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Discrimination of cathinone regioisomers, sold as ‘legal highs’, by Raman spectroscopy

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The discrimination of a cross section of cathinone regioisomers, sold as ‘legal highs’, using Raman spectroscopy, is reported here. Mephedrone and flephedrone were identified in ‘legal high’ products sold in Irish head shops, and their 2, 3 and 4-isomers were synthesized as reference standards. The 3,4-methylenedioxy substituted cathinones, methylone, butylone and methylenedioxypyrovalerone (MDPV), were also identified in ‘legal highs’ and their 2,3-isomers were synthesized for comparison. In addition, *alpha*- and *beta*-naphyrone were synthesized. Raman spectra of all the isomers were obtained using far-red excitation (785 nm) and it was found possible to discriminate the isomers of each substituted cathinone. In addition, Raman spectra were also recorded for a number of head shop products and, by comparison with the reference standards, correct isomer assignment for 4-mephedrone, 3-flephedrone, 3,4-methylone, 3,4-butylone, 3,4-MDPV, *alpha*-naphyrone and *beta*-naphyrone was achieved, thus providing a non-destructive, high-throughput and minimal sample preparation technique for the discrimination of such drug isomers.

Keywords: Raman; flephedrone; mephedrone; methylone; MDPV; naphyrone

Introduction

Ring-substituted cathinone derivatives have been present on the European recreational drugs market since the mid-2000s.[1,2] These compounds are claimed to have effects similar to those of cocaine, amphetamine, and ecstasy (MDMA/3,4-methylenedioxymethamphetamine).[3] Cathinone and methcathinone (Figure 1) are listed in Schedule I of the United Nations 1971 Convention on Psychotropic Substances. New analogs of controlled drugs are encountered on an ongoing basis in forensic laboratories and difficulties arise when only one isomeric form of a drug is controlled by legislation. The responsibility lies with the forensic scientist to prove that a forensic sample contains the controlled substance and not a closely related, uncontrolled isomer. In Ireland, for instance, under S.I. No.199 of 2010, Misuse of Drugs Act 1977 (Controlled Drugs), the 4-isomer of methylmethcathinone (mephedrone) was controlled, but not the 2- or 3- isomers (Figure 1).[4] Fluoromethcathinone (flephedrone), a mono-substituted cathinone, is another drug that poses problems for the forensic scientist, as the fluorine substituent may be on the 2-, 3- or 4- position of the aromatic ring (Figure 2). It has been shown that it is possible to distinguish the three isomers by ^{19}F nuclear magnetic resonance (NMR).[5] However, the use of NMR, particularly ^{19}F NMR, is generally not feasible in forensic laboratories, mostly due to the expense involved with such instruments.[6] Raman spectroscopy has shown potential as an effective forensic tool as a result of recent technological developments such as increasingly sensitive detectors, coupling of Raman with hyphenated techniques (e.g. coupled to high performance liquid chromatography (HPLC)) and improvements in notch filters. This is particularly evident with the development of portable Raman spectrometers used for the detection and identification of controlled substances by customs and border control authorities.[7–9] Raman spectroscopy is becoming an established forensic analysis technique, similar to Fourier transform infrared spectroscopy (FTIR), offering advantages such as rapid screening/throughput of samples, non-destructive analysis, and little or no sample preparation. It can also be used non-invasively, thus minimizing exposure to potentially dangerous substances.[10] Water is Raman inactive and therefore controlled substances that are damp or aqueous can be analyzed. Its usefulness for illicit drug composition profiling has been demonstrated.[11–13]

The use of Raman spectroscopy to discriminate isomers of mono-substituted cathinones and methylenedioxy substituted cathinones is reported here. It was also the objective to investigate whether a particular isomer could be identified in a seized sample (containing a cathinone and adulterants). Such products frequently contain caffeine and lignocaine along with the principal psychoactive substance. The compounds selected for analysis by Raman spectroscopy were the mono-substituted cathinone methcathinone, the ring-positional isomers of the mono-substituted cathinones flephedrone and mephedrone, 3,4-methylenedioxymethamphetamine (MDMA) and the methylenedioxy substituted cathinones, methylone, butylone and methylenedioxypyrovalerone (MDPV) and alpha-/beta-naphyrones. These were all identified in Irish head shop

