EPS NPS PROJECT

INTERMEDIATE REPORT
CRIMINOLOGICAL ANALYSIS

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EPS NPS PROJECT

The Project **EPS/NPS - Enhancing Police Skills on Novel Psychoactive Substances** is coordinated by RiSSC and developed in cooperation with University of Hertfordshire Higher Education Institution (UH) (UK), University of Szczecin (US) (PL), Eotvos University (ELTE) (HU) and INTERPOL (associate partner), with the financial support of the EU Commission - Targeted call on cross border law enforcement cooperation in the field of drug trafficking - DG Justice/DG Migrations and Home Affairs (JUST/2013/ISEC/DRUGS/AG/6429). The Advisory Board is composed by experts from Arma dei Carabinieri, EUROPOL, INTERPOL, Swiss Federal Police, UNODC and US Drug Enforcement Administration. The overall objective of the Project is to contribute at enhancing a knowledge-based joint EU approach to effectively addressing the rapid spread of NPS, by promoting in particular the generation of data/knowledge, information-sharing, and cooperation.

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The University of Hertfordshire (UH) was established in 1952 as Hatfield Technical College in 1952, being granted University status in 1992. The University is the UK's leading business-facing university and an exemplar in the sector. It is innovative and enterprising and challenges individuals and organisations to excel. In the 2014 Research Excellence Framework 55% of the University's research was regarded as 'world leading' and 'internationally excellent'. The present project is being supported by an interdisciplinary team from the Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit (formerly the Centre for Clinical Practice, Safe Medicines and Drug Misuse Research). Work on this project continues and further develops into new areas a series of innovative and ground-breaking EU-funded projects led by Professor Schifano over the last 15 years regarding the Internet and drugs, especially 'legal highs' and Novel Psychoactive Substances (NPS). The aims of current NPS research being undertaken include: identifying and characterising both emerging substances and their consumers; contributing to an understanding of how to establish psychoactivity of unknown NPS; developing techniques for hand-held Raman spectroscopy 'in the field'; identifying serious adverse physiological, psychological and psychiatric consequences of NPS use and how to treat them; developing epidemiological tools/techniques to monitor emerging NPS.

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INTRODUCTION

Legal highs or new psychoactive substances (NPS) are drugs of abuse (i.e., initially legal) that intend to mimic the effects of illegal drug substances. They include analogues of well-established drugs of abuse, psychoactive substances researched in the past, and pharmaceutical substances that are newly abused. The United Nations Office on Drugs and Crimes (UNODC) stated that up to December 2013, over 445 NPS have been reported worldwide. In Europe alone, approximately two new NPS were notified weekly to the Early Warning System (EWS) in 2013 [1]. As they are advertised as legal alternatives to cocaine and ecstasy, they are often perceived as safe; however, there remains limited information on their pharmacology. In addition, they are often taken in combination with other drugs/alcohol or in repetitive doses within a short timeframe. According to Corkery et al., the reported deaths cases in the UK in which an NPS has been implicated in a death has rose from 10 in 2009 to 68 in 2012 [2].

A key issue associated with these substances is that they often do not comply with their label claim, but contain a wide range of drug mixtures and/or impurities that may or may not be psychoactive. This chemical complexity provides challenges as well as opportunities for chemical analysis and monitoring. Thus the project activities thus far have focused on two key pathways:

1.The rapid in-field identification of the psychotropic/narcotic active ingredients in NPS products using hand-held Raman spectroscopy. Although NPS products are notoriously chemically complex, the use of hand-held Raman spectrometers can enable a diverse range of professionals/officers, e.g. the police, border control and paramedics, to identify the index NPS. Handheld spectroscopic instruments offer the advantage of carrying the laboratory to the sample. A number of studies report on the use of portable Raman instruments for the identification of drugs of abuse; however, these are limited to classical drugs of abuse such as heroin, cocaine and amphetamine. The use of laboratory-based Raman spectroscopy for screening NPS products has shown promise [3], but challenges with incomplete reference library and fluorescence need further investigation. Our previous investigations have found similar challenges with hand-held Raman [4] which are further explored in this project to improve applicability for the end user.

