# Detection of drugs of abuse by Raman spectroscopy

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**Raman spectroscopy can provide rapid, sensitive, non-destructive analysis of a variety of drug types (e.g. amphetamines, alkaloids, designer drugs, and date rape drugs). This review concentrates on developments in the past 15 years. It considers identification and quantification of drugs of abuse in different types of forensic evidence, including bulk street drugs as well as traces found in drinks, on fibres/clothing, in fingerprints, on fingernails, on bank notes, and in body fluids. Copyright © 2010 John Wiley & Sons, Ltd.**

**Keywords:** Raman spectroscopy; drugs of abuse; forensic science.

## Introduction

The use of drugs of abuse is the cause of many serious problems. Drug addiction has resulted in young people dropping out of education, and it can prevent parents caring for their children. It draws people into crime and poverty, destroys ambition, and ruins lives. As part of the fight against drugs, forensic scientists and law enforcement agencies need quick and reliable methods of drug identification which can be adapted to the ever increasing number of available drugs.

Raman spectroscopy is employed to detect vibrations in molecules and is closely related to infrared (IR) spectroscopy.[1] The Raman experiment involves irradiating a sample with a laser light source. Most of the light is elastically scattered at the same wavelength as the light source (Rayleigh scattering), but a small fraction (approx $10^{-5}$%) of the incident radiation is scattered at a different energy (Raman scattering). The difference in energy between the incident source and the Raman emission corresponds to molecular vibrations. Whilst historically IR spectroscopy has been used more extensively than Raman spectroscopy, developments in Raman instrumentation have led to it becoming the technique of choice in many applications. This, coupled with the development of surface enhanced Raman spectroscopy (SERS) and surface enhanced resonance Raman spectroscopy (SERRS), means that the technique is now sufficiently sensitive for trace forensic analysis.[2] In some respects information provided by Raman spectroscopy is complementary to that provided by IR spectroscopy. Changes in dipole moment give rise to IR activity whilst changes in polarisability are required for Raman activity. Transitions that are strong in an IR spectrum are often weak or absent in a Raman spectrum and vice versa. Raman spectroscopy tends to highlight the structural carbon elements in an organic molecule while IR spectroscopy emphasises the functional groups.

Modern Raman instruments can provide rapid, sensitive, non-destructive analysis on microscopic samples combined with increasing portability. Raman spectroscopy has been established as a valuable forensic tool in the past 20 years with rapid development in the last decade. With regard to drug analysis, the unique vibrational spectrum (Figure 1 shows spectra of four typically encountered drugs) of a molecule results in a high degree of confi-dence in identification. The weak Raman signal from water allows spectra to be obtained from aqueous solutions or moist materials.

The two most common forms of Raman spectrometers are dispersive and Fourier transform (FT) spectrometers.[1] The former employs a UV or visible or near infrared (NIR) laser for excitation, a dispersive spectrometer and a CCD for detection. The latter employs an NIR laser for excitation and an interferometer-based detection system that requires an FT programme to produce a spectrum. Both can be used in conjunction with microscopes to examine small samples. The development of portable Raman systems means that it is now possible to provide rapid analysis at a scene such as a clandestine drug-manufacturing laboratory.[3]

One of the major disadvantages of Raman spectroscopy is that the weak Raman signals can easily be masked by fluorescence. However there is a range of effective strategies to overcome this problem, many of which will be mentioned in this review.

Raman spectroscopy has been applied to a variety of drugs types (e.g. amphetamines, alkaloids, designer drugs and date rape drugs). This review, which concentrates on developments in the past 15 years, considers the analysis of drugs of abuse dependent on the type of forensic evidence involved starting with bulk street drug samples and then considering trace samples found in drinks, on fibres/clothing, in fingerprints, on fingernails, and on bank notes as well as the detection of drug usage.

