Raman Spectroscopy – Basic Principle, Instrumentation And Selected Applications For The Characterization of Drugs of Abuse

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Abstract- *This review gives an overview of the developments in the analysis of drugs of abuse and other illicit substances by Raman spectroscopy for forensic purpose. The review covers the brief overview of basic principle and instrumentation of Raman spectroscopy along with selected and recent applications for characterization of drugs of abuse using this technique. These applications show the potential value of Raman spectroscopy in the qualitative and quantitative analysis of trace amounts of drugs of abuse and other illicit substances on different matrices such as cloth, currency notes, fiber etc., without extensive sample preparation in a non-destructive manner.*

Keywords- Raman spectroscopy ;Morphine ; Amphetamine; Barbiturates; Abused substances

I. INTRODUCTION

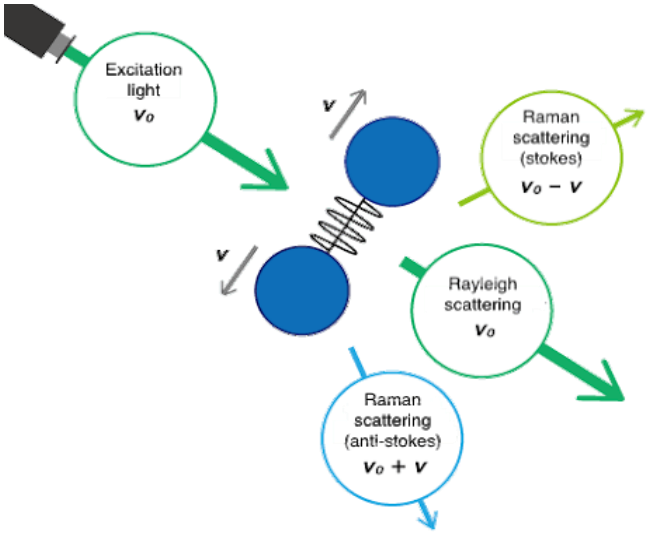
Spectroscopy is the study of interaction of electromagnetic radiation with matter. Spectroscopic methods can be based on phenomena of emission, absorption, fluorescence or scattering.1, 3 Different spectroscopic methods are frequently used for the characterization of a wide range of samples of forensic interest. These methods are used for qualitative and quantitative analysis of sample/s. The qualitative analysis is performed to establish the identity of sample while quantitative analysis is performed to estimate the concentration of analyte in sample.1 Some of the spectroscopic methods (e.g. UV–Vis Spectrophotometry) are used as a screening method since it gives the tentative identification of sample and are not specific in nature while other spectroscopic methods (e.g. Infrared Spectroscopy and Mass Spectrometry) are used as a confirmatory method since they give the reliable identity of sample and are specific in nature.3, 4, 10

Raman spectroscopy was named in the honor of its inventor, C.V. Raman, who, along with K.S. Krishnan, published the first paper on this technique.2 Raman spectroscopy (RS) is a versatile method for analysis of a wide range of forensic samples. It resolves most of limitations of other spectroscopic techniques. It can be used for both qualitative as well as quantitative purpose. Qualitative analysis can be performed by measuring the frequency of scattered radiations while quantitative analysis can be performed by measuring the intensity of scattered radiations.3, 4

A review unfolding the utility of Raman spectroscopy in the forensic analysis of different types of inks in questioned documents is available.5 A review presenting a recent progress in characterizing trace amounts of body fluids using Raman spectroscopy is available.6 A recent review describing the application of infrared and Raman spectroscopy to the identification of explosives is also available.7 Infrared spectroscopy is a complementary technique to Raman spectroscopy and is discussed in many cases for completeness. This article discusses the basic principle and instrumentation of Raman spectroscopy. The chief purpose of this review is to briefly present an overview of some important recent and selected applications of Raman spectroscopy in the analysis of drugs of abuse and related illicit compounds.

