Detection and Identification of Illicit Drugs and Cutting Agents in Seized Street Drugs:

Benchtop NMR Spectrometer and Databasing Software

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INTRODUCTION

Historically, law enforcement officers and the forensic community have relied primarily on the use of chemical tests, such as Nik Wipes, optical spectroscopy, such as handheld Raman spectrometers, and/or gas chromatography-mass spectrometry (GC-MS) to identify illegal drugs. However, the drastic increase in designer drugs and new psychoactive substances (NPS) over the last decade has made the detection and identification of new classes of drugs extremely difficult.

While not as common in drug detection, NMR Spectroscopy could provide value in identification and purity determination as it provides non-destructive, rapid analysis with a wide dynamic range that does not require blank runs, large amounts of flammable solvents nor the preparation of a calibration curve. One of the main reasons that high-field, superconducting NMR technology was overlooked in this regard, was the capital cost, the size and siting requirements, maintenance costs and the expertise required to operate the traditional NMR instrumentation.

Benchtop NMR spectrometers, provide an interesting alternative platform on which to develop an illicit drug database to place this powerful, information-rich technology in the hands of forensic scientists. Herein we describe the use of our ^{1}H 60 MHz benchtop NMR spectrometer for the acquisition of standard drugs, the preparation of a database using ACD/Labs Spectrus tools and show examples of how it can be used to identify seized street drug samples.

EXPERIMENTAL

Sample Preparation

Samples were prepared by LKA in their Hanover facility. For reference samples 60 µmol were dissolved in d_6-DMSO, and if insoluble in DMSO, D_2O was added to the vial. The vial was agitated until the sample fully dissolved and then it was transferred to an NMR tube. For pure samples, solubility was not an issue.

For unknown samples of street drugs, a spatula known to hold roughly 30mg of drug was filled and added to two vials and 0.6 mL of d_6-DMSO was added to one vial, and 0.6 mL of D_2O to the second. The vials were capped and agitated for 1-2 minutes. In unknown samples, solubility was often an issue presumably due to fillers in drug preparation, as standards were highly soluble, the liquid was transferred to an NMR and the ^{1}H NMR data was acquired.

Spectral Acquisition

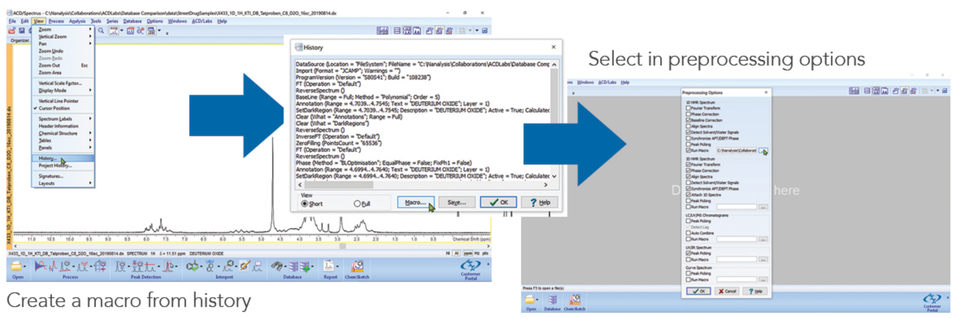
For spectral acquisition 1D ^{1}H NMR spectra was acquired with the following parameters:

SW = 80ppm	scan delay = 1sec
SW = 20ppm	ns = 16 or 64
np = 8192	time = 1 or 4 min

**It can be noted that some parameters, such as 80ppm were acquired at larger values than required to ensure flexibility for future data analysis.*

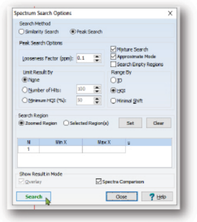
PRE-PROCESSING

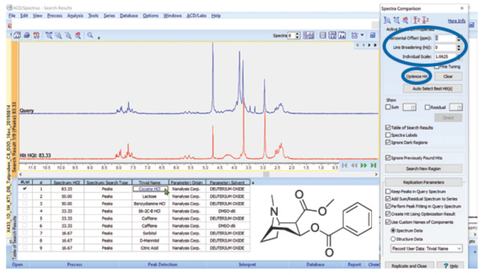
To ensure simple and repeatable processing between the operators, and accelerate the processing of 200+ samples, an ACD/Spectrus Processor macro was run to allow for zero filling, phase correction, baseline correction and creating 'dark regions' where the ^{1}H NMR chemical shifts of solvent or reference compounds (*e.g.*, TMS) are known to appear to prevent an masking or inaccurate matching within the database.