## Bulk street drugs

By far the most detailed work has been done on the analysis of macroscopic samples compared with the detection of trace evidence. Raman spectroscopy is attractive because it is potentially a rapid, specific form of analysis that requires little or no sample preparation and is non-destructive. All of these features are advantageous if a large number of samples need to be analysed

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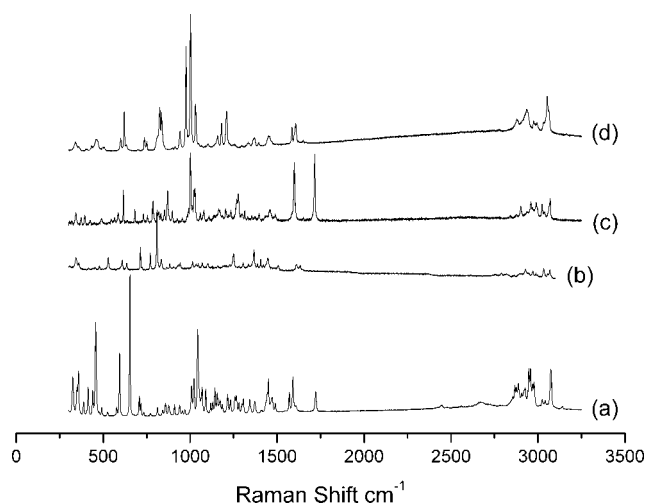
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**Figure 1.** Raman spectra of (a) ketamine, (b) MDMA, (c) cocaine and (d) amphetamine obtained using a helium-neon laser (632.8 nm).

or screened. It can be used to discriminate between and within drug types as well as to quantitatively analyse mixtures containing drugs of abuse. Raman spectral mapping allows the homogeneity of street samples to be tested.

Several reports have concerned the analysis of amphetamine samples. FT-Raman spectroscopy has been shown to be a reliable method for identifying methamphetamine hydrochloride (MA). FT-Raman spectra of MA have been successfully recorded through plastic packaging (polyethylene or polypropylene bags) typical of that used either by criminals for transportation or by law enforcement for containing and sealing evidence.[4] The technique readily discriminates between MA, amphetamine sulfate and ephedrine hydrochloride and MA is readily identifiable diluted in sodium chloride or water with a detection limit of 1% (w/w). FT-Raman is a popular form of Raman spectroscopy principally because it uses an NIR laser, usually a neodymium-doped yttrium aluminium garnet ($Nd^{3+}$: YAG) solid state laser emitting at 1064 nm.[1] Few compounds have excited states low enough in energy to be excited by this laser to give fluorescence. However, the Raman scattering is inherently weaker compared with dispersive systems using higher energy lasers, because the intensity of the Raman scattering is proportional to the fourth power of the frequency of the incident radiation. This is partially compensated by the fact that, since the exciting radiation does not absorb into most samples as efficiently as visible radiation, higher laser powers can be used and also interferometer detection systems are very sensitive. Practically if a weaker signal is observed then this will inevitably lead to an increase in acquisition time and thus an overall lengthening of the detection process.

The use of short wavelength excitation (e.g. 244 nm) is also effective in avoiding fluorescence as it is well separated from the Raman signal. Fluorescence, which is often associated with aromatic functionalities in the drug or other components of a street sample, generally occurs in the 300–700 nm region. This type of fluorescence can be avoided if the Raman signal is located in a different region (e.g. UV or NIR). As the Raman signal is located near the excitation wavelength the fluorescence can be avoided by choosing a laser with a UV (or NIR) wavelength. The technique is inherently more sensitive at higher frequencies due to the fourth power law and can also benefit from the resonance Raman effect,[1] which further enhances the sensitivity as the laser

wavelength is within the typical optical absorption band of most drug molecules. A 244 nm excitation Raman microspectroscope has been developed and successfully used to investigate a range of narcotics and explosives, both pure and contaminated. The instrument is reported to be quick and simple to operate and the simplification of spectra caused by resonance allows the easy identification of species contained in complex mixtures.[5] However, there have been relatively few reports of the use of UV-Raman for drug analysis possibly because potentially the high energy laser may damage the sample. Also the UV resonance enhancement tends to be localised to the vibrational modes of relatively rigid chromophores so that the spectra are less sensitive, compared with visible or NIR excitation, to different polymorphic forms.[6]