II. BASIC PRINCIPLES AND INSTRUMENTATION

Raman spectroscopy is a popular technique for the analysis of molecular structure and is considered complementary to infrared spectroscopy. Raman spectroscopy is based on the Raman effect, which was first identified by the Indian physicist Chandrasekhara Venkata Raman in 1928. The Raman effect is based on scattering of light, which includes both elastic (Rayleigh) scattering at the same wavelength as the incident light, and inelastic (Raman) scattering at different wavelengths, due to molecular vibrations. Raman scattering is about a million times less intense than Rayleigh scattering. Therefore, to obtain Raman spectra, it is necessary to prevent Rayleigh scattering from overpowering the weaker Raman scattering.



Raman spectra are measured by exciting a sample using a high-intensity laser beam, with the resulting scattered light being passed through a spectrometer. The Raman shift is the energy difference between the incident light and the scattered light. In the resulting spectrum, the vertical axis is the intensity of the scattered light and the horizontal axis is the wavenumber of the Raman shift (cm-1).

In Raman spectroscopy, sample is illuminated with a monochromatic laser beam which interacts with the molecules of sample and originates a scattered light. The scattered light having a frequency different from that of incident light (inelastic scattering) is used to construct a Raman spectrum. Raman spectra arise due to inelastic collision between incident monochromatic radiation and molecules of sample. When a monochromatic radiation strikes at sample, it scatters in all directions after its interaction with sample molecules. Much of this scattered radiation has a frequency which is equal to frequency of incident radiation and constitutes Rayleigh scattering. Only a small fraction of scattered radiation has a frequency different from frequency of incident radiation and constitutes Raman scattering. When the frequency of incident radiation is higher than frequency of scattered radiation, Stokes lines appear in Raman spectrum. But when the frequency of incident radiation is lower than frequency of scattered radiation, anti-Stokes lines appear in Raman spectrum. Scattered radiation is usually measured at right angle to incident radiation.3, 4, 9

Stokes shifted Raman bands involve the transitions from lower to higher energy vibrational levels and therefore, Stokes bands are more intense than anti-Stokes bands and hence are measured in conventional Raman spectroscopy3, 4, 9 while anti-Stokes bands are measured with fluorescing samples because fluorescence causes interference with Stokes bands.3 The magnitude of Raman shifts does not depend on wavelength of incident radiation.3 Raman scattering depends on wavelength of incident radiation.1 A change in polarizability during molecular vibration is an essential requirement to obtain Raman spectrum of sample. Since Raman scattering due to water is low, water is an ideal solvent for dissolving samples. Glass can be used for optical components (mirror, lens, sample cell) in Raman spectrophotometer.3, 4, 9

A Raman spectrum is presented as an intensity-versus-wavelength shift.1 Raman spectra can be recorded over a range of 4000–10 cm−1(10). However, Raman active normal modes of vibration of organic molecules occur in the range of 4000–400 Δcm−1. Depending on spectrophotometer's design and optical components, typical Raman spectra cover the wavenumber region between 400–5 Δcm−1 and 4000–3800 Δcm−1(8). A Raman spectrum is significantly simpler than their Infrared (IR) counterparts because in normal Raman overtones, combination and difference bands are rare.1

Raman spectrophotometers can be dispersive or non-dispersive. Dispersive Raman spectrophotometer use prism or grating while non-dispersive Raman spectrophotometer uses an interferometer such as Michelson interferometer in Fourier Transform Raman spectrophotometer.1

Mercury arc lamp was used as light source in Raman spectrophotometers in early days. 435.8 nm line of coiled low-pressure mercury arc lamp was used as light source until 1960's.1, 3 Laser sources became available in late 1960's and completely replaced the mercury lamp.1 These laser sources provide stable and intense beam of radiation. Wide range of lasers such as Argon ion laser (488 and 514.5 nm), Krypton ion laser (530.9 and 647.1 nm), Helium–Neon (He–Ne) (632.8 nm), Near Infrared (IR) diode lasers (785 and 830 nm), Neodymium–Yttrium Aluminum Garnet (Nd:YAG) and Neodymium–Yttrium Ortho-Vanadate (Nd:YVO4) (1064 nm) and frequency doubled Nd:YAG and Nd:YVO4 diode lasers (532 nm) can be used as light source in Raman spectrophotometers.8 Short wavelength sources such as argon ion and krypton ion lasers can produce significant fluorescence and cause photodecomposition of the sample. However, long wavelength sources such as diode or Nd:YAG lasers can be operated at much higher power without causing photodecomposition of sample and eliminates or reduces fluorescence in most cases.3