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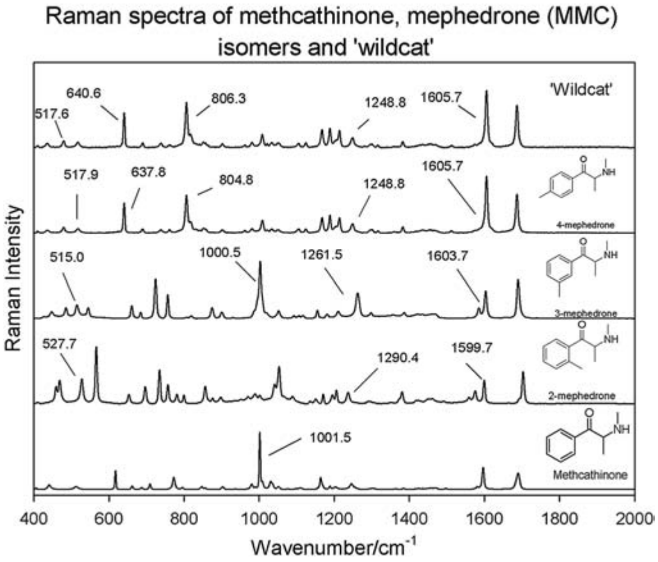

Figure 1. Raman spectra of methcathinone, mephedrone (MMC) isomers and ‘wildcat’.

products (except for methcathinone and MDMA) and were also available through online head shops.[14,15]

Materials and methods

Reagents and materials

The isomers of mephedrone, flephedrone, methylone, butylone, and MDPV were synthesized as described previously.[5,16] Methcathinone was synthesized using propiophenone as the starting ketone, by a similar method and the naphyrone isomers were synthesized from the respective naphthaldehydes using a previously published protocol.[17] Caffeine and lignocaine were obtained from Sigma Aldrich (Arklow, Co. Wicklow, Ireland). The following ‘legal high’ products were purchased (March–April, 2010) from head shops (Dublin, Ireland): ‘Wildcat’ ‘White Ice’, ‘Craic’, ‘Mint Mania’, ‘Doves’, ‘Ivory Wave’, ‘Snow’, ‘Ivory Wave’, ‘Mind Melt’, and two different samples of ‘Pure NRG’. These products have been previously analyzed by gas chromatography–mass spectrometry (GC-MS) to identify the specific new psychoactive substances present. The two individual ‘Ivory Wave’ samples were found to contain unique new psychoactive substances by GC-MS; MDPV was present in one, and beta-naphyrone in the other. In the case of the two individual ‘Pure NRG’ samples, both were found to contain beta-naphyrone by GC-MS analysis.[14,15]

Sample analysis

Raman

Raman data were acquired using a Horiba Jobin Yvon LabRAM HR800, a microscope based system using a 300 mW 785 nm CLDS point mode diode laser as source. All microscope data were collected using a 100x objective, described recently by Bell *et al.*[18] Samples were prepared by placing several mg onto a glass slide and compressing the powder to an area of approximately 1cm x 1cm and approximately 2 mm in depth. The sample spectra were acquired for 20 s with 10 x 3 accumulations. For each sample, several points were sampled (3–6 points) to check for spatial consistency of the spectral profiles. All acquired spectra were normalized when plotted.

Infrared (IR)

IR data was acquired using a Perkin Elmer Precisely Universal ATR Spectrum65 FT-IR Spectrometer, using 16 scans over a range from 400cm^{-1} to 550cm^{-1}. Spectra were obtained in triplicate.

Results and discussion

A Raman spectrum of methcathinone, a mono-substituted cathinone, was compared to other mono-substituted cathinones mephedrone and flephedrone, as it has previously been reported that mono-substituted cathinones can be distinguished from 1,4-disubstituted cathinones possessing a methyl group on the aromatic ring (*i.e.*4-mephedrone) and also from 3,4-disubstituted cathinones containing a methylenedioxy group such as methylone, butylone and methylenedioxypyrovalerone (MDPV).[18]

Mono-substituted cathinones and 1,3-disubstituted cathinones (3-flephedrone and 3-mephedrone) can be distinguished from 1,2- and 1,4-disubstituted cathinones (i.e. 2-flephedrone, 2-mephedrone, 4-flephedrone and 4-mephedrone). The aromatic in-plane C-H deformation vibrations that occur in the region 1290–990cm^{-1} are useful for characterization purposes and they are often observed as very intense bands.[19] In the case of methcathinone, a very strong band is observed at 1001.5cm^{-1} (Figure 1), this is the ring-breathing mode of a mono-substituted benzene (assigned as ν_{12} mode). An equally strong band is observed in 3-mephedrone (1000.5cm^{-1}, Figure 1) and in 3-flephedrone (1001.5cm-1, Figure 2). These bands arise from the ν_{12} mode (benzene in-plane ring deformation) which is very strong in Raman, always occurring at 1010+/−10cm^{-1}, and are usually the strongest band in the Raman spectrum. The ν_{12} mode is dependent on the ring breathing motion of three alternate carbons and is independent of the type of substituent once the substituent is at the 1- (mono), 1,3- (*meta*) or 1,3,5- positions.[20] Therefore, a strong Raman band at this wavenumber, as seen in Figures 1 and 2, is indicative of mono- or *meta*- substitution and not *ortho*- or *para*-.