It has been demonstrated that conventional dispersive Raman spectroscopy, with far-red excitation, of N-methyl-3, 4-methylenedioxyamphetamine (MDMA) and related compounds can be very rapid and effective.[7] Using 785 nm excitation the level of fluorescence is low and good quality data can be obtained in around 2 min. The spectra can be used to distinguish between closely related substances such as the geometric isomers N-ethyl-3,4-methylenedioxyamphetamine (MDEA) and N-methyl-1-(1,3-benzodioxol-5-yl)-2-butamine (MBDB) as well as different polymorphic/hydrated forms of the same drug. Excipients and bulking agents used to prepare the tablets can be identified, giving useful composition profiles. It is also possible to identify the specific amphetamine present even in the presence of multiple adulterants which is a key requirement of any technique to be applied to seized drug samples.

A study of 400 ecstasy (MDMA) tablets all of similar appearance and carrying the same logo from a large seizure of more than 50 000 tablets showed that they could be classified on the basis of the excipients used.[8] The study highlighted that the simple physical descriptions coupled with active drug content do not in themselves fully characterise the nature of the tablets. There is considerable variation within a single seizure that can be detected by Raman spectroscopy, which could be useful in tracing distribution networks. Inhomogeneity was observed in many of the tablets highlighting the problem of using microscopic collection of spectra potentially leading to erroneous conclusions. Therefore it is important to sample more than one area or to sample over larger areas of a tablet to obtain fully representative data.

In 2003 the results of an even larger study were reported.[9] The ability of Raman spectroscopy to profile large numbers of tablets was demonstrated by screening approximately 1500 tablets from different seizures in Northern Ireland. Typical accumulation times were 40 s per tablet. The ratios of the peak heights of the prominent MDMA bands at 810 $cm^{-1}$ and 716 $cm^{-1}$ (which vary with hydration state of MDMA) and the MDMA band at 810 $cm^{-1}$ against the largest clearly discernible excipient band in the spectrum were measured. It was possible to decide that two independently seized batches of a drug may have originated from the same source based on similarities in the impurities present using Raman spectroscopy even allowing for in-house batch to batch variation. It was also found that there was a large range in the homogeneity and MDMA content even from tablets with the same logo and from the same batch. This could mean that users may accidentally overdose if they assume that the tablets they acquired all contained the same level of MDMA when this may not be the case.

A study has been undertaken in order to determine the most important experimental parameters for automated, quantitative

analysis of seized and model ecstasy tablets.[10] Spectra recorded at single points on the surfaces of seized MDMA-caffeine-lactose tablets with a Raman microscope (785 nm laser, 3 μm diameter spot) were dominated by one or another of the three components, which was consistent with Raman mapping and showed the component micro-crystals to be approximately 40 μm in diameter. Quantification was performed using the microscope and a macro-Raman (150 μm diameter spot) system and it was found that the macroscopic system was much more reliable. This is consistent with the increased sampling volume arising from a combination of the larger spot size and the depth of focus. It was also found that combining 64 grid points (0.5 mm spacing and 1–2 s accumulation per point) to give a single average spectrum for a tablet gave a practical balance between minimising sampling error and keeping sampling times at an acceptable level.

A recent detailed assignment of the Raman spectra of MDA and MDMA has been performed based on structural analysis carried out by theoretical methods.[11] This work provides information regarding the physicochemical properties of MDMA and any synthetic impurities, which is useful for both forensic and toxicological studies. The Raman spectra obtained, using an Ar$^+$ laser at 514.5 nm, allowed the characterisation of MDMA, MD, and some common precursors of amphetamines. The identification of the precursors present could be used to determine the synthetic pathways used in the drugs synthesis which in turn may help to link seizures to a common source.

The identification of $\beta$-Methyl-$\beta$-nitrostyrene derivatives, which are synthetic precursors of amphetamine-like drugs, has been performed using Raman spectroscopy with conformational analysis being used to confirm the assignment of Raman bands.[12] The results of this work suggest that future identification of such precursors will be rapid and accurate. This will mean that the composition of seized illicit samples of drugs can be identified and these could possibly be linked to clandestine laboratories.