2.Evaluation of impurities/cutting agents present in NPS products using computational approaches to observe trends in production/distribution. This can give an indication if a group of Internet products were cut or produced at the same location, thus supporting in particular supply chain analysis.

THE RAPID IN-FIELD IDENTIFICATION OF PSYCHOTROPIC - NARCOTIC ACTIVE INGREDIENTS IN NPS PRODUCTS USING HAND-HELD RAMAN SPECTROSCOPY.

It was determined that the main challenges of hand-held Raman instruments for the purpose of NPS identification are the following:

A. Signal interference from a variety of cutting agents/adulterants (e.g., talc and microcrystalline cellulose(MCC)
B. Signal interference from fluorescence
C. Limited reference libraries due the lack of availability of standards
D. Spectral searching algorithm capabilities
E. Various formulations of NPS available
F. Presence of more than one NPS

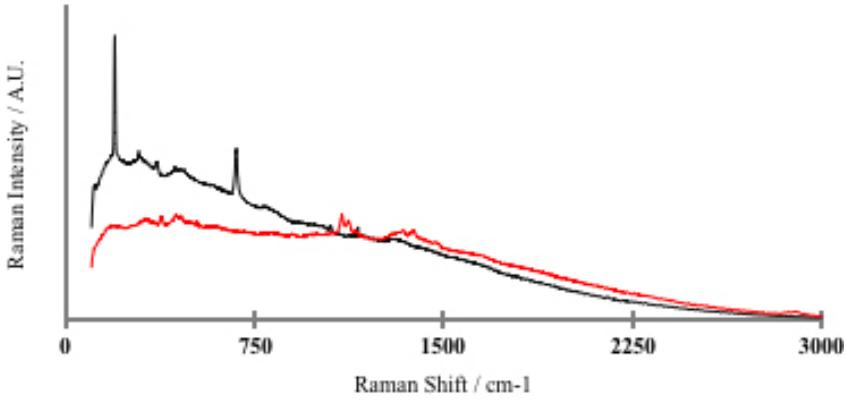
A literature review was conducted to explore 'main challenge a.' and select the most common adulterants and cutting agents found in NPS products. A total of 25 excipients were selected for study with a range of functional categories. These ranged from local anaesthetics to painkillers.
A selection of the excipients are found in Table 1.

Table 1: A selection of the excipients studied including their functional categories

EXCIPIENT	FUNCTIONAL CATEGORY[1]
Adulterants	
Caffeine	Mild stimulant
Lidocaine	Local anaesthetic
Phenacetin	Painkiller; chemically related to paracetamol
Cutting agents	
Dextrose	Tablet and capsule diluent, therapeutic agent
Microcrystalline cellulose (MCC)	Absorbent, suspending agent
Talc	Anticaking agent, glidant

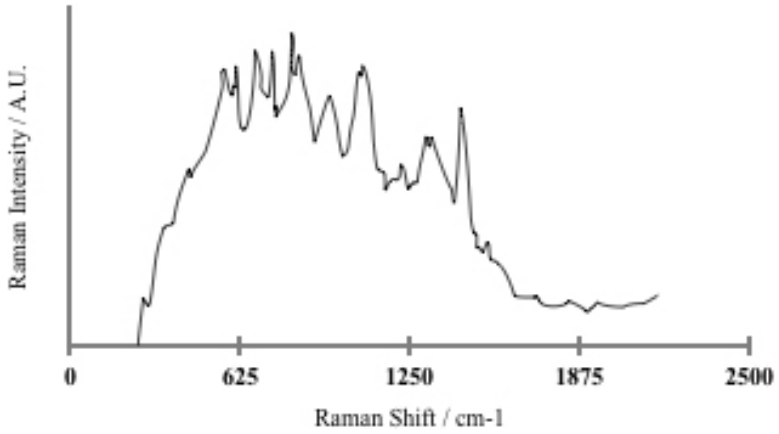
For example, two cutting agents that can interfere (i.e., mask) the signal from the psychotropic/narcotic active ingredient are talc and MCC. Figure 1 shows the Raman spectrum of both talc and MCC showing the considerable raised background, especially at lower Raman shifts.