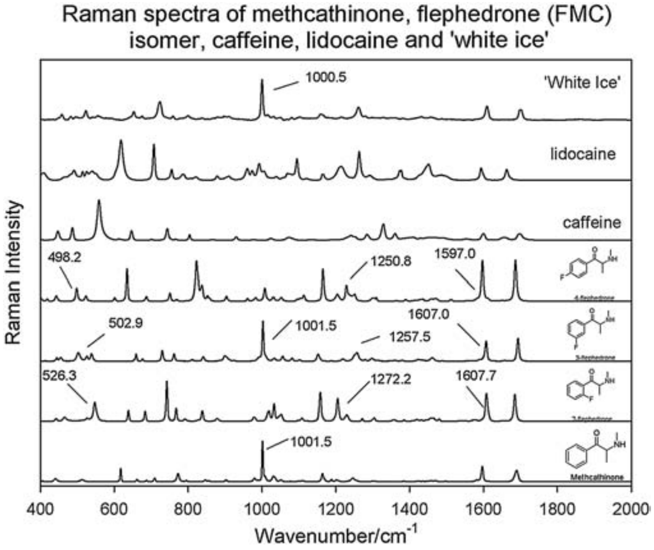

Figure 2. Raman spectra of methcathinone, flephedrone (FMC) isomers, caffeine, lidocaine and ‘white ice’.

The isomers of the mono-substituted cathinones, flephedrone, and mephedrone and the methylenedioxy substituted cathinones, methylone, butylone, and MDPV have also been shown to be distinguishable from each other using Raman spectroscopy. Three specific regions in the Raman spectra of each mephedrone and flephedrone isomer were selected for comparison with methcathinone (another mono-substituted isomer) due to the intensity of the stretches and the significant shifts in wavenumbers. Bands of significance were also identified in the methylenedioxy substituted isomers in comparison with 3,4-methylenedioxymethamphetamine.

The first region that can be used to distinguish between the isomers of mephedrone and flephedrone is the aromatic C = C stretching vibration which occurs at ~1600cm^{-1}. This band is sharp and strong, and is observed in all isomers at 1600cm^{-1}+/—10cm^{-1} (Table 1). This is assigned as the $\nu_{8\beta}$ mode, which is normally weak to very weak in intensity, but actually increases significantly when a substituent to the benzene ring is unconjugated. This effect is apparent in Figures 1 and 2, where the C = C stretching vibration for methcathinone is less intense than the same peak for the isomers of mephedrone and flephedrone.

The second region of interest is 1300–1240cm^{-1}. Bands are observed due to aromatic = C-H in-plane deformation vibrations for 1,2-, 1,3- and 1,4-disubstituted benzenes. In the case of the 2-, 3- and 4-isomers of flephedrone and mephedrone, bands should be observed at 1290–1250cm^{-1}, 1300–1240cm^{-1} and 1270–1250cm^{-1}, respectively (Table 1). There is a consistent shift in wavenumbers comparing methcathinone to the 2-, 3- and 4- isomers of both mephedrone and flephedrone.

The final region that can be used to discriminate in particular the flephedrone isomers in comparison to methcathinone and the mephedrone isomers is 540–490cm^{-1} (Figures 1 and 2). In this region, bands due to ring breathing coupled with C-X (X = F, or CH_3) stretching are observed. A previous study has shown that the position of a fluorine substituent on the ring 'leads to significant structural changes and redistribution of the atomic charges in the ring'.[21] Table 1 shows the effects that these changes have on the wavenumbers of these bands in this spectral region in comparison to a methyl substituent (observed in mephedrone). It was noted that, as the fluorine substituent changes from the *para* position through to the *meta* and then *ortho* position, there is a consistent and significant increase in the wavenumber of the specific bands caused by the field effect that fluorine has on the ring.

There is another region that can be considered for discrimination purposes and that is at ~ 690cm^{-1}. This strong band arises from ring puckering vibrations and is assigned to the ν_4 mode, whereby alternate carbons are displaced both above and below the plane of the benzene ring. Thus, a mono-substituted isomer (methcathinone) could be discriminated from an *ortho* isomer (i.e. 2-flephedrone and 2-mephedrone) based on whether a band was observed in the 690cm^{-1} region, in addition to a strong band in the 750–730cm^{-1} region. Likewise, if this latter band appeared above 770cm^{-1}, it could be suggested that this was more likely evidence of the *meta* isomer (3-mephedrone or 3-flephedrone).[20] The C-H out-of-plane bending and ring puckering vibrations for all of the isomers discussed are represented in Table 2 which shows the presence of the band observed in the 690cm^{-1} region for methcathinone (706.6cm^{-1}) but not for any of the remaining isomers.

