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Editorial

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Fighting the War on Drugs: What Weapons for Analysis and Detection?

Elise Champeil[1*]

[1]*John Jay College of Criminal Justice, USA*

The abuse of drugs has become one of the most serious social problems in the world. According to the "United Nations Office on Drugs and Crime" (UNODC) latest report, between 149 and 272 million people used illicit substances at least once in the year 2008. The world population of "Problem drug users", defined as regular users of illicit substances is estimated at between 15 and 39 million. Amphetamines, cocaine, opiates and cannabis are the most abused substances. In addition non-medical use of prescription drugs is reportedly a growing health problem in a number of developed and developing countries. Moreover, in recent years, several new synthetic compounds have emerged. Many of these substances are marketed as 'legal highs' and substitutes for illicit stimulant drugs such as cocaine or 'ecstasy'. Two examples are piperazine and mephedrone, which are not under international control. A similar development has been observed with regard to cannabis, where demand for synthetic cannabinoids ('spice') has increased in some countries. The health consequences of drug use are dramatic: 2.8 million people who inject drugs are HIV positive. This means that nearly one in five injecting drug users is living with HIV. The prevalence of Hepatitis C among injecting drug users at the global level is estimated at 50%, suggesting that there are 8.0 million injecting drug users worldwide who are also infected with HCV. Deaths related to or associated with the use of illicit drugs are estimated between 104,000 and 263,000 deaths each year, equivalent to a range of 23.1 to 58.7 deaths per one million inhabitants aged 15-64. Over half of the deaths are estimated to be fatal overdose cases. These facts clearly point to a crucial need for developing and improving analytical methods to identify such drugs. It is also critical to develop methods for the analysis of drugs and their metabolites in biological specimen such as urine, blood, sweat and saliva; particularly in a forensic context.

Many methods are commonly used in forensic laboratories and have already been well researched and accepted in the scientific community. However, these methods are prone to certain downfalls. Immunoassays are presumptive tests that are not definitive and are subject to high rates of false negatives or false positives due to cross-reactivity or adulterants in the samples tested. Chromatographic methods (LC and GC/MS) require sample preparation such as extraction and derivatization of the compounds and extensive operator training; they are also time consuming. Another powerful technique for the detection of drugs of abuse is Nuclear Magnetic Resonance (NMR) spectroscopy. NMR has many advantages: It allows definite positive identifications, very little sample preparation or operator training is needed, and a spectrum can be gathered in only a few minutes. Furthermore, it is a non-destructive method and analyzed samples can be recovered. All those are important considerations in a forensic setting. NMR spectroscopy also shows signals from all NMR-active materials, and therefore is not limited to screening for specific drugs. In addition, NMR spectra can be obtained directly from the biofluid specimen (urine, plasma, saliva), providing a water suppression technique is used. Problems of extraction, recovery, and chemical derivatization or those that may be encountered with pH sensitive compounds are consequently avoided. Finally, quantitation analysis can easily be performed. All these facts indicate that NMR spectroscopy is a great technique for the detection of drugs of abuse in biofluids in a forensic situation. Previous examples include the use of NMR to identify and quantitate levels of methanol and ethylene glycol [1], methylenedioxymethamphetamine (ecstasy) [2] or *gamma*-hydroxybutyric acid [3]. However, compared with most chromatographic and other spectroscopic techniques, NMR is relatively insensitive. Indeed the limit of detection (LOD) of NMR ranges between 10^{-9} and 10^{-11} mol whereas as UV–vis absorbance reaches 10^{-13} to 10^{-16} mol.

To conclude, NMR analysis of biofluids for the detection of drugs is a rapid, convenient and conservative technique. In a forensic context, biofluids could be quickly pre-analyzed by NMR in cases where there is a strong suspicion of the presence of drugs. NMR analysis could be used as a "pre-screening" method. However, for detections at lower levels, MS or UV based analyses are required. To that end using LC-NMR in a synergistic way for rapid and unequivocal identification of unknowns has shown great promise. MS and NMR can also be combined with one LC to operate as LC-NMR-MS, and this combination has attracted considerable interest [4]. Targeted analytes have included acetaminophen metabolites in human urine [5]. The forensic community would greatly benefit from the development of dedicated instruments to further improve the performance of these synergetic techniques for routine use in the analysis of drugs in biofluids. LC-NMR-MS^2 is another hyphenated technique in which the rapid and ultra-sensitive screening capability of MS (or the advanced information content of real-time MS/MS), could be used to identify peaks of interest in complex mixtures.

***Corresponding author:** Dr. Elise Champeil, John Jay College of Criminal Justice, 445 West 59th Street, New York, USA, 10019, E-mail: echampeil@jjay.cuny.edu

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