Quantifying the drug content of a street sample by Raman spectroscopy can be difficult because of the range of possible adulterants, but is potentially much quicker than chromatography-based methods and is non-destructive. A Raman spectroscopic method for determining amphetamine content in street-seized samples has been developed which involves dissolving the samples in an acidic solution containing sodium dihydrogen phosphate as the internal standard.[13] The method, which works even if the sample contains unknown adulterants and impurities, compares favourably to gas chromatography and is very rapid; results are usually obtained within 1 min. Quantification, which is accurate enough for routine forensic analysis, can be performed by either a traditional calibration method or by using principal component analysis (PCA) and partial least squares (PLS) methods.

Similarly by dissolving samples of 'crystal meth' (mixtures of methyl sulfone (MS) and methamphetamine (MA)) in water and obtaining Raman spectra it is possible to get an indication of the composition of the mixture in minutes without the need for separation.[14] This is achieved by comparison to mixtures of known composition of MS and MA. The Raman spectrum of MA is much weaker than that of MS and for this reason it can be harder to detect at low concentrations. The technique has also been used in a semi-quantitative way to analyse MA in these samples. The ratio of MA : MS at which equal peak heights are observed is approximately 68 : 32. It may be possible to determine a more precise mathematical relationship between the relative peak heights in mixtures which in future would allow for more accurate quantification.

Surface enhancement is a well-known method of increasing the sensitivity of Raman spectroscopy. In surface enhanced Raman spectroscopy (SERS) the analyte is adsorbed on an enhancing medium, normally a colloidal metal suspension (typically gold or silver) or a roughened electrode giving an enhancement of up to 10$^6$ in Raman scattering efficiency. Note however that a roughened surface is not an absolute requirement.[15] When SERS is utilised, band intensities decrease as the vibrational frequency increases meaning that C-H stretches are usually weak. In addition, selection rules are relaxed meaning that Raman bands appear that would normally be forbidden.[16] Furthermore, in many cases, fluorescence is almost completely quenched.

SERS using a matrix-stabilised silver halide dispersion has been demonstrated as an effective method of identifying a range of seized amphetamine powders and ecstasy tablets.[17] The method established was suitable for the high throughput that may be required by a forensic laboratory. Samples were extracted into cyclohexane which was found to extract the amine drug compounds leaving the other excipients in the residue. Many of the tablets examined contained food colours that were likely to interfere spectroscopically; however, these components did not migrate into the cyclohexane phase. In order to compare the obtained spectra, they were divided into 10 regions and the relative contributions of each segment calculated. The results obtained showed that the active ingredient of the drug was successfully detected even in the presence of other excipients.

Colloidal suspensions of gold and silver have been used for the detection of amphetamine sulfate.[18] Colloids are an attractive substrate for this application as they are relatively cheap and provide a fresh surface for each analysis thereby reducing contamination, which can be a problem due to high sensitivity. In particular, identification and semi-quantitative estimation of amphetamine sulfate can be made using suspended colloid and an aggregating agent. Gold colloids, which were more effective than silver at detecting low levels of amphetamine, were able to detect concentrations of 10$^{-5}$ mol dm$^{-3}$ and had the advantage of a better signal to noise ratio. The choice of aggregating agent was important and it is suggested that adsorption of the amphetamine and the aggregation process can in some cases interfere making acquisition of the spectrum more difficult.

An interesting development has been on-tablet SERS to enhance the signal from a low concentration drug.[19] Some ecstasy-type compounds are potent at significantly lower doses. 2,5-dimethoxy-4-bromoamphetamine (DOB) is often present in tablets in sub milligram quantities compared with MDMA in the range 50–100 mg although recent studies suggest that the MDMA content is now typically in the region of 10–30 mg. This means that spot testing for DOB is not likely to be successful, but detection is important as the chemical is active at concentrations as low as 0.2 mg. Also there is a long delay between consumption and effect which increases the chance of accidental overdoses. Once the silver colloid is applied there is a differential enhancement of the Raman signal from the DOB, or other amphetamines present, because these compounds spontaneously adsorb to the silver nano-particles whereas other excipients such as lactose or cellulose do not. Model tablets containing lactose and DOB at concentrations ranging from 1 mg down to 15 μg were successfully tested for DOB. However, due to the low levels of DOB usually present in seized ecstasy tablets SERS will not be suitable for its detection in the presence of MDMA at much higher levels. This is because although the signals from both compounds will be enhanced, the enhancement of the MDMA at a much higher

concentration will produce a signal that drowns out the relatively weak signal from the DOB.