The Raman spectrum of the head shop product, 'Wildcat' (Figure 1), which was found to contain 4-mephedrone (by GC-MS), displayed strong and characteristically similar bands to 4-mephedrone but not to 2- or 3-mephedrone. The Raman spectrum of the head shop product, 'White Ice' (Figure 2), which was found to contain 3-flephedrone, caffeine and lignocaine by GC-MS, displayed a strong and characteristic band at approximately ~1000cm^{-1} which was not evident in either the caffeine or lignocaine spectra. This indicates the presence of 3-flephedrone as the band was absent in the other two isomers (Figure 2).

The methylenedioxy substituted cathinones, methylone, butylone and MDPV, possess two significant bands between ~1600 and ~1700cm^{-1}, a feature of substituted cathinones also observed in flephedrone and mephedrone. A distinguishing feature of the band observed at approximately 1600cm^{-1} in the 3,4-methylenedioxy substituted cathinones, however, is the presence of a shoulder at between 1610–1630cm^{-1}. This has also been reported to be present

Table 1. The characteristic bands and changes in wavenumbers, comparing methcathinone (mono-substituted) to the mephedrone and flephedrone isomers (*ortho*, *meta* and *para*)

Isomer	Aromatic C = C Stretching Vibration (cm^{-1})	Δ wavenumber between isomers compared to methcathinone (cm^{-1})	Aromatic = C-H In-Plane Deformation Vibration (cm^{-})	Δ wavenumber between isomers (cm^{-1})	C-X Stretching (X = F) (cm^{-1})	Δ wavenumber between isomers (cm^{-1})
Methcathinone (mono)	1596.9		1246.9		509.2	
2-mephedrone (*ortho*)	1599.7	2.8	1290.5	43.6	527.7	18.5
3-mephedrone (*meta*)	1603.7	6.8	1261.5	14.6	515.0	5.8
4-mephedrone (*para*)	1605.7	8.8	1248.8	1.9	517.9	8.7
Methcathinone (mono)	1596.9		1246.9		509.2	
2-flephedrone (*ortho*)	1607.7	10.8	1272.2	25.3	526.3	17.1
3-flephedrone (*meta*)	1607.0	10.1	1257.5	10.6	502.9	6.3
4-flephedrone (*para*)	1597.0	0.1	1250.8	3.9	498.2	11.0

Table 2. C-H out-of-plane bending and ring puckering vibrations for methcathinone and the isomers of mephedrone and flephedrone

Isomer	Region 730–860 cm-1 (cm-1)	Region 710–690 cm-1 (cm-1)
Methcathinone (mono)	771	706.6
2-mephedrone (*ortho*)	755.6	Not present
3-mephedrone (*meta*)	752.8	Not present
4-mephedrone (*para*)	804.8	Not present
2-flephedrone (*ortho*)	704.2	Not present
3-flephedrone (*meta*)	808.7	Not present
4-flephedrone (*para*)	819.9	Not present

in the Raman spectrum of MDMA but is not observed in disubstituted cathinones or 2,3-methylenedioxy substituted isomers (Figure 3).[18] These shoulders were observed at 1622.4cm^{-1}, 1624.8cm^{-1} and 1611.0cm^{-1} for 3,4-methylone, 3,4-butylone and 3,4-MDPV respectively (Figures 3–5). Bands at 1250.8cm^{-1}, 809.7cm^{-1} and 841.8cm^{-1} were also present for 3,4-methylone but not for 2,3-methylone. For butylone, bands at 1245.5cm^{-1}, 1286.1cm^{-1}, 850.7cm^{-1}, 828.3cm^{-1}, 805.9cm^{-1}, 744.4cm^{-1} and 720.6cm^{-1} were observed for the 3,4-isomer but not for the 2,3-isomer. Bands at 1352.4cm^{-1} and 809.0cm^{-1} were observed in 3,4-MDPV only.

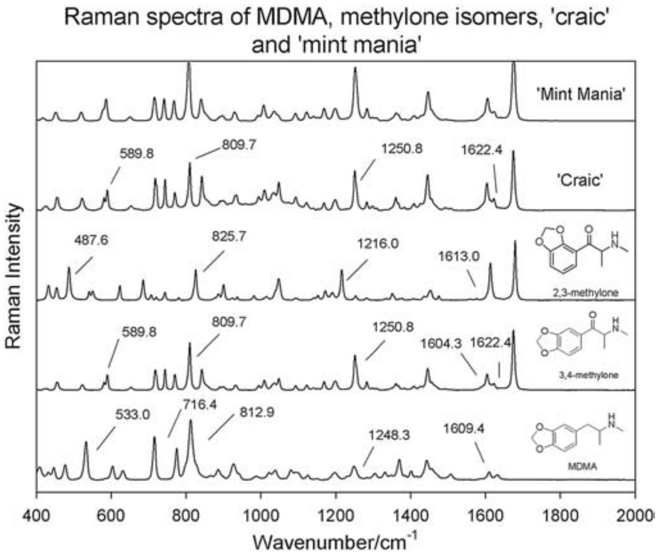

Figure 3. Raman spectra of MDMA, methylone isomers, 'craic'and 'mint mania'.

