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Analysis of Drugs of Abuse

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Preface

Since ancient times, humans have ingested mind-altering substances. The earliest reports of human interactions with these materials indicate that they were often used in the context of healing, ceremonial, and/or religious practices. Most were derived from plants such as khat, opium poppy, peyote cactus, and cannabis, among many others. Although the use of these substances may have become chronic as a consequence of dependence, the circumstances leading to the current drug abuse pandemic emerged in the early nineteenth century when it was demonstrated that a psychoactive active ingredient could be isolated and obtained in highly purified form from plant material. Morphine, isolated from the opium poppy, serves as an early example. Less than a quarter of a century after its isolation, it was marketed and freely dispensed. The revelation of its highly addictive characteristics had two consequences. The first was that chemists began systematic efforts to introduce structural changes to the core scaffold, in order to design drugs that retained the analgesic activities while reducing or eliminating their propensity to cause addiction. Heroin, synthesized by diacetylation of morphine, is a case in point and can be labeled as one of the earliest "synthetics." Unfortunately, it turned out to be more potent and more addictive than the morphine from which it was derived, characteristics that were not discovered until there were numerous casualties and addiction had become rampant! The second consequence was the institution of legislation of mind-altering substances as a means to control their abuse. The former has resulted in the development of a plethora of synthetic and semisynthetic compounds, some of which are used in medicine and others which are not. The success of the latter (i.e., legislation) has hinged on the development of technologies that could be used reliably to prove the presence and identity of outlawed compounds.

The modern history of drug abuse and the concurrent development of legislation to curtail abuse have been important in shaping current approaches to the development of the analytical methods used in crime labs. Forensic science relies on two types of tests: presumptive and confirmatory. The former tend to be rapid, require little if any instrumentation, can usually be carried out on-site by law enforcement, and provide results that are readily interpreted and enable informed decisions to be made about what further analysis steps need to be undertaken. Confirmatory tests on the other hand usually leverage the expertise of highly trained scientists and rely on the use of sophisticated instrumentation. The methods developed were shaped by the technologies available and the usual goal of identifying structurally familiar purified or semi-purified substances (e.g., prescription drugs, crack cocaine, THC, and mescaline). The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) defines three categories of tests. Category A approaches, including mass spectrometry and nuclear magnetic resonance spectroscopy, exhibit high discriminating power. Category B includes separation techniques such as gas and liquid chromatography and capillary electrophoresis, while Category C includes presumptive color tests, immunoassays, and fluorescence spectroscopy, among others. Furthermore, SWGDRUG recommends that for definitive identification of a substance, at least one other technique from Category A, B, or C be used in conjunction with a bona fide validated Category A method. The robustness of the instrumentation, its relatively low cost when

compared with other technologies, and the fact that the experimental results are independent of the lab or brand of instrument used, among other factors, caused GC-MS to emerge as the gold standard for drug identification, and it remains the mainstay of crime labs to this day. It conforms to SWGDRUG recommendations in that it conveniently combines a Category A and a Category B method. On the presumptive test front, colorimetric tests provided yes/no answers in identifying classes of illicit substances, were easy to perform in the field, could be readily packaged into "kits," and were straightforward to conduct. These factors, along with their cost-effectiveness and the fact that they could be rapidly performed, resulted in their emergence as the most viable options for routine field use by crime labs, even though some are burndened by high false positive/false negative rates. Additional analysis approaches exploit the use of various spectroscopic methods such as infrared, hyphenated MS methods such as LC- and capillary electrophoresis-MS, immunoassays, and others. All of these approaches have served drug labs very well for several decades.

However, over the last 10 years, the drug abuse landscape has undergone a sea change. Abuse of well-known substances with which crime labs have great familiarity has given way to the rapid and unrelenting emergence of novel psychoactive substances of unknown identity. These synthetic compounds are derivatives of known cathinones, opioids, and other psychoactive scaffolds. As these compounds are unscheduled, they are termed "legal highs" and are viewed by users as a means of avoiding prosecution for possession and use of outlawed substances. The influx of these compounds, coupled with a rise of drug abuse cases in general, has resulted in sample analysis backlogs in crime labs that last from months to years. Furthermore, they are often encountered as compounded mixtures containing both known and novel variants of known drugs. Crime laboratories, already burndened with sample analysis backlogs, are usually not positioned to routinely undertake the time-consuming process of first characterizing the new structures and then developing standard operating protocols (SOP) for their routine identification. Even when developed, the SOP may face rapid obsolescence, as the newly outlawed drug is rapidly replaced with unscheduled novel variants, beginning the cycle anew. Another category of legal highs is those derived from plants. The United Nations Office on Drugs and Crime has identified 20 "plants of concern," so designated because of the extent to which they are increasingly abused. These plants and their products are readily available via the Internet. Most remain unscheduled and there are few if any SOPs for their routine identification, which further retards efforts to legislate them.