In a similar manner to the identification of amphetamines, Raman spectroscopy has been used to identify and quantify cocaine samples. NIR (785 nm) excitation has been used to obtain Raman spectra from solid mixtures containing cocaine, caffeine, and glucose (9.8–80.6% by weight cocaine).[20] Quantitative calibration models were generated using PLS algorithms. Quantification by Raman spectroscopy of seized drugs is problematic due to the presence of unknown excipients which may fluoresce making quantification impossible. The other problem that occurs when excipients present have very strong Raman signals, compared with the signals from the drug, is that the signals from the drug can be masked. PLS, after suitable calibration, was found to accurately determine the concentration of cocaine in a three-component mixture. However, it was also found that when the caffeine concentration was high (50%) some of the cocaine bands were difficult to identify.

Raman spectroscopy can readily discriminate between cocaine hydrochloride and freebase cocaine (crack) and can identify *in situ* drugs separated by thin-layer chromatography (TLC).[21,22] SERS data for cocaine in solution using colloidal silver has been reported. It was found that the two forms of cocaine were easily distinguished even in the presence of other excipients.[21,22] Spectra from seized samples were obtained from within plastic containers without interference. Adulterants such as lidocaine or benzocaine, common cutting agents for cocaine, did not hinder the detection process. More complex mixtures were analysed after separation using TLC with spectra being obtained directly from the TLC plates after the addition of deionised water to prevent the laser burning the TLC plate. SERS spectra were also obtained from lower concentrations of cocaine solution and initial results indicated that the technique may be useful for toxicological samples.

In the case of cocaine hydrochloride, Kerr gated fluorescence rejection Raman spectroscopy has been shown to be very effective in the analysis of street samples. However, the technique is relatively expensive and not portable.[23] The Kerr gate comprises of two cross polarisers and a Kerr medium ($CS_2$). When the gate is closed, the light collected from the sample is blocked by the polarisers. A pulse opens the gate for a brief time when the Raman spectrum is collected. The gate, however, remains closed for the time in which the main body of fluorescence occurs. By using this method it is possible to discriminate between the Raman signals and the interfering background fluorescence.

NIR-FT Raman has been utilised for the identification and quantification of alkaloids in poppy capsules without interference from fluorescence or any sample preparation.[24] ATR-IR was also investigated, but this suffered from problems associated with strong absorption bands from water which overlapped with key bands from the alkaloids. It was also possible to determine whether there was a high or low alkaloid content in plants.

Considerable progress has been made in the analysis of narcotics mixed with common cutting agents. For example, cocaine, heroin, and MDMA dispersed in solid dilutants of different concentrations have been analysed using NIR (785 nm excitation) micro-Raman spectroscopy.[25] The dilutants investigated were foodstuffs (flour, baby milk formula), sugars (glucose, lactose, maltose, mannitol), and inorganic materials (talc powder, $NaHCO_3$, $MgSO_4.7H_2O$). In most cases it was possible to detect the presence of drugs at levels down to 10% by weight. The detection sensitivity of the Raman technique was found to be dependent on a number of factors, such as the scattering cross-sections of drug and dilutant,

fluorescence of matrix or drug, complexity of dilutant Raman spectrum, and spectrometer resolution. Raman spectra from a series of 20 mixtures of cocaine and glucose (0–100% by weight cocaine) were collected and analysed using multivariate analysis methods. An accurate prediction model was generated using a PLS algorithm that can predict the concentration of cocaine in solid glucose from a single Raman spectrum with a root mean standard error of prediction of 2.3%.