The Raman spectra of the reference standards of the methylenedioxy substituted cathinones were compared with the spectra of head shop products that were known to contain those ingredients (based on previous GC-MS analysis).[14,15] The spectra of two head shop products, 'Craic' and 'Mint Mania', containing methylone (Figure 3), demonstrated the presence of the 3,4-isomer. Another product ('Doves') was found to contain 3,4-butylone (Figure 4). 'Ivory Wave' and 'Snow' were found to contain 3,4-MDPV (Figure 5). These findings were in agreement with GC-MS results. The results highlight the presence of the 3,4-isomer, which was expected.

The Raman band values that were obtained in this study for 4-mephedrone, 3-flephedrone, 3,4-methylone and 3,4-butylone were also compared to values published in the literature by Bell *et al.*[18] This comparison is outlined in Table 3 and highlights the consistency between the Raman bands obtained in both studies.

The Raman spectra of the *alpha*- and *beta*-isomers of naphyrone were found to be distinguishable, thus facilitating correct isomer assignment in the 'head shop' products (Figure 6). The following bands were present in the *alpha*-isomer: 561.0cm^{-1}, 657.6cm^{-1}, 899.7cm^{-1}, 1367.3cm^{-1}, 1573.1cm^{-1}, and 1687.0cm^{-1}. The distinctive bands present in the *beta*-isomer were 516.2cm^{-1}, 771.0cm^{-1}, 1393.9cm^{-1}, 1627.6cm^{-1}, and 1671.0cm^{-1}. Isomer assignment, based on the Raman spectra, correlated with the results of GC-MS analysis.

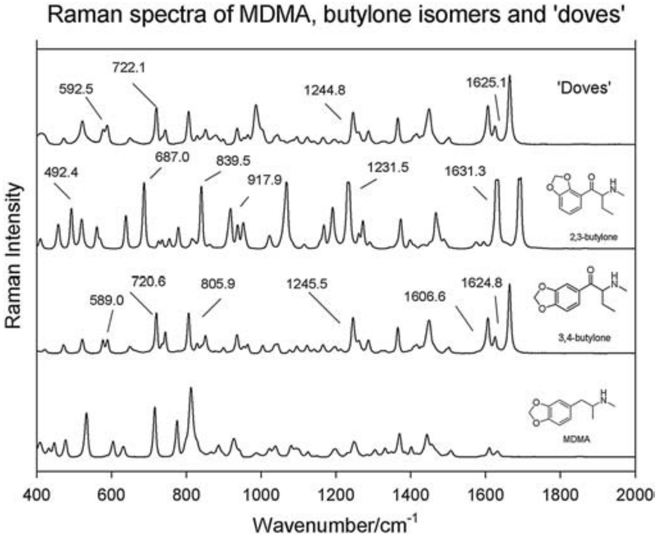

Figure 4. Raman spectra of MDMA, butylone isomers and 'doves'.

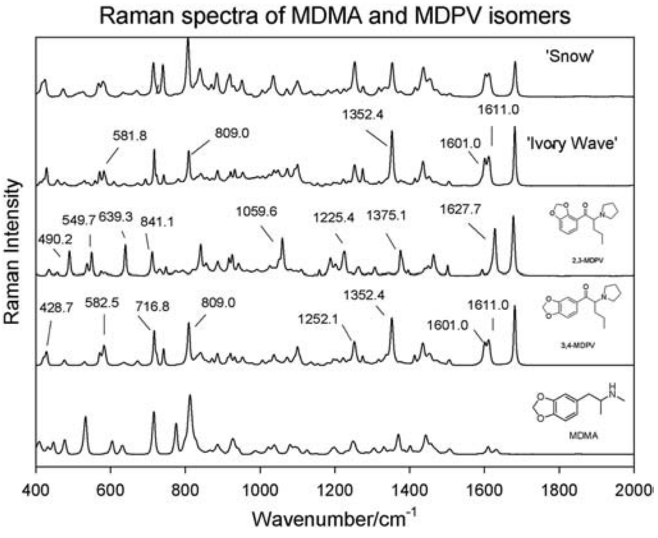

Figure 5. Raman spectra of MDMA and MDPV isomers.