Band pass filters are used to isolate a single laser beam. A combination of notch filter and high quality grating monochromator is most frequently used in dispersive

instruments. Double or even triple grating monochromators, super notch filters, rejection filters, holographic notch or edge filters and holographic filters are used to separate relatively weak Raman lines from intense Rayleigh scattered radiations.1, 3, 11, 12

Thermoelectrically cooled photomultiplier tubes and photodiode array detectors were used in early models of dispersive Raman spectrophotometers.3 Advances in instrumentation and technology replace these detectors with more sensitive charge transfer devices (CTDs) such as charge-coupled devices (CCDs) and charge-injection devices (CIDs). These devices act as a detector and used in the form of arrays. In CTD's arrays, photosite converts the incoming optical signal into charge which is integrated and transferred to readout devices.1 Multichannel CCD detectors are used with laser wavelengths of less than 1 μm while single element low band-gap semiconductor such as Germanium (Ge) or Indium–Gallium–Arsenic (InGaAs) detectors are used with laser wavelengths of greater than 1 μm.11, 12

Commercial Fourier Transform-Raman spectrophotometers (FT-Raman) were introduced in late 1980's to improve the detection system capable of overcoming the limitations of CCD and other detectors for operating in the near-IR region when using 1064 nm laser excitation.11 FT-Raman spectrophotometer uses a Michelson interferometer and continuous wave laser such as Nd–YAG which emits the radiation at 1064 nm. InGaAs and germanium (Ge) detectors are operated at cryogenic temperatures in order to reduce noise and thus raise the signal-to-noise ratio.3 Cryogenic temperature is a temperature at which molecular motion comes as close as theoretically possible to ceasing completely. At cryogenic temperature, materials are as close to a static and highly ordered state as is possible.39 Since water absorbs in the 1000 nm region, aqueous samples cannot be analyzed by FT-Raman spectrophotometer.1

Depending on the area of use, Raman spectrophotometers can be categorized into two broad classes: lab based spectrophotometers and in-field, in-situ or down-field use Raman spectrophotometers which include portable and hand-held devices or remote or stand-off systems.8 The basic principle is same in each case and these systems are differentiated by versatility of an instrument and size and relative cost of its components. More compact components are used in on-site Raman spectrophotometers. Benchtop, handheld, portable, remote or stand-off Raman spectrophotometers are available for on-site analysis and research purpose.8

Low sensitivity due to weak Raman scattering is the major problem associated with this technique. However, sensitivity can be enhanced using Resonance Raman Spectroscopy (RRS) and Surface Enhanced Raman Spectroscopy (SERS). In RRS, frequency of incident radiation matches with an electronic transition of molecule and as a result of this match, much more intense Raman spectrum is obtained.13 SERS was first reported in 1974 by Fleishman and colleagues.14 SERS is a modified technique in which sample is adsorbed on a colloidal metallic surface (silver, gold or copper) and thereby improves the intensity of Raman signals and also quenches the fluorescence caused by cutting agents, diluents and matrices.1, 13 The combination of RRS and SERS techniques (i.e. Surface Enhanced Resonance Raman spectroscopy (SERRS) can amplify the sensitivity up to ten orders of magnitude as compared to Raman spectroscopy.15 In conventional Raman spectroscopy, concentration of solutions must be high. Fluorescence can also be reduced by exciting the sample with near IR laser such as Nd–YAG at 1064 nm.1