DATABASE OPTIMIZATION OF ILLEGAL DRUG

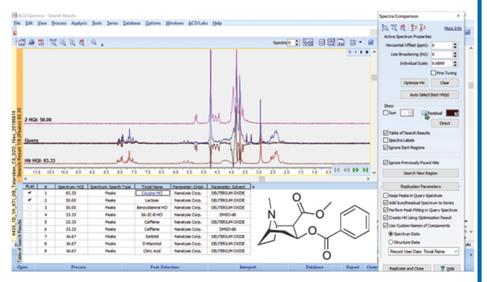
Once the database has been filled, we explored its efficacy using unknown samples. The ^{1}H NMR file is loaded in Spectrus so the preprocessing is immediately performed. From here the user can select the database and load search options. As the unknown sample is anticipated to be a mixture composed of a many components, we select 'peak search', specify that it is a 'mixture search' in 'approximate mode' to account for any changes that arise due to slightly different experimental parameters, *e.g.*, pH of the sample, different quality shims. From here the user selects 'search'.





The search returns as a result a number of compounds, in the case of the unknown street drug sample shown here, there are 9 possible hits. The main component is cocaine, with an 83.33 HQI factor, and the remainder of the matches correspond to potential fillers.

To get the best match between the query and the drugs, the user can employ the spectra comparison toolbar on the right-hand side to manually optimize (using the horizontal offset to move chemical shifts in 0.01ppm increments, the line broadening to widen or narrow the peak, and the scaling factor to increase or decrease the intensity) or automatically using the 'optimize hit' button.



The quality of the fit between the spectra can be visualized using either spectral 'residuals' or'sums'.

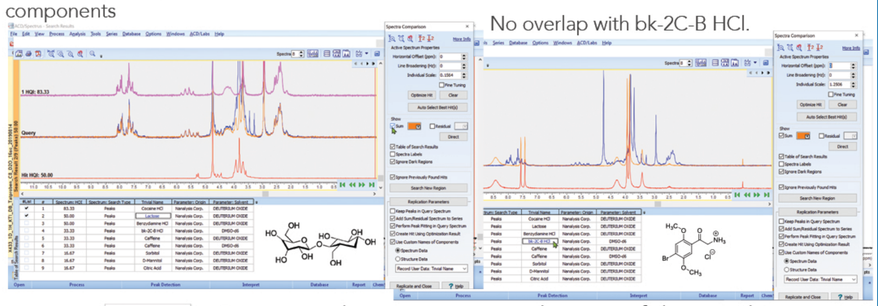
DATABASE OPTIMIZATION OF CUTTING AGENTS

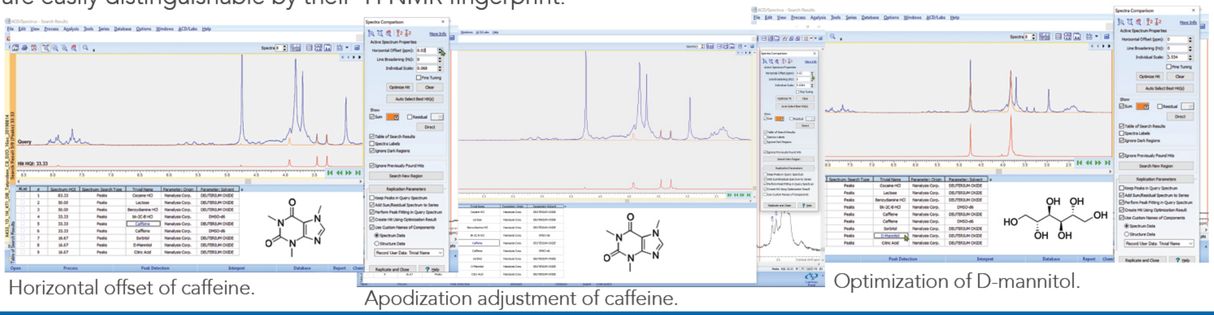
Once the cocaine spectrum has been optimized the user than starts to optimize the cutting agents. Lactose appears to be the second largest component in the sample.

The user then visually inspects the remaining 9 hits. The two samples in DMSO are discounted because the unknown sample was prepared in D_2O, benzyldiamine, bk-2C-B HCl (shown here), sorbitol and citric acid are excluded because they don't have suitable peak overlap. However, caffeine in d_6-DMSO and D-mannitol do show good peak overlap with street drug sample and are optimized in a similar way to cocaine and lactose. Interesting to note, sorbitol and D-mannitol are diastereomers, and indistinguishable in traditional GC-MS methods, although they are easily distinguishable by their ^{1}H NMR fingerprint.

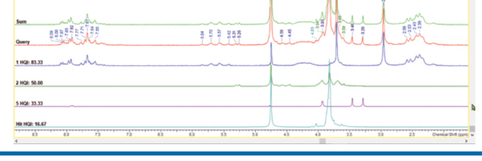
Spectral sum of optimized lactose & cocaine components

No overlap with bk-2C-B HCl.





Once complete, one can see the sum of the matching components on the query and get the residual sum of squares, the relative residual and other parameters associated with the match. Additionally, when compared with GC-MS analysis on the same sample, there is excellent agreement.



CONCLUSIONS AND FUTURE WORK

On-going work looks to build fingerprint regions to reliably flag designer drugs that don't match with standards within the database and increase the automation of the matching software further to ease the use of this technique by forensic analysts.

Our collaborators at the LKA are deploying this in mobile laboratory vans to allow forensic analysts to analyze unknown samples directly onsite, thus facilitating faster decision making and designer drug identification.

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