Studies):


2-Phenylethylamine (Phenethylamine) and related compounds:


**Poppy Tea:**


**Psilocybin and Psilocin:**


**Steroids:**


Caerhati, T.; Forgacs, E., "Effect of beta-cyclodextrin derivatives on the retention of steroidal..."


Theophylline:

II) Novel Syntheses of Illicit Drugs, Precursors and Essential Chemicals

Problem/Issue:

Forensic chemists must maintain familiarity with existing and new clandestine syntheses of illicit drugs in order to assist enforcement activities, to ensure safety and effectiveness during enforcement operations, and to provide expert testimony in legal proceedings.

Solution:

Illicit drug seizures and clandestine laboratory operations are continuously monitored to maintain a comprehensive overview of the field. In cases where new drugs are synthesized, or new methodologies are utilized, case reports are generated for the forensic and enforcement communities.

Recent Developments:

Expanding use of the InterNet has spread a wide variety of both new and old synthetic procedures for all drugs throughout the world. In the United States, most new syntheses have concentrated on reduction of ephedrine or pseudoephedrine to methamphetamine. Use of active metal reductions (i.e., with lithium or sodium metals in ammonia) continues to increase throughout the midwest, while a wide variety of red phosphorus/hydriodic acid or red phosphorus/iodine based reductions have been seen in the west. New reductions based on hypophosphorous acid have appeared, and some older methods, including reductive aminations of phenylacetone, have reappeared. Use of unusual sources of ephedrine (notably ground ephedra) and pseudoephedrine (primarily commercial tablets) have increased. Use of unusual solvents for salting out procedures, including new refrigerants (freons) and camping stove fuels, has dramatically increased. Counterfeit flunitrazepam (Rohypnol) tablets have appeared. Hydroponics-based marijuana operations continue to spread throughout North America, with hash oil use remaining popular in Canada.
In Europe, most new syntheses have concentrated on production of variants of methylenedioxyamphetamine; however, it remains unclear whether these new analogs are by design or rather unintended errors. In Europe and Southeast Asia, amphetamines and methylenedioxyamphetamine are commonly produced on industrial scales.

In South America, cocaine production continues to be simplified, and a large variety of commercially available farming and industrial products have been used as effective substitutes for "classic" reagents, especially in Colombia. Production of heroin continues to increase.

Summary:
Since 1995, a variety of alternate precursors, unusual substitutes for essential chemicals, and new or modified synthetic methods have been reported.

References:

Clandestine Laboratory Updates:


New or Unusual Drugs and/or Precursors:


Clandestine Laboratory Appraisals and Safety

Problem/Issue:

Forensic chemists must maintain familiarity with clandestine laboratory procedures, setups and techniques in order to assist enforcement activities, to ensure safety and effectiveness during enforcement operations, and in order to provide expert testimony in Court proceedings.

Solution:

Clandestine laboratory operations are continuously reviewed to provide a comprehensive overview of the field. In cases where new methodologies are noted, or unusual safety concerns are salient, case reports are generated for the forensic and enforcement communities.

Recent Developments:

Expanding use of the Internet has spread a wide variety of clandestine laboratory methodologies throughout the world, including basic set-up procedures, adaptations of standard consumer products as substitutes for laboratory glassware, equipment, and essential chemicals, concealment techniques, covert surveillance and countersurveillance techniques, and booby trapping.

In the United States, widespread use of active metal reductions of ephedrine (i.e., with lithium or sodium metals in ammonia) represents a serious threat to forensic, law enforcement and fire department personnel. Continuing increases in the numbers of "confined space" clandestine laboratories (e.g., buried vehicles, caves, underground chambers or hidden internal compartments in residences, etc.) has necessitated new guidelines and training for enforcement and forensic personnel entry and disassembly/cleanup. Use of booby-traps in clandestine laboratories and storage sites continues.
Summary:

Since 1995, a number of reports concerning safety in confined space laboratories or unusual hazards associated with certain methamphetamine syntheses have been reported.

References:

**Safety Issues - Case Reports:**


**Confined Space Laboratories:**


IV) Reference Drug Standards

Problem/Issue:
Many reference drug standards or structurally related internal standards are either commercially unavailable, or if available are extremely expensive.

Solution:
Controlled substances and their structural or isotopically labelled analogs are synthesized as needed. Internal standards are also prepared as needed. Case reports are published for new or unusual standards or improved synthetic approaches.

Recent Developments:
Increasing use of single ion-monitoring techniques for identification and quantitation of controlled substances and/or precursor compounds and essential chemicals has necessitated the development and use of isotopically labelled analogues or closely related structural isomers.

Summary:
Since 1995, several reports detailing "total syntheses" of various controlled substances have been reported.

References:


V) 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 large numbers of exhibits. Improved analytical and data handling techniques are needed.

Solution:

In-depth analysis via improved instrumental methodologies help 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, a number of comparative analysis protocols were reported.