First Raman microspectrophotometer was developed in France in 1976. In Raman microspectroscopy, Raman spectrophotometer is interfaced to an optical microscope which enables both visual and spectroscopic examinations as either as single point, mapping or imaging measurements. Microscope is used to focus the laser beam onto the sample. Raman microspectrophotometry enables the visual inspection of sample and facilitates spectroscopic analysis of a limited amount of sample or a selected small region within a sample. Sample size of about 1 × 1 × 5 μm can be examined by Raman microspectrophotometer equipped with short wavelength visible laser.3, 8, 16 Coupling of Raman spectrophotometer to microscope and advent of portable and handheld Raman spectrometers improve the application space of this technique. In-situ analysis is possible nowadays without any sample pretreatment. Portable Raman spectrophotometers are useful for the examination of large or very fragile objects and artefacts.8

The incorporation of short wavelength lasers in Raman spectrophotometers opens the doors for use of telecommunications-type optical fibers such as remote-fiber-optic probes which can be operated over long distances (>10 m in some instances) and are well suited for in-situ or on-site analysis of samples. These fiber optic probes can also be used to record the Raman spectra in locations remote from the sample site and thereby prevent the exposure of investigator to hazardous environment.3, 8

3.Selected applications for the analysis of drugs of abuseNumbers of papers describing the utility of Raman

spectroscopy are available in the literature. It is not possible to include all these papers in this review. Therefore, this article has selected a number of papers describing the recent applications of Raman spectroscopy in analyzing drugs of abuse.

Raman spectrophotometric method was presented to analyzed eight barbiturates (phenobarbital, pentobarbital, barbital, secobarbital, amobarbital, hexobarbital, butabarbital, mephobarbital) and three sodium salt analogs.17 Characteristic Raman frequencies of carbonyl stretching and ring breathing vibrations of the pyrimidine ring were used to identify all barbituric acids and their salts. Bands arises due to carbonyl stretching vibrations of pyrimidine ring were observed at 1692 ± 6 Δcm−1 and 1737 ± 8 Δcm−1 in free acids. Strong band at 629 ± 8 Δcm−1 (for free acids) and 652 ± 4 Δcm−1 (for sodium salts) was assigned to the symmetric breathing of the pyrimidine ring. Specific band locations were utilized to distinguish most barbiturates. 488 nm argon ion laser was used with 300 mW and 60 mW power at sample. Individual compounds were characterized by unique vibrations of substituents. Only secobarbital possesses an alkyl group containing a double bond and showed characteristic, well resolved intense bands at 653 and 1640 cm−1. Phenobarbital possesses a monosubstituted phenyl group and showed characteristic bands at 620, 1002, 1039, 1585 and 1597 Δcm−1. Methyl group at 1-postion was used to distinguish mephobarbital from phenobarbital. A very strong band at 652 ± 4 Δcm−1 was used to distinguish barbiturate salts from free acids. A weak band at 1585 ± 15 Δcm−1 was present in all spectra of sodium salts while it was absent in corresponding free acid spectra and was useful in differentiating salt form from acid form. Intense characteristic bands due to substituents at 5-position on the pyrimidine ring were used to distinguish between compounds such as phenobarbital and secobarbital or pentobarbital. Method presents a reliable discrimination between these drugs.17

A method of using Fourier transform-Raman and infrared spectroscopy to characterize benzodiazepines (delorazepam, fludiazepam, flurazepam, tetrazepam) was described.18 These drugs could be distinguished from diazepam by substituents at positions 1 and 5 of the diazepine ring. These methods could be used to discriminate benzodiazepines.18

A rapid method for in-situ identification of free base cocaine and cocaine hydrochloride was proposed.19 The analysis was performed using portable Raman spectrophotometer equipped with a fiber-optic Raman probe. The potential utility of Surface Enhanced Raman Spectroscopy (SERS) in toxicological drug screening and preliminary SERS data for cocaine in solution using colloidal silver was also presented. A significant difference was observed between spectra of cocaine hydrochloride and free base cocaine. Raman spectra of common cutting agents and impurities such as benzocaine and lidocaine were easily distinguishable from free base cocaine and cocaine hydrochloride. Method could be used to identify drugs in transparent plastic evidence containers and thus maintain the chain of custody.19