Table 3. Comparison of literature obtained Raman values to the values obtained in this study

Bell et al. 4-mmc (cm^{-1})	This study 4-mmc (cm^{-1})	Bell et al. 3-fmc (cm^{-1})	This Study 3-fmc (cm^{-1})	Bell et al. Methylone (cm^{-1})	This study Methylone (cm^{-1})	Bell et al. Butylone (cm^{-1})	This study Butylone (cm^{-1})
639	637.8	462	454.5	523	522.3	525	525.6
804	804.8	487	502.9	589	589.8	580	580.5
851	857.4	526	526.3	653	652.8	592	589.0
1006	1008.2	657	659.3	720	721.5	652	652.8
1048	149.9	679	676.2	744	743.5	722	720.6
1123	1126.0	726	730.2	770	769.6	746	746.9
1168	1159.2	762	762.2	810	809.7	808	805.9
1189	1187.7	1004	1001.5	843	841.8	854	853.8
1213	1216.2	1082	1082.0	898	896.6	938	938.0
1249	1248.8	1098	1101.5	933	931.3	967	966.1
1299	1297.4	1161	1151.9	1010	1008.9	1046	1046.3
1383	1385.8	1221	1219.4	1095	1093.7	1097	1097.6
1606	1605.7	1264	1257.5	1124	1120.9	1125	1123.5
1687	1682.0	1611	1607.0	1171	1168.9	1167	1166.3
		1703	1693.2	1199	1196.1	1199	1197.4
				1253	1250.8	1247	1245.5
				1285	1281.7	1262	1261.5
				1363	1360.4	1289	1286.9
				1412	1409.2	1367	1365.1
				1448	1445.3	1417	1415.9
				1499	15021	1451	1450.0
				1607	1604.3	1503	1502.1
				1624	1622.4	1608	1606.6
				1677	1674.3	1627	1624.8
						1666	1663.8

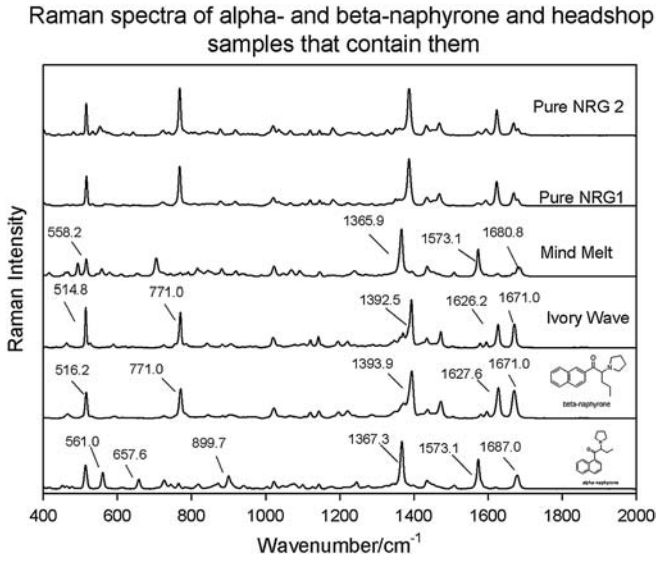

Figure 6. Raman spectra of alpha- and beta-naphyrone and headshop samples that contain them.

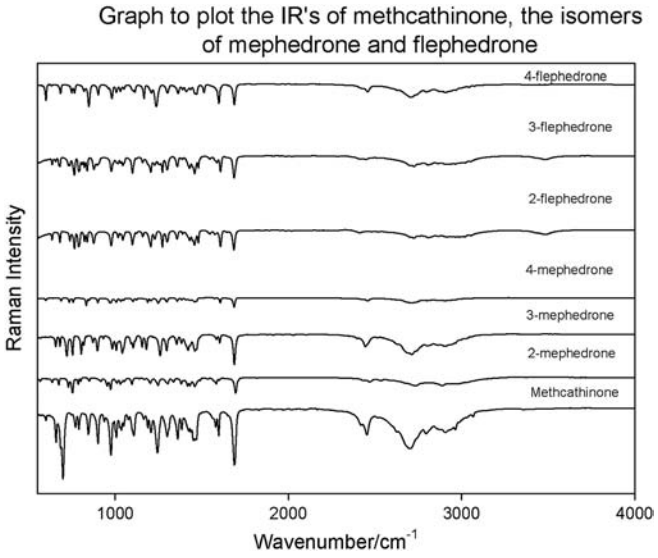

Figure 7. Graph to plot the IR's of methcathinone, the isomers of mephedrone and flephedrone.

Beta-naphyrone was identified in 'Ivory Wave' and both of the 'Pure NRG' samples whereas *alpha*-naphyrone was found in 'Mind Melt'.

