Interpol Review of Forensic Chemistry – Controlled Substances, 2016 – 2019
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ASCLD Forensic Research Committee
Future Forensics Subcommittee

<u>Analysis of Controlled Substances 2016-2019</u> (Summarized by Thomas Duncan, Jeff Comparin, Richard Meyers and Henry Marche)

- There is an increasing demand to have faster and more reliable testing options available for field work. This push has partly stemmed from increases in the number of seizures and turnaround times at forensic labs, as well as an increased focus on compounds which are sometimes present at low concentrations. Efforts in this area include:
    - automated fast screening method for Cocaine identification in seized drug samples using a portable Fourier transform infrared (FT-IR) [35]
    - lateral flow assay combined with a smartphone application for detection of cocaine [68]
    - comparison of portable IR spectrometers, portable Raman spectrometers, and color-based field tests for the on-scene analysis of cocaine [104]
    - portable Raman spectroscopy for the detection of the flunitrazepam in spiked beverages [186]
    - colorimetric sensor detection of ketamine in illicit drug samples with comparison to levels detected with FTIR-ATR and LC [216]
    - development of a library search-based screening system for MDMA in ecstasy tablets using a portable near-infrared (NIR) spectrometer [292]
    - thermal desorption- IMS method for obtaining spectral fingerprints of single cannabinoids from Cannabis plant extracts [673]
    - wearable sensor device for the rapid and sensitive detection of amphetamine-type stimulants [874]
    - fluorescence based lateral flow competition assay for the screening of four classes of drugs, THC, cocaine, opiates and amphetamine present in the sweat of a fingerprint [1306]
    - field detection of Illicit substances in 304 samples using RAMAN during drug checking service in electronic music events [1529]
    - thermal desorption acetone-assisted photoionization miniature ion trap mass spectrometer for onsite identification of illegal drugs at checkpoints [1533]
    - analytical validation of a portable mass spectrometer featuring interchangeable, ambient ionization sources for high throughput forensic evidence screening [1571]
    - portable infrared laser for the identification of psychoactive substances and of their main precursors [1680]

<u>Fentanyl(s) and Fentanyl-Related Compounds</u>:
- The prevalence of fentanyl and fentanyl-related compounds were the focus of significant research efforts. The timely detection, identification, and evaluation of these compounds are detailed in the following references:

- o analytical challenges of cyclopropylfentanyl and crotonylfentany (using HPLC-DAD, LC-MS/MS and LC-QTOF-MS) [126]
- o synthesis, characterization and differentiation of cyclopropylfentanyl from E-crotonylfentanyl, Zcrotonylfentanyl, and 3-butenylfentanyl using NMR, GC-MS and FTIR [127]
- o 160 distinct compounds were identified using GC/MS and LCMS/MS-TOF in conjunction ICPMS to classify 87 route specific chemical attribution signatures (CAS) associated with the synthesis of fentanyl to determine origin [170];
- o identification and analytical characterization of a new fentanyl derivative, 4-fluorobutyrfentanyl (4-FBF), in seized powder and in the ecigarette liquid [187]
- o GC-MS, QTOF-MS, MALDI-Orbitrap-MS, NMR and IR for confirmation of the presence of acrylfentanyl in seized material [1011]
- o HPLC-DAD for simultaneous detection and quantification of heroin, fentanyl and ten fentalogues [1304]

Marijuana and Hemp Characterization:
- Changes in the United States law which related to the analytical distinction between hemp and marijuana were reflected in the continued publication of marijuana research. Surveys, characterizations, and quantitations from throughout the world were also prevalent. A full summary can be found by reference to Section 1, pgs. 27-32 of the Interpol Review [references 615 - 782]. Select research topics include:
    - o GC-MS of cannabigerol, cannabinol, cannabidiol, cannabichromene, delta 9-tetrahydrocannabinol (THC) and other terpenoids in seized cannabis seeds [621]
    - o analysis of the change in potency of cannabis samples in the five French forensic police laboratories over 25 years (1992-2016) [644]
    - o variations in potency and price in legal cannabis markets [654]
    - o analysis of Delta 9-THC, cannabidiol (CBD), and cannabinol (CBN) in confiscated cannabis using UPLC-MS/MS [660]
    - o composition of a collection of hemp cultivars and accessions of different geographical origins grown under the same conditions for 1 year [745]

Analytical Advancements/Applications/Instruments
- Raman technologies continue to be an area of focus as it allows the detection of compounds through some containers and with no sample handling. Due to Raman's inherent limitations with low purity samples, techniques such as Surface Enhanced Raman Scattering (SERS) were represented in an increasing number of manuscripts.
    - o SERS detection of "difficult" aromatic targets such as 3,4-methylenedioxymethamphetamine with unmodified aggregated Au colloids [300]
    - o SERS for detection of trace quantities of fentanyl alone and as an adulterant in heroin [1074]
    - o SERS, Raman, and DFT analyses of fentanyl and carfentanil [1288]
    - o SERS methods detect trace levels of Cocaine, Heroin, Methamphetamine, and THC [1292]
- DART continues to be an increasingly used technique due to the minimal sample preparation required and its high screening throughput.