Summary:

Since 1995, comparative analyses have been conducted on amphetamines, heroin, LSD blotter papers, marijuana, opium, and tablet and capsule logos. Comparative analysis has also been addressed in general terms.

References:

Amphetamines:


Heroin:


LSD:


Marijuana:

Opium:


Source Determination (Ballistics/Toolmarks):


General Discussions:

Source Determination of Drugs (Impurity Profiling)

Problem/Issue:

Impurity profiling of drugs is important for comparative analysis protocols, geosourcing and synthetic route determinations. 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 profiles of trace-level impurities, ions, trace metals and stable isotopes. 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:

Since 1995, the ongoing and systematic effort to identify impurities and establish signature profiles via in-house syntheses has continued and expanded. Heroin impurity profiling continues in the United States, Germany and Australia. Cocaine impurity profiling continues in the United States and Europe, and has expanded in South America. Analysis of occluded solvents in finished products (notably cocaine, heroin and methamphetamine) continues, and stable isotope analyses have expanded.

Summary:

Since 1995, impurity profiling has been conducted on amphetamine, cocaine, heroin, marijuana, methamphetamine, methylenedioxyamphetamines, and precursors.
References:

Amphetamine:


Cocaine:


Moore, J.M.; Casale, J.F., "Lesser alkaloids of cocaine-bearing plants. Part 1: nicotinoyl-, 2'-pyrroloyl, and 2'- and 3'-furanoylmecgonine methyl ester - Isolation and mass spectral..."


**Heroin:**


**Marijuana:**


**Methamphetamine:**


Precursors:


General Discussions:


Occluded Solvent Analyses:


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, and 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 continuously monitored to provide a comprehensive overview of adulterants and diluents. Case reports providing standard analytical data for new and/or unusual 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:
In the United States dimethylsulfone and dimethylphthalate (or its isomers) were commonly identified in methamphetamine and cocaine, respectively. Additional programs for simultaneous identification of moderate quantities (i.e., 5 - 20 %) of certain cutting agents in cocaine or heroin by FT-IR spectroscopy were reported. Several unusual cutting agents were identified. Adulterants and diluents were the focus of several general surveys.

Summary:
Since 1995, several reports detailing common cutting agents were published. In addition, a number of simultaneous determinations of controlled substances and cutting agents were reported.
References:

Adulterants/Diluents:


Chew, S.L., "1,4-Butanediol in Liquid Exhibit," Microgram, 1997, 30 (7), 154.


Simultaneous Analyses of Drugs and Adulterants/Diluents:


Bautista, R.D.; Jimenez, A.I.; Jimenez, F.; Arias, J.J., "Resolution of ternary and quaternary mixtures of drugs in pharmaceutical preparations by use of spectrophotometric data in


VIII) Analytical Artifacts

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:

Nitrites have been recognized to be problematic for analyses of cannabinoids.

Summary:

Since 1995, several case reports on artifact appearance in GC and/or GC/MS analyses of various controlled substances were reported.

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 both routine and specialized analyses of drugs. In cases where improved performance is observed, case reports are generated for the forensic community.

Recent Developments:

Capillary electrophoresis and related techniques (electrokinetic chromatography, capillary electrochromatography, and micellar electrokinetic capillary chromatography) have moved to the forefront in liquid chromatographic analyses of controlled substances. Applications have included direct chiral discrimination of optical isomers without derivatization or specialized columns. Specialized injection techniques have enhanced detection limits for a variety of liquid chromatographic techniques. Raman spectroscopy has been investigated for identification of controlled substances. Laser-induced fluorescence has been utilized for ultra-trace level detection of both controlled substances and their impurity profiles.

Summary:

Since 1995, a variety of new and/or improved/existing instrumental methods have been utilized for drug analysis; most have been based on capillary electrophoretic techniques.
References:

Capillary Electrophoresis (and related CE techniques):


Altria, K.D., "Determination of drug-related impurities by capillary electrophoresis," I.


Gas Chromatography (and GC/MS):


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


Duenas, E.V.; Forero, M.E., "Standardized Methods to Separate and Identify Cocaine, Morphine, Heroin, Codeine, Papaverine, Benzocaine, Procaine, Lidocaine by High-Efficiency, Liquid Chromatography with Diode Array Detector (HPLC-DAD)," Microgram, 1996, 29 (8), 207.


Micellar Electrokinetic Capillary Chromatography:


**Other General Analytical Methods:**


X) Portable Detection and Analytical 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 detection and/or analytical equipment.

Solution:

Development of portable and highly sensitive detectors for drug detection and analyses allows law enforcement personnel and/or 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 ion mobility spectrometers has 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, GC/MS, and ion mobility-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 1995, a variety of new, portable vapor and/or particle detectors have been reported for drug analyses. Several instruments based on fast neutron analyses have also been reported.
References:


References:


Zedeck, M., "Drug Enforcement Administration (DEA) Chemists Erred in Calculating Quantity of Methadone that could be synthesized from precursor chemicals," *J. Forensic Sci.*, 1997, 42 (2), 349.


**General Surveys:**

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