Finally, to supplement the information provided by the Raman spectra of all the isomers and to demonstrate a more comprehensive discrimination, the IR spectrum of the isomers was obtained (Figures 7, 8 and 9). Infrared spectroscopy has also been shown to be useful in the discrimination of these drug isomers.[16,22] The two spectroscopic techniques are indeed complementary. However, Raman spectroscopy has the advantage that benchtop spectrometers can routinely measure as low as 100cm^{-1}, whereas bench-top FTIR instruments are commonly limited to a low frequency cut-off of ~600cm^{-1}. Thus Raman is particularly useful

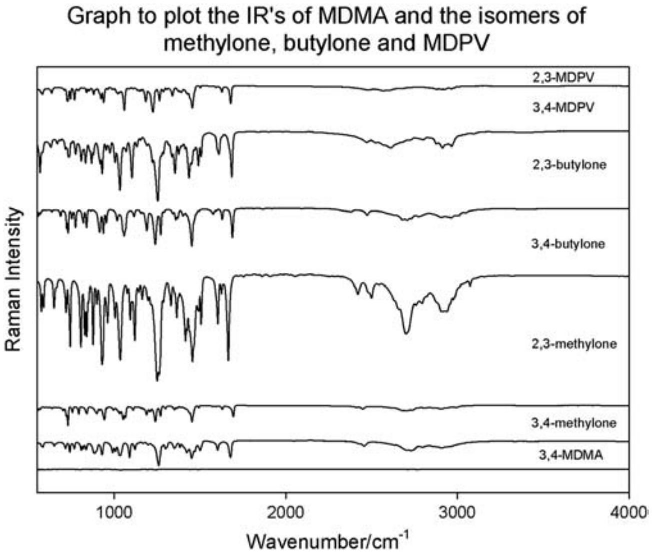

Figure 8. Graph to plot the IR's of MDMA and the isomers of methylone, butylone and MDPV.

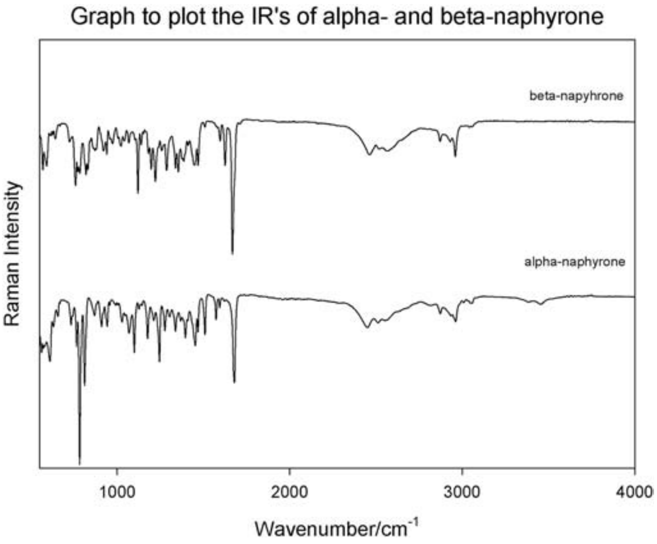

Figure 9. Graph to plot the IR's of alpha- and beta-naphyrone.

for the flephedrone isomers which display characteristic bands in the 540–490cm^{-1} region, signatures of the ring-breathing coupled with carbon-fluorine stretching.

Conclusion

The discrimination of the ring substituted isomers of mono-substituted and methylenedioxy substituted cathinones by Raman spectroscopy has been demonstrated. The Raman spectra for all of the isomers were distinguishable due to significant and characteristic shifts in their bands. The mono-substituted isomers of mephedrone and flephedrone could also be discriminated, as could the methylenedioxy substituted isomers of methylone, butylone MDPV and naphyrone. 'Legal high' products were analyzed using Raman spectroscopy and, in each case, the spectra clearly showed the presence of one isomer, which was in agreement with GC-MS results. Notably, it is beyond the scope of this study to address all of the commercially available cathinones, and indeed the number is ever increasing. Nevertheless, the study represents a proof of concept using a representative cross section. To implement the technology, a full library of the spectroscopic signatures of this family of compounds would be required. Efforts in this direction are ongoing. The availability of a broader dataset would facilitate more sophisticated data analysis techniques based on multivariate statistics to enhance sensitivity and selectivity and the potential of these methods are currently being examined.

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References

[1] EMCDDA. Drug profiles, Synthetic Cathinones. Available at: http://www.emcdda.europa.eu/publications/drug-profiles/synthetic-cathinones [03 July 2013]

[2] UNODC. The challenge of new psychoactive substances. Available at: http://www.unodc.org/documents/scientific/NPS_2013_SMART.pdf [03 July 2013]

[3] L.D. Simmler, T.A. Buser, M. Donzelli, Y. Schramm, L.H. Dieu, J. Huwyler, et al. Pharmacological characterization of designer cathinones in vitro. *Brit. J. Pharmacol.* **2013**, *168*, 458.