- o DART-HRMS for spectral profiling of biological material including Mitragyna speciosa (Kratom) and Datura (Jimsonweed) [834]
  - o DART-MS and NMR spectroscopy for screening and detection of synthetic cannabinoids in herbs and powders [1232]
  - o DART-MS method for the analysis of 11 NPSs including four cathinones, one phenylethylamine, and six synthetic cannabinoids [1265]
  - o Review of DART use in forensic and security applications [1542]
- Desktop NMR is a burgeoning area of study as efforts are being made to bring the analytical capabilities of NMR to laboratories that have not traditionally had easy access to this instrument.
  - o differentiation of 65 fentanyl and related substances, including various types of positional isomers, using low-field (62 MHz) H-1 NMR [181]
  - o benchtop NMR for the analysis of samples from suspected clandestine laboratories [250]
  - o application of a desktop NMR spectrometer to qualitatively analyze samples in drug-related cases to identify new drugs [1575]

New and Novel Precursors:
- Several studies focused on the advent of new precursors. The identification of these precursors and their potential impact on the manufacture of controlled substances were highlighted in the following citations:
  - o identification of specific markers for amphetamine synthesized from the pre-precursor APAAN following the Leuckart route and retrospective search for APAAN markers in profiling databases from Germany and the Netherlands [13]
  - o identification and characterization of N-tert-butoxycarbonyl-MDMA: a new MDMA precursor; using a combination of NMR, GC-MS, IR spectroscopy, and synthesis [295];
  - o detection of t-Boc-methamphetamine (t-Boc-MP) by DART-TOF-MS and evaluation of the method in comparison with GC-MS and LC-TOF-MS [880]

Impurity Profiling/Fingerprint(ing):
- There have been a wealth of studies related to the impurity profiling of various controlled substances. Enhanced statistical approaches were commonly applied to support these efforts. Select references on this topic include:
  - o impact of different storage conditions on the stability of amphetamine impurity profiles [25]
  - o source attribution of fentanyl through impurity and stable isotope and trace element profiling [175]
  - o signature profiling of illicit fentanyl and fentanyl-related seizures for tactical and strategic intelligence [176]
  - o $^{87}Sr/^{86}Sr$ Isotopic analysis of Heroin-HCl to differentiate Mexican and South American Heroin [191]
  - o impurity profiling of methamphetamine synthesized from clandestine methylamine [251]
  - o isolation and characterization of trans-N-methyl-4-methyl-5-phenyl-4-penten-2-amine hydrochloride, trace processing impurity found in some methamphetamine samples [257]

- o assignment of batch membership of 3,4-methylenedioxy methylamphetamine hydrochloride by comparison of organic impurity profiles reported as similarity measures (Pearson correlation coefficient, reported as the modified Pearson distance, and its Fisher transform) between impurity content of pairs of samples manufactured using four common reductive amination routes [294]
- o synthesis impurity profiling using the combination of flash chromatography coupled with LC-MS, and multivariate data analysis for synthetic cannabinoids [1253]
- o overview of drug profiling including implementation of new technologies and continued process improvements [1664]

Chemometrics/Multi-variate/optimization:
- Advanced statistical methods are increasingly applied to forensic data to support the existing conclusions and allow the discernment of trends that were previously obscured. The following references highlight some of the recent applications of chemometrics to forensic analysis:
    - o combination of analysis of trace cocaine alkaloids, stable isotopes, and multivariate statistical analyses to classify illicit cocaine as originating from one of 19 growing regions within South America [58]
    - o chemometrics applied to chemical profiles of Cocaine seizures [78]
    - o changes in illicit cocaine hydrochloride processing identified and revealed through multivariate analysis of cocaine signature data [99]
    - o estimation of the synthetic routes of seized methamphetamines using GC-MS and multivariate analysis [247]
    - o integration of NIR spectroscopy with chemometrics for the determination of AKB48 (N-1-Adamantyl-1-pentyl-1H-indazole-3-carboxamide) [1206]
    - o cold EI based fast GC-MS analysis of cocaine and heroin (focus on the optimization of flow programming) [1290]
    - o near infrared (NIR) spectroscopy coupled to chemometrics calibration to detect new psychoactive substances in street sample [1508]

NPS/designer/synthetic drug:
- Newly emerging drugs of abuse continue to represent a significant portion of the published forensic science literature. The timely identification, characterization, and syntheses of these compounds are of benefit to the forensic community at large. A full summary can be found by reference to Section 2, pgs. 64-66 of the Interpol Review (references 1464 – 1501). Select research topics include:
    - o detection of ethylphenidate, methiopropamine and methoxiphenidaine, the sedative etizolam and the third generation synthetic cannabinoids 5F-AKB-48, AB-FUBINACA, MDMB-CHMICA on letters impregnated with NPS [1302]
    - o overview of NPSs: chemistry, pharmacology, metabolism, and detectability of amphetamine derivatives with modified ring systems [1464]
    - o multidisciplinary approach comprising LC-MS/MS, GC-MS and NMR analysis for the identification of three NPS including 1-(benzofuran-5-yl)-N-methylpropan2- amine, 2-amino-1-(4-bromo-2,5- dimethoxyphenyl) ethan-1-one (bk-2C-B), and 3-(2-aminopropyl) indole (amethyltryptamine) in seized materials [1477]
    - o separation of structural isomers of NPS including 2-, 3-, and 4- structural isomers of fluoroamphetamine, fluoromethamphetamine, and methylmethcathinone, isomeric

pairs of the synthetic cannabinoids UR-144/UR-144 degradant, XLR-11/XLR-11 degradant, JWH-015/JWH-073, and JWH-019/JWH-122, as well as amphetamine and several stable isotope-labeled amphetamine internal standards with UHPSFC-MS/MS and compared with UHPLC-MS/MS [1492]
- o Raman spectroscopy for the identification and classification of seized Customs samples into three NPS families [1498]

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