A method of using Raman spectroscopy for the determination of drug content of street samples of amphetamine was described.20 Samples were dissolved in an acidic solution of sodium dihydrogen phosphate (internal standard). Two different methods were used for quantification purposes: (1) relative peak heights of characteristic signals of amphetamine and internal standard, (2) multivariate calibration by partial least square (PLS) based on second derivative of spectra. Peak height ratio [h(amphetamine at 994 cm−1)/h(internal standard at 880 cm−1)] was calculated, where h denotes the peak height of amphetamine and internal standard respectively. 830 nm laser with power of 100 mW was used. Diameter of measurement spot was 0.5 mm. Spectra were recorded in the range of 2000–0 cm−1. Region of 1300–630 cm−1 was used for PLS analysis. Pure compounds could not be used as standard samples for PLS analysis because they did not contain any impurities and therefore, their spectra lack information regarding impurities. Characteristic bands of amphetamine and internal standard were used for identification and quantification of amphetamine. Common diluents such as lactose, caffeine did not interfere with the determination of amphetamine. PLS results were independent of long storage time while the traditional peak height method depends on it. Storage time study showed a rise in the concentration of amphetamine with passage of time after 2 h. Authors recommended that sample should be analyzed before 2 h by using the traditional peak height method. The method is rapid and accurate for quantitative analysis of street samples containing illicit drugs, unknown impurities and adulterants.20

The modified surface enhanced Raman spectroscopic method was proposed to analyze seized tablets of 2,5-dimethoxy-4-bromoamphetamine (DOB).21 5 μl of centrifuged silver colloid and 5 μl of 1 mol/dm3 of sodium chloride solution were dispensed onto upper surface of tablets and 785 nm diode laser was directed onto treated area and spectra were recorded. Method improves the signal from low concentrations of DOB and detection limit was 15 μg. Strongest DOB band was observed at 706 cm−1. The method permits the simple, rapid and accurate discrimination between low concentration DOB tablets and tablets with non-active constituents.21

The potential utility of Raman spectroscopy to detect the cocaine hydrochloride on human nail was described.22 An added difficulty in the analysis of drug crystals on nail surface due to the presence of nail varnish coating was reduced by employing confocal Raman spectroscopy. 785 nm NIR diode laser (5 μm spot diameter) was used to record Raman spectra of drug crystals on uncoated nail surface and under a coating of nail varnish. 50× objective lens was used. Spectra were recorded in the range of 100–3200 cm−1. Drug particles with an average size of 5–20 μm could be analyzed by this method. Fluorescence due to nail varnish was reduced by use of NIR laser. This method provides the discriminating potential of confocal Raman microscopy in the analysis of drug particles on uncoated nail surface and under a coating of nail varnish. Method permits the rapid identification of drug particles on nail surface and under a coating of nail varnish without any interference from nail or nail varnish.22

Displaced Raman spectroscopic method was developed to detect cocaine concealed within alcoholic beverages.23 830 nm diode laser was used with 250 mW power at sample. Diameter of laser spot was 1 mm and acquisition time for each spectrum was 1 second. Intensities of ethanol and cocaine bands were used to determine the relative concentration of cocaine in ethanol. Limit of detection was 9 g/0.7 L (0.04 moles/L). The method provides fast, noninvasive detection of concealed illicit compounds inside alcoholic beverages thus preventing drug trafficking more effectively.23

Raman spectroscopic method for rapid and in-situ identification of drugs of abuse in an airport environment was developed.24 Street samples of cocaine hydrochloride, 3,4-methylenedioxymethamphetamine (MDMA) and amphetamine sulfate of unknown composition were analyzed using portable Raman spectrophotometer equipped with 785 nm diode laser and thermoelectrically cooled charge coupled device (CCD) detector. Power of laser at sample was 50 mW. Method permits the fast and easy discrimination between these drugs in an airport environment and thus can be used as first pass screening technique in law enforcement applications.24