Figure 1: Raman spectrum of talc (black) and MCC (red), common cutting agents of NPS



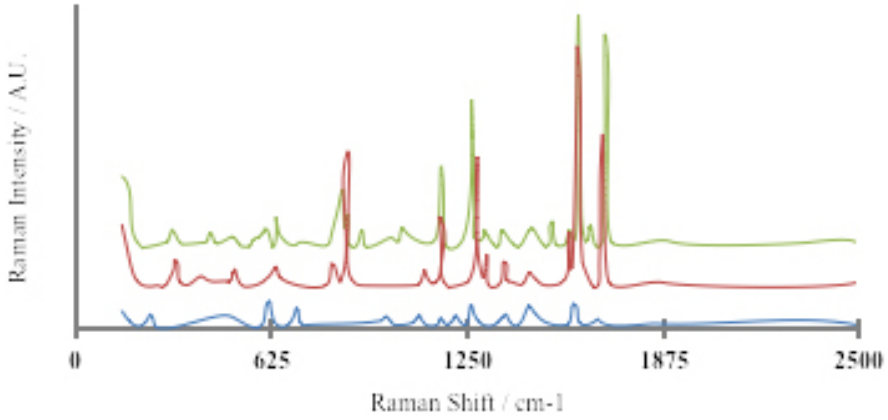
Below is an example of a Raman spectrum of the NPS product labelled as methiopropamine (MPA); GC-MS results confirmed the presence of MPA. The spectrum shows a raised baseline, which could be the signature of a cutting agent or adulterant as the MPA itself does not demonstrate such fluorescence.

Figure 2: Raman spectrum of NPS product labelled as methiopropamine (MPA)



Many adulterants added to NPS products are strong Raman scatterers. For example, the local anaesthetics such as benzocaine and procaine give a number of relatively high intensity peaks which can overlap with Raman peaks of the psychotropic/narcotic active ingredients of interest.

Figure 3. Raman spectra of lidocaine (blue), benzocaine (red), and procaine (green)



A preliminary study was conducted to determine the response of these cutting agents and adulterants using handheld Raman spectroscopy. This was compared to Fourier transform infrared spectroscopy (FTIR) and gas chromatography-mass spectrometry (GC-MS), which are two common techniques used in forensic identification. The spectral fingerprints were qualitatively evaluated for spectral complexity (i.e., spectral information) and compared across techniques. The results indicate that most adulterants respond well using each technique, whereas cutting agents such as carbohydrates and sugars are more detectable using FTIR. Furthermore, many of these substances did not dissolve in typical solvents used for GC-MS. This suggests that the spectral masking of NPS by carbohydrate/ sugar cutting agents is less prone using the hand-held Raman spectrometer than FTIR. Carbohydrates and sugars contain many polar C–O and O–H bonds, which are strong infrared absorbers and weak Raman scatterers. This also suggest that on the whole the addition of adulterants have the potential to cause more spectral masking (i.e., of the NPS) than cutting agents. In the case of mixtures with adulterants, or other NPS, identification may require further processing of spectra.

[1] EMCDDA-Europol, European Drug Report 2013: Trends and developments. 2013, European Monitoring Centre for Drugs and Drug Addiction: Lisbon.

[2] J. M. Corkery, H. Claridge, B. Loi, C. Goodair, and F. Schifano, Drug-related deaths in the UK: January-December 2012, Annual Report 2013, National Programme on Substance Abuse Deaths (NPSAD) New Psychoactive Substances, London, 2014.

[3] L.E. Jones, A. Stewart, K.L. Peters, M. McNaul, S.J. Speers, N.C. Fletcher, S.E.J. Bell, Analyst, 2016, 141, 902.

[4] S. Assi, A. Guirguis, S. Halsey, S. Fergus, J. L. Stair, Anal. Methods, 2015, 7, 736.

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