[4] Irish Statute Book. Available at: www.irishstatutebook.ie/pdf/2010/en.si.2010.0199.PDF [03 July 2013]

[5] R.P. Archer. Fluoromethcathinone, a new substance of abuse. *Forensic Sci. Int.* **2009**, *185*, 10.

[6] S. Bell. Forensic Chemistry, Annual Review of Analytical Chemistry. Annual Reviews, California, USA, **2009**, pp. 297–319.

[7] C. Weyermann, Y. Mimoune, F. Anglada, G. Massonnet, P. Esseiva, P. Buzzini. Applications of a transportable Raman spectrometer for the in situ detection of controlled substances at border controls. *Forensic Sci. Int.* **2011**, *209*, 21.

[8] M.D. Hargreaves, A.D. Burnett, T. Munshi, J.E. Cunningham, E.H. Linfield, A.G. Davies, et al. Comparison of near infrared laser excitation wavelengths and its influence on the interrogation of seized drugs-of-abuse by Raman Spectroscopy. *J. Raman Spectrosc.* **2009**, *40*, 1974.

[9] M.D. Hargreaves, K. Page, T. Munshi, R. Tomsett, G. Lynch, H.G.M. Edwards. Analysis of seized drugs using portable Raman spectroscopy in an airport environment—a proof of principle study. *J. Raman Spectrosc.* **2008**, *39*, 873.

[10] A.D. Burnett, H.G. Edwards, M.D. Hargreaves, T. Munshi, K. Page. A forensic case study: The detection of contraband drugs in carrier solutions by Raman spectroscopy. *Drug Test. Anal.* **2011**, *9*, 539.

[11] J.M. Chalmers, E.G.M. Howell, M.D. Hargreaves. Infrared and Raman Spectroscopy in Forensic Science. John Wiley & Sons Ltd, Chichester, West Sussex, **2012**.

[12] S.E. Bell, D.T. Burns, A.C. Dennis, L.J. Matchett, J.S. Speers. Composition profiling of seized ecstasy tablets by Raman spectroscopy. *Analyst* **2000**, *125*, 1811.

[13] S.E. Bell, L.J. Barrett, D.T. Burns, A.C. Dennis, S.J. Speers. Tracking the distribution of "ecstasy" tablets by Raman composition profiling: A large scale feasibility study. *Analyst* **2003**, *128*, 1331.

[14] C. Keller, R. Christie, K. Lalor, J. Fox, M. Bowden, C. O'Donnell. An Overview of New Psychoactive Substances and the Outlets Supplying Them. National Advisory Committee on Drugs. Available at: http://www.nacd.ie/index.php/publications/38-an-overview-of-new-psychoactive-substances-and-the-outlets-supplying-them.html [03 July 2013]

[15] P.V. Kavanagh, S. McNamara, D. Angelov, S. McDermott, D. Mullan, S.A. Ryder. The Characterization of 'Legal Highs' Available from Head Shops in Dublin. Available at: http://drugs.ie/downloadDocs/Poster.pdf [03 July 2013]

[16] P. Kavanagh, J. O'Brien, J. Fox, C. O'Donnell, R. Christie, J.D. Power, et al. The analysis of substituted cathinones. Part 3. Synthesis and characterisation of 2,3-methylenedioxy substituted cathinones. *Forensic Sci. Int.* **2012**, *216*, 19.

[17] J.D. Power, P. McGlynn, K. Clarke, S.D. McDermott, P. Kavanagh, J. O'Brien. The analysis of substituted cathinones. Part 1: Chemical analysis of 2-, 3- and 4-methylmethcathinone. *Forensic Sci. Int*. **2011**, *212*, 6.

[18] S.P. Stewart, S.E. Bell, N.C. Fletcher, S. Bouazzaoui, Y.C. Ho, S.J. Speers. Raman spectroscopy for forensic examination of β-ketophenethylamine "legal highs": Reference and seized samples of cathinone derivatives. *Anal. Chim. Acta* **2012**, *711*, 1.

[19] G. Socrates. Infrared and Raman Characteristic Group Frequencies. John Wiley & Sons Ltd, Chichester, West Sussex, **2001**.

[20] D.W. Mayo, F.A. Miller, R.W. Hannah. Course Notes on the Interpretation of Infrared and Raman Spectra. John Wiley & Sons Inc., Hoboken, New Jersey, **2004**.

[21] P. Wojciechowski, K. Helios, D. Michalska. Theoretical anharmonic Raman and infrared spectra with vibrational assignments for monofluoroaniline isomers. *Vib. Spectrosc*. **2011**, *57*, 126.

[22] S.D. Brandt, P.F. Daley, N.V. Cozzi. Analytical characterization of three trifluoromethyl-substituted methcathinone isomers. *Drug Test. Anal.* **2012**, *4*, 525.