Using Benchtop NMR to identify the unknown in forensic drug testing

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Testing for illegal drugs is an ongoing battle. With approximately 100 new psychoactive substances (NPS) appearing at border checkpoints every year [1], the rapid detection and identification of these drugs is critical to prevent their widespread sale.

In recent years, death rates from drugs have ramped up to more than 40,000 a year in the US alone [2]. This 'opioid epidemic' specifically refers to the growing number of deaths and hospitalisations from opioids including illicit drugs such as NPS, and drug overdose is now the leading cause of accidental death in the United States.

This presents significant challenges to the authorities. The main issue here is that testing relies on matching substances to libraries of known substances. NPS, however, are developed to mimic drugs such as heroin and cannabis, and avoid detection through changing their molecular structure. This 'camouflage' removes the possibility of forensics testing finding a match to the recognised drug.

Police forces and criminal investigators need a new, accurate and, importantly, rapid way to track the unknown as well as the known.

Identifying the unknown

A key objective of analysing suspect substances is to provide legally admissible evidence that proves a drug's chemical make up. Materials are sent to a testing lab for identification and quantification, but providing unequivocal evidence is hampered by many issues.

MS screening

Current drug testing relies mainly on mass spectrometry (MS) screening. This tried and trusted method produces reliable results but quantification is limited by the need to compare the spectral peak of the unknown substance with a reference substance and to display a known peak in the vicinity. This is a compound-specific reference standard. Using this method, any mimic molecule will display different fractural patterns in analysis and will slip through the net.

NMR methods

NMR spectroscopy systems are a well-established testing method in clinical research sectors, as well as in forensics at police, customs and border control labs. NMR can identify and quantify unknown substances without requiring a compound-specific reference. Its use is supported by a European Commission report, which states that, "The chemical identification of many unknown substances found by customs and suspected to be NPS requires the use of more sophisticated analytical techniques such as NMR […] [3].

The significant advantage of NMR in forensics applications is its ability to detect, identify and quantify unknown substances without needing a pre-qualified reference. On analysis, a mimic molecule is shown in the resulting spectrum with slight differences to a known substance. This new substance can be investigated further and added to the library for immediate matching and identification in future.

High specification NMR systems are only accessible at major scientific centres and traditionally rely on highly trained staff to operate them. This, together with the high initial investment cost as well as the total cost of ownership, has restricted the uptake of NMR.

Double testing for legal admissibility

In most countries across the globe, a minimum of two orthogonal analytical methods must be used in drug testing to provide sufficient and admissible evidence. The goal is that the second method provides completely different selectivity from the first, in order to validate the findings. Using two entirely independent methods, however, can be both time consuming and resource-intensive and, in practice, this is often hard to carry out. For this reason, two library-based methods like MS and FT-IR are mostly used and the results are widely accepted as proof of identification for known substances.

Accurate quantification, however, remains a critical part of the process due to the need for compound specific reference material.

In the case of an NPS - or unknown substance – being identified and quantified, NMR plays a key role because it is independent of the availability of compound specific reference material. The growing occurrence of NPS and the fast increasing need for NMR testing, however, can cause substantial sample bottlenecks at central scientific hubs, which has an adverse impact on time to results.

Reducing screening time

The fast turnaround of NMR cuts screening time from days to minutes. In a situation where drugs have been seized, in any quantity, the paperwork needed to hold a suspect for the time it takes to identify and analyse the chemical composition of the drugs may well be prohibitive. Time-to-result for a benchtop NMR instrument to deliver a conclusive identification is dramatically shortened compared to conventional NMR analyses, where samples may need to be sent away to scientific hubs for testing. Any airport or police authority, for example, can now own a suite of benchtop NMR instruments to deliver routine screening results rapidly using the global database, without needing highly trained operators to run the test and interpret the findings.

Unlike traditional large scale NMR instruments, benchtop models operate using a single plug socket, with no need to recharge with high maintenance cryogenics like helium. New benchtop NMR instruments offer a cryogen-free magnet design, making it accessible and cost effective for any lab to provide the definitive results unique to NMR analysis.

Database maintenance

Organisations such as the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), the European Network of Forensic Science Institutes (ENFSI) and the Customs Laboratories European Network (CLEN) are driving the adoption of a global database of substances. The maintenance of this database plays an essential role in the fight against illegal trafficking of drugs.

Once a new substance is identified by NMR, anywhere in the world, its spectral data can be uploaded into a global database, from where any lab across the globe with a similar benchtop NMR instrument could identify and quantify that substance at the touch of a button, using spectral fingerprinting. Using MS alone would not be feasible, as this approach would require designing a deuterated species of the substance and making the reference compound available to any lab, which, at a rate of two new NPS a week, is simply not possible.

Centralised integration

The true potential of NMR can be unlocked when full sized instruments can be integrated with benchtop systems. Operators familiar with NMR software can take control of the benchtop system without needing additional training, and an inexperienced NMR user can benefit from push button interfaces and dedicated workflows.