In a related study PCA was employed to classify the samples according to narcotic type.[26,27] The best sample discrimination was obtained by using the first derivative of the Raman spectra. Furthermore, by restricting the spectral variables for PCA to 2 or 3% of the original spectral data according to the most intense peaks in the Raman spectrum of the pure narcotic, a rapid discrimination method for classifying samples according to narcotic type resulted. This method allowed for the easy discrimination between cocaine, heroin, and MDMA mixtures even when the Raman spectra were complex or very similar. Cocaine and MDMA being moderately strong Raman scatterers were well discriminated. However, the weaker scatterer, heroin, was not discriminated as successfully. This was due to the presence of strong Raman bands in other excipients that overlapped with and masked bands from the drug itself. An additional observation made was that prolonged storage of hydrochloride salts of the drug samples with $NaHCO_3$ may result in reactions creating different derivatives or causing decomposition. In one case, a sample of cocaine HCl was found to have been converted to the free base crack cocaine.

Using PCA, it is possible to resolve the spectral differences between benzocaine, lidocaine, isoxsuprine, and norephedrine and correctly classify them 100% of the time.[28] Mixtures including up to three cutting agents were prepared with drug concentrations ranging from 10 to 100%. Optimal pre-processing for the data set included truncating, Savitzky-Golay smoothing, normalisation, differentiating, and mean centring.

In recent years, portable Raman spectrometers have become available for in-field applications. A recent study has used two commercially available Raman spectrometers in order to detect street samples of cocaine, ecstasy, and amphetamine *in situ* in an international airport arrivals area.[29] Spectra were obtained and identified within 30 s or less without requiring the sample to be removed from its container. This reduces the potential for contamination and also has the advantage that the operator does not come into contact with an unknown substance that could possibly be harmful. In most cases, high quality spectra were obtained with high throughput of samples, however, some samples did prove problematic due to fluorescence from cutting agents.

The analysis of street samples of cocaine hydrochloride, heroin, MDMA, cannabis, cocaine free base, and amphetamine using two NIR laser excitation wavelengths (785 and 1064 nm) has shown that 1064 nm is favourable.[30] The use of NIR laser excitation is attractive as this lower energy radiation is less likely to cause molecules of the drug or cutting agents present to fluoresce. NIR laser excitation does, however, have a disadvantage. The Raman intensity is inversely proportional to the fourth power of the laser wavelength and hence is weaker than when using ultraviolet or visible excitation. This also means that the acquisition times are increased. Portable Raman systems have a reduced spectral range; however, the range is more than adequate for the purpose of spectral identification of drug samples. Portable systems also have a slight broadening of Raman bands but do not lose spectral detail. The data obtained from the 1064 nm excitation was far superior, making the identification of the drug easier. Also it

was found that no meaningful Raman spectra were obtained using 785 nm excitation for both heroin and cannabis, thus making this wavelength of excitation unsuitable for these samples. There is a problem with using 1064 nm for *in situ* analysis as all current portable systems are dispersive based with most using 785 nm excitation. It is suggested that dispersive systems using 900–1100 nm excitation may offer a solution to this problem.

## Detection of drugs in drinks

Raman spectroscopy is a very attractive technique for detecting drugs in drinks. Not only is it non-destructive and quick, but it is also possible to record spectra through plastic and glass containers negating the need to open sealed bottles or bags. Importantly, compared with IR spectroscopy, the low Raman scattering of water means there is little interference from the solvent. The analysis of cocaine in alcoholic drinks has been undertaken in the fight against smuggling, while the analysis of gamma-hydroxybutyric acid (GHB) in liquids is of interest in the prevention of drug-facilitated sexual assaults.

Alcoholic drinks such as rum have been used to smuggle cocaine into the UK; this has recently been highlighted by the death of an innocent victim who drank from a bottle of adulterant rum, which was subsequently found to contain 246 g of cocaine.[31] The ability of smugglers to conceal such a large quantity in a single bottle, which could be hidden in a genuine consignment of drink bottles makes detection difficult without opening each individual bottle. Displaced Raman spectroscopy, a variant of spatially offset Raman spectroscopy, can detect cocaine dissolved in rum contained in transparent bottles with an estimated detection limit of 9 g per 0.7 L which is significantly higher than the concentrations expected to be encountered in samples seized by customs and other agencies.[32] This form of Raman spectroscopy has the advantage that any interfering Raman and fluorescence emissions from the bottle are suppressed. Fluorescence can be particularly severe with coloured bottles (e.g. brown or green) using conventional Raman spectroscopy. If a sample produced a spectrum that was highly fluorescent it may suggest suspicious content, perhaps from a cutting agent, as rum itself is not fluorescent.