These circumstances have placed crime labs between the proverbial rock and a hard place. On the one hand, successful prosecution of cases requires analysis approaches that are validated, vetted, and will stand up in court. However, the release of novel products continues to outpace the ability of laboratories to develop such methods. The new paradigm has forced crime labs to confront the fact that the approaches that were relied upon over the past several decades for detection and analysis of drugs of abuse are no longer adequate to address the current range of challenges. In this regard, forensic science practitioners, industrial scientists, and academicians are bringing their collective expertise to bear on resolving emerging issues. While some of the experimental methods rely on the development of new technologies that offer special advantages over conventional methods (e.g., ambient ionization mass spectrometry), others leverage technological advantages to more conventional techniques (such as instrument sensitivity enhancements), or the coupling of color tests with spectroscopic methods.

This volume features a range of techniques that have been developed to analyze current drugs of abuse. Given that the first tests performed in the field are often presumptive, Chapter 1 illustrates how color tests can be applied to the presumptive identification of various classes of new psychoactive substances. Raman spectroscopy is a highly versatile spectroscopic tool in drug analysis, particularly since portable instruments that can be used in the field are available. Chapter 2 illustrates how the coupling of this technique to light microscopy-based particle imaging can be used for the forensic identification and determination of the sources of drugs of abuse.

Chapters 3 through 6 illustrate conventional approaches for the analysis of new psychoactive substances and commonly abused prescription drugs. Thus, Chapter 3 describes a GC-MS protocol for analysis of some of the most commonly encountered drugs of abuse, and Chapter 4 demonstrates the coupling of capillary electrophoresis with mass spectrometry in a portable device for field detection and identification of common drugs of abuse. The problem of sample backlogs has necessitated the development of screening approaches that can be used to rapidly classify samples and determine what subsequent more definitive analyses should be conducted. For many crime labs, DART-MS analysis has proven very useful in this regard, and Chapters 5 and 6 illustrate this technique.

Chapters 7 through 11 feature detection of drugs in complex matrices such as urine, hair, and blood. Chapter 7 describes identification of abused drugs and their metabolites in urine by ultra-performance liquid chromatography-high-resolution mass spectrometry, with low limits of detection and rapid analysis times. This approach can serve as an alternative to samples not amenable to analysis by GC-MS. In Chapter 8, the sensitivity enhancement that can be achieved in detection of drugs in urine through the use of magnetic particles as solid phase extraction sorbents and subsequent analysis by capillary electrophoresis is described. A high-throughput method for detecting drugs in urine using DART-MS is the subject of Chapter 9, while an approach to the detection of trace amounts of drugs in human hair using ultrahigh-performance LC-tandem MS is described in Chapter 10. A novel method for comprehensive drug screening of urine and blood using thermal desorption and DART-MS is described in Chapter 11.

A fairly recent development has been the detection of drugs in fingerprints, which is an approach that can establish, in a forensics context, a direct link between an individual and drugs with which they've come into contact. Chapter 12 illustrates how this type of an experiment can be performed by MALDI-mass spectrometry imaging of plant-derived psychoactive biomarkers in fingerprints. Determination of localization of drugs in tissues is important for pharmacological and toxicological studies, and Chapter 13 provides a protocol by which this can also be accomplished by MALDI-MS imaging.

The emerging field of wastewater epidemiology, which is enabling the tracking of drug abuse trends through detection in real time of compounds in sewage, has necessitated the development of methods for the detection of drugs in this medium. Chapters 14–16 illustrate approaches to accomplish this using LC-MS/MS and HPLC-ESI-MS/MS.

Detection and quantitative analysis of trace drugs on porous surfaces, as well as psychoactive components in plant-derived legal highs by DART-MS, are described in Chapters 17 and 18. The challenge of deciphering the structures of emerging cathinone unknowns by statistical analysis processing of DART-MS data is outlined in Chapter 19.

I extend my gratitude to all the authors not only for their knowledgeable contributions but also for their patience in awaiting the completion of this volume; to Professor Emeritus Dr. John M. Walker at the University of Hertfordshire, for affording me the opportunity to

take on this project and for his patient and unending support and guidance; and to the publisher, Springer. I hope this compilation of experimental protocols will prove useful for those wishing to embark on experimental work on analyzing drugs of abuse and/or learn about approaches that can be taken to tackle the ever-increasing challenge of analyzing drugs of abuse by both well-established and emerging techniques.

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