The application of Raman microscope for the detection of drugs of abuse (cocaine, amphetamine, ecstasy, ketamine) deposited in latent fingerprints after development with iron or aluminum based fingerprint powders and recovery with adhesive lifter and hinge lifters were described.25 A 632.8 nm laser beam from helium–neon laser with a power of 4 mW at sample was used. 50× objective lens was used to focus and analyzed drug particles. A liquid nitrogen cooled charge coupled device detection array was used. Particles with diameter in the range of 10–40 μm were analyzed. Spectra were recorded in the range of 3250–300 cm−1. Identification of these drugs was more complex with or in the presence of hinge lifters as these lifters exhibited strong Raman bands and therefore spectral subtraction was used to remove peaks due to hinge lifters. Detection process was not affected by application of powders, lifting process, evidence bag and identity of drugs could be established. Method was not suitable for in-situ detection of drugs of abuse deposited on fingerprint and on large items. However, powder dusting increases the analysis time, characteristic bands were used to discriminate these drugs by using this method. They also analyze these drugs of abuse on different wool, linen and cotton fibers in colors ranging from white to black after recovery with adhesive lifters and concluded that textile fibers, lifting process, adhesive lifters and evidence bags did not interfere with the identification of drug particles embedded in fibers.26

Raman spectroscopic method was developed to analyze and classify simulated street drug mixtures.27 Helium–neon laser and portable Raman spectrophotometer with 785 nm laser were used to analyze the drug samples. Principal component analysis (PCA) was used to resolve the spectral differences between lidocaine, norephedrine, benzocaine and isoxsuprine and rapidly and correctly classify them.27

The potential utility of Raman spectroscopy in the analysis of mixtures of “crystal meth” (usually comprised of methyl sulfone and methamphetamine) was discussed.28 Samples were dissolved in water and spectra were recorded in the range of 2000–100 cm−1 with 785 nm laser. Semiquantitative determination of methamphetamine concentrations in such exhibits could be performed by comparing spectra of such samples with spectra of known concentration of methamphetamine and methyl sulfone. Raman spectra of aqueous solution of methamphetamine and methyl sulfone were relatively simple. Most intense bands of methyl sulfone and methamphetamine were 703 and 1004 cm−1. Methamphetamine was difficult to detect at low concentrations (<20%) because Raman bands of methamphetamine was weaker than equal concentration of methyl sulfone. Height of peak at 1004 cm−1 was used to distinguish methyl sulfone from mixture of methamphetamine and methyl sulfone (1:9). Methamphetamine possesses characteristic peaks at 1208, 826 and 748 cm−1 while N-isopropylbenzylamine hydrochloride (IBA) possesses characteristic peaks at 1216, 851, 784 and 748 cm−1. Peak shift was observed from 825 to 851 cm−1 as relative concentration of N-isopropylbenzylamine hydrochloride to methamphetamine increases. Method provides quick results without any requirement of separation of active component from matrix.28

The application of one benchtop and two portable Raman spectrophotometer for in-situ detection of cocaine hydrochloride in clothing was described.29 Spectra were recorded from undyed natural (wool, silk, cotton) and synthetic (polyester) fibers and dyed textiles impregnated with drug. A 785 nm laser from a high power NIR diode laser was used in benchtop Raman spectrophotometer. Spectral range and resolution of benchtop Raman spectrophotometer were 3200–100 cm−1 and 2 cm−1. A 785 nm laser from a diode laser with a power of 49 mW at sample was used in one portable Raman spectrophotometer. Spectral range and resolution of this instrument were 2100–100 cm−1 and 10 cm−1. A 785 nm laser from a diode laser with a power of 37 mW at sample was used in second portable Raman spectrophotometer. Spectral range and resolution of this instrument were 2000–200 cm−1 and 8 cm−1. Thermoelectrically cooled CCD detector was used in all instruments. Characteristic bands of cocaine hydrochloride were observed in spectra collected from cocaine impregnated with cotton, wool, silk, polyester and denim. Characteristic bands of cocaine hydrochloride were clearly observed irrespective of broad fluorescent background. Characteristic bands due to drugs were more intense than bands due to matrices. Spectral bands due to substrate and dye presented no difficulty in establishing the identity of drug. Method provides rapid, non destructive, non contacting identification of drugs on dyed and undyed, natural and synthetic fibers.29