Gamma-hydroxybutyric acid (GHB), a central nervous system depressant, is used recreationally and has been associated with drug-facilitated sexual assaults. In the UK it is a Class C drug of abuse. GHB is normally administered via alcoholic drinks as this increases its sedative effects. A detailed study has examined its detection in spiked drinks in a variety of containers such as glass and plastic vials and also plastic bags using bench-top and portable Raman spectrometers.[33] It was found that the limit of detection of both GHB and GBL (the corresponding lactone gamma-butyrolactone) using either bench-top or portable systems is lower than the common dosage level. It was important to detect both GHB and GBL as the compounds undergo inter-conversion in solution. Band broadening was observed in the spectra of GHB in solution due to extensive hydrogen bonding of GHB in water.

## Detection of drugs on clothing

Two recent studies have investigated the detection of drugs on clothing fibres by Raman spectroscopy.[34,35] Pure and seized samples of cocaine hydrochloride, MDMA, ketamine and amphetamine can readily be detected on a range of natural,

synthetic, and dyed textiles in a range of colours from white to black. Care needs to taken to focus on the drug particle to avoid background spectra and fluorescence from the textile fibres. This can be achieved with normal or confocal Raman microscopy and the spectra can be obtained after the fibre has been recovered with an adhesive lifter and from within evidence bags. If any bands associated with the fibre are present, they can be easily removed with spectral subtraction. These results could be used to establish links between drugs of abuse and individuals suspected of being involved in the drug trade or of drug abuse. However, it is important to remember when dealing with trace residues that, in the absence of other evidence, their presence may not always indicate criminal activity. These studies were based on samples of powdered drug and, as MDMA are usually supplied in tablet form, further work is needed in order to fully understand how tablets will transfer trace amounts of drugs to clothing.

Recently it has been demonstrated that Raman spectroscopy can detect cocaine hydrochloride that has been impregnated into clothing, a technique used by smugglers who pour cocaine solutions onto clothing and then allow the solvent to evaporate.[36]

## Detection of drugs in fingerprints

Drugs of abuse, which may be present on individual's fingers due to handling, can be deposited in latent fingerprints. Recovery and identification of the fingerprints coupled with characterisation of an embedded substance offers the possibility of associating a suspect with a controlled substance, but again remembering that such residues may arise by innocent transfer. Raman spectroscopy can identify codeine phosphate, cocaine hydrochloride, amphetamine sulphate, barbital, nitrazepam, GHB, MDMA, and ketamine particles in fingerprints as well as a range of over the counter (OTC) drugs and common cutting agents.[37,38] The non-destructive nature of Raman spectroscopy means that the fingerprint can still be used in the subsequent identification of the individual.

Usually a latent fingerprint needs to be enhanced to make it visible. Studies have shown that these substances can still be detected in fingerprints that have been cyanoacrylate-fumed or developed with fingerprint powders.[39] The presence of additional material in the fingerprints developed with powders caused an increase in the time taken to locate particles of drugs; typically a 4- or 5-fold increase in time. In fingerprints developed with cyanoacrylate, unreacted monomer particles or other impurities arising from cyanoacrylate may hinder the unambiguous identification of drugs of abuse.[40]

Some samples were moderately fluorescent; however, this was often overcome by photobleaching typically for 5–30 min. Fluorescence is often attributed to the sebum in the fingerprint itself and an interesting observation is that fingerprints developed with powders showed a reduction in this fluorescence.[41] It is suggested that as the fingerprint powders are designed to adhere to the sebum content of the fingerprint, then this obscures the sebum from the laser and so the background fluorescence is diminished or even removed completely. The detection process was also not compromised by recovering the fingerprint with lifting tapes or by recording the spectrum through a polythene evidence bag. Any interfering bands associated with either the lifting tape or the evidence bag can be removed by spectral subtraction. It was noted that the location of drugs within a

fingerprint could be potentially determined by the use of Raman mapping or imaging.