Therefore, if an ambiguous sample identification is returned, NMR experts from a central scientific hub can log in to the system and help with parameter optimisation and data processing issues in case both system using the same software interface and set of protocols for ease of use. This level of integration opens up exciting potential for global collaboration beyond the current drug library sharing – with the possibility of national workflow definitions and method harmonisation, critical for evidence generation, with local users and the centralised control all working on the same system in real time.

Decentralising NMR analysis to put an instrument in every drug testing centre not only opens up the potential to dramatically scale up throughput and deliver a faster time-to-result, but also frees up the centralised high specification laboratory instrument and operator expertise to work on more specialist testing.

The future is benchtop

With bodies like EMCDDA [4], stating one of their goals is to, "Increase the ability of forensic science and toxicology laboratories to identify new substances, […] which requires support for training, resources for testing, and a mechanism for production and sharing of analytical data, reference materials and expertise," benchtop NMR instruments are well placed to support the new substance testing, data sharing and reference library creation to support this objective.

Offering the same functionality as high specification NMR, benchtop NMR requires no specialist operation or installation and can be easily integrated into any laboratory to give a rapid, automated, easy-to-use and unrestricted method of drug screening that is accessible for widespread and practical use.

Author profile

Dr Joerg Koehler studied physics and holds a doctoral degree from the Institute of Biophysics and Physical Biochemistry of the University of Regensburg, where he had also worked as a Postdoctoral Research Scientist with focus on NMR based studies of folding intermediates of biochemically active macromolecules. Dr Joerg Koehler held several positions in sales, sales management and business administration before joining Bruker as Head of Business Unit Industrial. Today he is accountable for Bruker's global activities in magnetic resonance in various industrial market segments including forensics.

References

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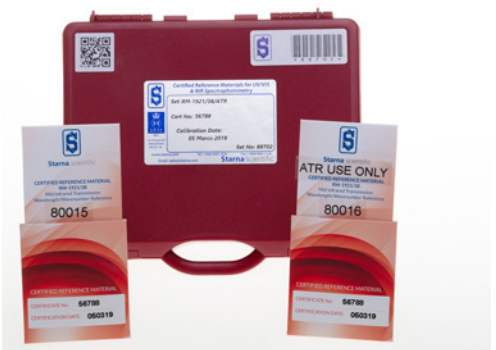
New ATR Mode Certified Polystyrene Reference Films



Starna now supply an 'ATR' set of polystyrene film references to assist compliance with the new European Pharmacopoeia Chapter 2.2.24. This is supplied as a kit of two films: a RM-1921/38 film certified film for normal Transmission measurements; and an accompanying film specifically certified for 'ATR only'.

This new set expands the Starna range of polystyrene film references for use in FTIR, MidIR and NIR Wavelength Calibration to include both Transmission and ATR modes. Existing films are available in two thicknesses: RM-1921/38 is a 38 µm polystyrene film with 14 certified peaks from 540 cm-1 to 3080 cm-1 (18.5 µm to 3.25 µm) whose values are traceable to NIST SRM 1921b. A thicker version, RM-1921/65, is 65 µm thick and in addition to the 14 peaks in the MidIR eight peaks are certified in the NIR from 3060 cm-1 to 8750 cm-1 (3.25 µm to 1.15 µm). These peaks are traceable to NIST SRM 2065.

They comply with the latest revisions of the European Pharmacopoeia Chapter 2.2.24, and US Pharmacopoeia General Chapters 854 and 1854 on Mid-Infrared Spectroscopy.

The references are presented as card mounted films in the conventional industry pattern; ATR film unmounted. Easy to use, they simply slip into the standard sample holder of any FTIR instrument.

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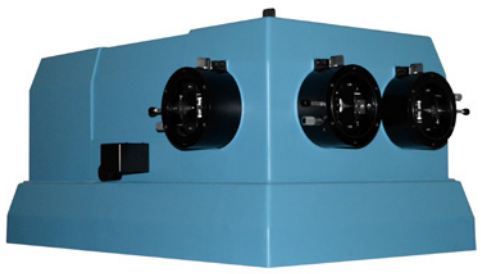
A fast spectrometer is essential to collect light in both the VUV and the IR regimes of the spectrum. Whether the spectrometer is being used as a light source to deliver the most light possible or is used to collect a signal, the higher collection efficiency of faster f number and optimised optics coating is essential. This makes the Model 207 and the Model 207V ideal spectrometers for experiments conducted in the VUV or the IR.



The new Model 207 is a 670mm focal length, optically fast, f/4.7 monochromator. The Model 207V is available in a VUV version for use down to 105nm and in the vacuum IR. It is also now available with off-axis parabolic optics for better imaging, if required. The off-axis parabolic (OAP) mirrors provide both low f/number and stigmatic monochromator performance. The Model 207A with OAP optics provides coincident sagittal and tangential foci as well as perfect collimation and focusing, which is beneficial in source systems. The combination of OAP with either the Model 207 or the Model 207V make this an ideal system for small compact images, such as for use in Raman, with small laser exited sources, or with imaging detectors.

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