A model based on Raman spectroscopic analysis of simulated illicit street drug samples followed by partial least square (PLS) regression for quantitative analysis was developed.30 A homebuilt Raman spectrophotometer equipped with rotating sample holder and 10 mW He–Ne laser was used to record the spectra of drug samples. Each drug sample contained one drug surrogate (isoxsuprine, norephedrine, benzocaine or lidocaine) and up to three different cutting agents (d-mannitol, α-lactose monohydrate, and methylsulfonyl methane, baking soda, cornstarch and procaine hydrochloride). Spectral pre-processing including smoothing, differentiation, mean-centering and auto-scaling was used to develop separate models for each drug surrogate. This method was developed to determine the amount of drug surrogate in the presence of up to three cutting agents. Method provides a rapid, hand-held, portable drug analysis system effective for on-site analysis of drugs of abuse.30

A sensitive and rapid Raman spectroscopic method to detect the presence of cocaine (0.5–10%w/v) in colored alcoholic solutions concealed in different colored containers was presented.31 Each sample was analyzed in brown and transparent glass vial, light and dark green glass bottles, purple and cream colored plastic bottles. Due to the fluorescence caused by green color, it was difficult to analyze samples in green glass containers with 785 nm laser but analysis could be made easy by using 1064 nm laser. Cocaine was identified at concentrations above 8%w/v in rum. Characteristic peaks of cocaine at 1730, 1603 and 1003 cm−1 were detected until 4%w/v with 1064 nm laser from FT-Raman spectrophotometer and 6%w/v with 785 nm laser from "Inspector Raman" and Renishaw RX210 Raman spectrophotometer. 785 nm laser was more effective than 1064 nm laser for analysis of samples through brown glass vials. Limit of detection was 1.55%. Method provides the rapid, non-contacting and non destructive detection of contraband drugs dissolved in carrier solutions smuggled through ports and airports.31

A method to enhance the SERS detection of MDMA by modifying the surface of metal colloids with self-assembled monolayers (SAM's) composed of ω-functionalized alkyl or aryl thiols was reported.32 Best results were observed for colloids modified with mixed SAM's of sodium mercaptopropanesulfonate (MPS) and benzyl mercaptan (BZM) in the ratio of 6:4. Mixed ω-functionalized thiols promote the adsorption of MDMA to silver colloids and thus improve detection limits (<50 ppm). Method improves the detection of poorly adsorbing target molecules on metal colloids as well as reduces the signals from interfering species present in sample.32

Surface enhanced Raman spectroscopic method for the identification of trace amounts of morphine, codeine and hydrocodone in their base form was discussed.33 785 and 633 nm lasers with a power of 100 mW and 20 mW at sample were used to record the spectra from 2 μl of drug solution. Intense peaks of hydrocodone at 640, 568, 583 and 615 cm−1 were used to discriminate it from morphine and codeine. Characteristic peaks at 889, 1035 and 1627 cm−1 were used to confirm the identification of morphine. Method provides the immediate identification of these prohibited substances without any fluorescence caused by cutting agents.33

The potential utility of confocal Raman microscopy for in-situ analysis of trace amounts of street samples of cocaine hydrochloride and MDMA on natural (wool, silk and cotton) and synthetic (polyester) textiles was discussed.34 785 nm near infrared diode laser and CCD detector were used to record the spectra in the range of 1800–100 cm−1 from drug particles with dimensions in the range of 5–15 μm. 50× objective lens was used to obtain laser spot diameter of 5 μm. Bands due to drugs were stronger than excipients. Bands due to excipients and fiber substrate did not interfere with the identification of drugs. Method permits rapid, non-invasive

detection of street drug particles embedded within highly fluorescent fiber substrate.34