## Detection of drugs on fingernails

Contamination of a fingernail may result from the handling or abuse of a drug and hence its detection could possibly establish a link between a suspect and a substance. Spectra can be readily obtained using a 785 nm NIR diode laser from paracetamol, pure cocaine hydrochloride, and street cocaine crystals on human nails.[42] Spectra can also be obtained if the sample has been embedded in the nail when the rubbing of finely powdered drug particles into the nail has occurred. Use of confocal microscopy allows spectra or Raman point maps to be obtained from under a layer of nail varnish. The advantage of confocal Raman spectroscopy is being able to focus the beam below the surface of the nail varnish but above the nail itself thus focusing directly on the drug particle itself. Interference from the nail, including background fluorescence, was avoided by careful focusing of the laser beam.

## Detection of drugs on banknotes

Measurement of illicit drugs on paper currency is of interest for evidentiary purposes in legal cases involving the drug trade. Current methods, primarily based on mass spectrometry, can be destructive and prevent re-analysis of the evidence. Raman microspectroscopy can collect spectra from individual crystals on the surface of paper currency. As the technique is non-destructive, the banknotes can be re-examined a number of times and in different laboratories if required. One series of studies involved mixtures of isoxsuprine and norephedrine, which are non-pharmacologically active drug surrogates, as well as lidocaine and benzocaine, common excipients in street drugs, which were doped in small quantities onto US currency.[43,44] Significant fluorescence interference resulted from the underlying dollar bill. Photobleaching and background subtraction, were both effective at reducing the fluorescence background. A quantitative study indicated that the fluorescence background from the dark green and gray areas of the dollar bill is much weaker than from the light green or white areas. A method for determining the percent composition of individual components in heterogeneous mixtures has been developed by systematically sampling the surface of the dollar bill. Results are accurate to within a few percent, although the method is quite time consuming.

## Detecting narcotic usage

Raman spectroscopy has been used to detect drugs in human blood or urine.[45] The potential for the detection of drugs of abuse such as ethanol and codeine was investigated by studying the samples which were dissolved in water. The errors of the Raman tests for acetaminophen and ethanol were lower than their toxic levels in serum, but the sensitivity of codeine failed to reach its toxic level. The detection of protein, albumin, triglyceride, and glucose in human sera was attempted with NIR-Raman spectroscopy and PLS was used to estimate their concentrations. The errors in the results varied between 1% and 10% which is acceptable for clinical diagnosis.[45]

Surface enhanced Raman spectroscopic analysis of saliva can detect usage of heroin, methamphetamine and methadone.[46] Saliva samples from 44 narcotic users and 52 non-users were examined using SERS and the samples from the users showed a characteristic band at 1030 cm$^{-1}$ that was not observed in the non-users. Thus it is possible to rapidly identify users and non-users with this technique. The detection in saliva is important as it is non-invasive and sample collection is easier than for urine samples.

Raman spectroscopy has been utilised to study the interactions of cocaine and opiates at a molecular level.[47] Raman spectra were obtained from morphine, both basic and protonated forms, heroin and cocaine. Spectra were also obtained from mixtures of cocaine-heroin and cocaine-morphine, both basic and protonated. The results obtained indicated a clear interaction between cocaine and morphine that was not observed between cocaine and heroin. In the 50 cm$^{-1}$ to 1750 cm$^{-1}$ range, the Raman spectrum of morphine was strongly affected by the presence of cocaine. In the range 2800 cm$^{-1}$ to 3200 cm$^{-1}$ a number of new features was observed and some of the bands associated with the individual drugs spectra disappeared or were greatly diminished. This work has increased knowledge of cocaine-opioid interactions at a molecular level and may lead to effective therapies for the treatment of co-drug abuse.

## Conclusions

Significant progress has been made in the application of Raman spectroscopy to drug analysis in recent years. The technique is capable of identification of trace evidence and quantification of bulk samples in a rapid and non-destructive manner. Drugs can be detected and identified in a wide range of forensically important environments. Advances in instrument design will increasing see Raman spectroscopy move out of the specialised laboratory and into the field with the use of portable systems. Automated database recognition algorithms to identify drugs will assist the non-spectroscopist in data evaluation.

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