The Application of Stable Isotope Ratio Mass Spectrometry to Illicit Drug Profiling

The Application of Stable Ratio Isotope Mass Spectrometry to Illicit Drug Profiling

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I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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List of Abbreviations

3,4-MDMA	3,4-methylenedioxymethamphetamine
3,4-MDMC	3,4-methylenedioxymethcathinone
3,4-MDPV	3,4-Methylenedioxypyrovalerone
4-FMC	4-fluoromethcathinone
4-MEC	4-methylethcathinone
4-MePPP	4-methyl-α-pyrrolidinopropiophenone
4-MMC/MCAT	4-methylmethcathinone
ACC	Australian Crime Commission
AFDL	Australian Forensic Drug Laboratory
AFP	Australian Federal Police
AIDIP	Australian Illicit Drug Intelligence Program
ATS	Amphetamine Type Substance
bk-MDMA	3,4-methylenedioxymethcathinone
Boc/Boc_2O	di-*tert*-butyl dicarbonate
BZP	Benzylpiperazine
CE	Capillary Electrophoresis
DANPS	Drug Analogue and New Psychoactive Substances
DCM	Dichloromethane
DEA	Drug Enforcement Administration
DMSO	Dimethyl sulfoxide
EA-IRMS	Elemental Analyser-Isotope Ratio Mass Spectrometry
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
ENIPID	Enhanced National Intelligence Picture of Illicit Drugs
EWS	Early Warning System
GC-C-IRMS	Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry
GC-FID	Gas Chromatography-Flame Ionisation Detector
GC-MS	Gas Chromatography-Mass Spectrometry
GUM	Guide to Uncertainty Measurement
ICP-MS	Inductively coupled plasma-Mass Spectrometry
IRMS	Isotope Ratio Mass Spectrometry
LC-ELSD	Liquid chromatography-Evaporating Light Scattering Detector

L-PAC	L-phenylacetylcarbinol
Na_2SO_4	Sodium sulfate
NMI	National Measurement Institute
NMR Spectroscopy	Nuclear Magnetic Resonance Spectroscopy
NPS	Novel Psychoactive Substances
P-2-P	Phenyl-2-propanone
PDB	Pee Dee Belemnite
PEA	Phenethylamine
PETN	Pentaerythritoltetranitrate
PMMC	4-methoxymethcathinone
qNMR spectroscopy	Quantitative Nuclear Magnetic Resonance spectroscopy
SLAP	Standard Light Antarctic Precipitation
SMOW	Standard Mean Ocean Water
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TATP	Triaceton triperoxide
TC-IRMS	Thermal Conversion-Isotope Ratio Mass Spectrometry
TFA	Trifluoroacetic acid
TFMPP	Trifluoromethylphenylpiperazine
TMSI	*N*-trimethylsilylimidazole
UPLC	Ultra Perfromance Liquid Chromatography
VPDB	Vienna Peedee Belemnite
VSMOW	Vienna Mean Standard Ocean Water
α-PVP	α-pyrrolidinovalerophenone
$\delta^{13}C$	$^{13}C/^{12}C$ isotope abundances relative to Vee Pee Dee Belemnite (VPDB)
$\delta^{15}N$	$^{15}N/^{14}N$ isotope abundances relative to Air
$\delta^{2}H$	$^{2}H/^{1}H$ isotope abundances relative to Standard Mean Ocean Water (SMOW)

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Abstract

The increase in appeal of IRMS for forensic investigations has been reflected in the number of forensic applications; which includes questioned documents, explosives and illicit drug profiling. Differences in isotopic abundances can be the result of variations in chemical processes and reaction conditions. The intelligence obtained through this analysis can be advantageous for law enforcement having both strategic and tactical value.

In this study, stable isotope ratio analysis was used to measure the carbon, nitrogen and hydrogen of two illicit drug types, namely designer cathinones and ephedrine, and assessed for its provision for strategic and tactical intelligence.

Following an observed increase in novel psychoactive compounds, IRMS was applied to the analysis of synthetic cathinones. Measurement of $\delta^{13}C$, $\delta^{15}N$ and $\delta^{2}H$ by EA/TC-IRMS showed sufficient variation allowing for the discrimination between samples. Variation in isotope profiles of the precursor material was the primary reason for differences with kinetic factors influencing the final isotope ratios, particularly where $\delta^{15}N$ were concerned. IRMS was found to be useful when tactically comparing synthetic cathinones and discriminating between different synthetic batches.

A novel method for the synthesis of ephedrine from *N*-methylalanine and benzaldehyde has received interest recently in peer-reviewed literature and online forums. Ephedrine synthesised from *N*-methylalanine was profiled using IRMS to develop its isotopic profile, thus furthering the capability of IRMS analysis currently employed at the NMI. $\delta^{13}C$ of ephedrine was recorded between -29.7 and -38.4‰, with values depleted below -32‰ not previously recorded. $\delta^{2}H$ fell between -39 and +335‰, primarily dependent on the source of benzaldehyde. The forensic intelligence obtained from the isotopic profile of ephedrine can be used both strategically and tactically, with the combination of a depleted $\delta^{13}C$ and enriched $\delta^{2}H$ unique to ephedrine synthesised from *N*-methylalanine. The $\delta^{15}N$, despite care taken to control conditions, fluctuated between synthetic batches and ranged from -24.3 and +10.1‰, proving to be useful in the tactical comparison of samples. These results satisfy the aims of the profiling and intelligence programs, providing an advantage to law enforcement as seizures manufactured via this route can be identified and monitored.