Raman spectroscopic method for the rapid characterization of reference and seized samples of β-ketophenethylamine 'legal highs' (KP) of cathinone derivatives was described.35 A collimated laser beam (40 μm diameter) from 785 nm diode laser with power of 300 mW at sample was used to record Raman spectra. The 20× objective was used in microscope to focus the laser beam on sample. Another Raman spectrophotometer with 785 nm diode laser with a power of 100 mW at sample was also used. 100 μm spot was analyzed by this system. Characteristic changes associated with pattern of substitution on aromatic rings were noted in spectra. Creatine and taurine were used as bulking agents in β-ketophenethylamines while calcium carbonate, paracetamol and sucrose were used as contaminants in seized samples of β-ketophenethylamines.35

Infrared and confocal Raman microscopic method was presented to characterize and discriminate eight barbiturates (barbital, pentobarbital, butalbital, phenobarbital, amobarbital, secobarbital, pentothal, butabarbital) in powdered form.36 532 and 633 nm lasers were used to record Raman spectra in the range of 3500–100 cm−1 by confocal Raman microscope. A prominent peak at 653 cm−1 (due to symmetric breathing vibration of pyrimidine ring) was used to identify barbiturates. Peaks observed in 3100–2800 cm−1 region of spectra were used to distinguish pentobarbital from butalbital. The method was useful to discriminate barbiturates without any need for sample pretreatment and in very short time (30 s) and helpful for the determination of barbiturates in blood, saliva and urine.36

The utility of Raman spectroscopy as a rapid, non destructive, screening method for the presence of methamphetamine encountered in clandestine laboratory liquid samples was discussed.37 Methamphetamine solutions of varying concentrations (0.5–10%) in ethanol, diethyl ether and Coleman fuel were prepared and spectra were recorded in the range of 100–3410 cm−1 with 785 nm laser from near IR laser operated at 10 mW. Characteristic intense peak of methamphetamine at 1003 cm−1 was used as a concentration dependent peak. Abundance of several characteristic peaks (3057, 1604, 1583, 1003, 750, 620 cm−1) in spectra of methamphetamine solution increases with an increase in concentration of methamphetamine solution. Concentration dependent peak (1003 cm−1) was observed at and above 4% solution of methamphetamine. Method permits the analysis of samples through glass containers and thus prevents the unnecessary exposure of analyst to hazardous chemicals.37

Raman microscopic method for the identification of different drugs of abuse, metabolites, degradation products and common cutting agents (allobarbital, amobarbital, barbital, phenobarbital, pentobarbital, secobarbital, chlordiazepoxide, diazepam, flunitrazepam, nitrazepam, cannabidiol, cannabinol, cocaine, ecgonine, amphetamine sulfate, fenethylline, methylenedioxyethylamphetamine (MDEA), methylenedioxymethamphetamine (MDMA), methamphetamine, 6-monoacetylmorphine, acetylcodeine, heroin, morphine, papaverine, thebaine, caffeine, diphenhydramine, methaqualone, pemoline, procaine) was described.38 Confocal Raman spectroscopy method was used to analyze drug particles on the top of tapes, trapped between glass slides and tapes, and after folding and unfolding the tape in case of green tape. A collimated 532 nm laser beam (25 μm diameter) with a power of 10 mW at sample was used to record the spectra in the range of 1800–400 cm−1. 10× or 20× magnification was used depending on sample. However, different tapes did not interfere with the identification of drug particles, authors advocate the use of transparent tape due to visual detection of drug particles and folded transparent tape reduces the potential contamination of sample. The method permits the rapid identification of these drugs of abuse without any interference from either tape or other contaminants present in sample.38

IV. CONCLUSION

Raman spectroscopy has established itself as a reliable and non-destructive technique for the qualitative and quantitative analysis of a variety of drugs of abuse and illicit substances of forensic interest. Technique is capable of analyzing solid and liquid samples quite rapidly and without removing from packaging and thereby maintaining the integrity of forensic samples. The simplification of spectra caused by resonance allows the easy identification of species contained in complex mixtures. However, low sensitivity due to weak Raman signals and strong fluorescence due to impurities or colored packaging material can be very well addressed by combing two developments of the technique namely resonance Raman and surface enhanced Raman spectroscopy.

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