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Rapid Identification of Synthetic Cannabinoids in Herbal Incenses with DART-MS and NMR [*,ǂ]

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ABSTRACT

The usage of herbal incenses containing synthetic cannabinoids has caused an increase in medical incidents and triggered legislations to ban these products throughout the world. Law enforcement agencies are experiencing sample backlogs due to the variety of the products and the addition of new and still-legal compounds. In our study, proton Nuclear Magnetic Resonance (NMR) spectroscopy was employed to promptly screen the synthetic cannabinoids after their rapid, direct detection on the herbs and in the powders by Direct Analysis in Real Time-Mass Spectrometry (DART-MS). A simple sample preparation protocol was employed on 50 mg of herbal sample matrices for quick NMR detection. Ten synthetic cannabinoids were discovered in fifteen herbal incenses. The combined DART-MS and NMR methods can be used to quickly screen synthetic cannabinoids in powder and herbal samples, serving as a complementary approach to conventional GC-MS or LC-MS methods.

Keywords: Forensic Science, Synthetic Cannabinoids, Spice, NMR, DART-MS, drug identification, JWH.

Since 2006, synthetic cannabinoids such as JWH-018 (Figure 1 and Figure 2a) have been reportedly mixed with natural herbs and sold as cannabis substitutes all over the world (1). When this trend migrated from Europe to the United States a few years ago, it instantly became popular among recreational drug users, especially those with experimental interest in “Research Chemicals” (RC). Smoking these synthetic cannabimimetic compounds in their pure form, and more commonly in herbal blends, has produced adverse effects in users such as anxiety attacks, vomiting and psychotic episodes, which resulted in increased emergency room visits. These incidents led to the eventual passage of S. 3187 that classified five classes of synthetic cannabinoids as Schedule I controlled substances (2). Millions of samples were confiscated after the passage, which created large backlogs for evidence processing. Despite efforts to remove these types of compounds from the market, legal analogs are still being made to circumvent the ban. They can be readily purchased as legal incenses or herbal potpourri in natural food shops or, more conveniently, through internet vendors. A recent survey on adolescent drug use suggested that “synthetic marijuana” has become the second most common drug of abuse in high schools (3). Due to the lack of quality control, drug users are often inhaling synthetic compounds that are misrepresented with varying concentrations. The identity of the synthetic cannabinoid is ever-changing (4). New generations of these so called “Spice” products are constantly being released into the international market and are continuing to cause harm (5). As a result, it has become urgent for forensic labs to be able to promptly detect and identify synthetic cannabinoids in their original powder form and in other consumer products, with minimal sample preparation and clean-up steps.

In the past three years, various efforts have been made by forensic scientists around the world to utilize spectroscopic methods and chromatographic separation methods to identify and quantify synthetic cannabinoids in powders as well as herbal mixtures. Auwärter et al. (6) first used GC-MS along with thin layer chromatography (TLC) to identify JWH-018 and CP-47,497 after a cumbersome chemical derivatization. Uchiyama and coworkers analyzed multiple herbal products on the Japanese market to identify synthetic cannabinoids, taking advantage of multiple spectroscopic techniques coupled with chromatographic separations (7-10). Uchiyama’s method involved a lengthy extraction of the compounds from the herbs, TLC separations, as well as a second extraction of the purified analytes from the TLC plate multiple times in order

to get enough material (several milligrams) for downstream analyses. The fractions subsequently combined, evaporated and crystallized prior to spectroscopic analyses.

Direct Analysis in Real Time-Mass Spectrometry (DART-MS) has been previously used to rapidly detect narcotics with essentially no sample preparation and ultra-fast analysis under atmospheric conditions (11). Uchiyama *et al* (8, 9) have also utilized DART-MS as one of their confirmatory methods for several purified JWH- compounds extracted and separated from herbal blends. DART ionization occurs by introducing the sample (powders or solutions) into the gas stream, sometimes via a coated glass rod (11). Peaks corresponding to protonated molecules are then detected within seconds by a high resolution Time-of-Flight Mass Spectrometer (TOF-MS). Using exact mass information, isotope peaks and fragmentation data under different cone voltage conditions, a compound of interest can be identified within minutes with minimal interference from the background. More recently, following rapid DART ionization, Musah *et al.* have successfully demonstrated how the fragmentation from the DART mass spectra can indicate the presence of specific structural features in synthetic cannabinoids (12, 13) and in cathinones (14), which complements our NMR study.

DART-MS, however, is not always able to differentiate between two isomers that have identical fragments. Thus it was recommended as a reliable screening tool for forensic drug analysis (11). Although time-dependent desorption can occur for compounds with differing volatility, the lack of a chromatographic separation method can in some cases limit the utility of the DART method. Additionally, when more than two synthetic components of varying concentrations are present in the herbal products, it may be difficult to interpret the overlapping fragment-ion mass spectra, thus resulting in the trace components possibly being overlooked. Consequently, additional confirmatory methods such as NMR can enhance the positive identification of positional isomers and all components in a mixture.

NMR has been extensively used to derive the structures of purified synthetic cannabinoids (1, 8, 11, 15, 16). JWH-series and AM-series compounds (Figure 1) have distinctive peaks in the proton NMR aromatic regions (6.5-9 ppm) as well as around 4 ppm, with little to no interference from natural components from the herbal base. Only a minimal amount of cannabinoid analyte is necessary to reach very low detection limits with a

small amount of herbs (~100 mg or less). To render the dosage effective, usually the concentration of the synthetic cannabinoid ranges from 1-40 mg/g of herb (10). When the synthetic compound is extracted from the surface of the herbs into an NMR solvent, the final concentration range is from 0.1-10 mg/mL, which exceeds the NMR detection limit (~1 μg/mL) by several orders of magnitude.

Conventional structural elucidation by NMR has required cumbersome sample preparation steps to collect enough purified compounds (5 mg or more) and lengthy NMR experiments with H1-NMR, C13-NMR, DEPT, COSY, HMQC and HMBC that can last several days (1, 9, 15). To ensure clean spectra, the cannabinoid samples were extracted from the herbal matrices and separated on TLC plates or chromatographic columns multiple times to obtain enough pure compounds (1, 7, 8). Our NMR sample preparation method is designed as a simplified protocol to dramatically reduce the time and sample size needed to positively identify cannabinoids in herbal products. The combination of rapid DART-MS and NMR can provide concrete cannabinoid structural information with no ambiguity, which can be a useful alternative, or complement, to conventional GC-MS and LC-MS methods.

Materials and Methods

Materials:

Powder cannabinoid samples (as held in a plastic vial indicated in Figure 3a) were initially purchased online from Mountain Industry (California, USA), which was a major online distributor for other online sellers of “Spice” products. The Mountain Industry powders were found to be of low quality with mixtures and/or mislabeled compounds identified within these samples (Tables 1 and 2). Standard cannabinoids (see Table 2) with reliable quality control were purchased from Cayman Chemical (Ann Arbor, MI, USA). The structures of the standard cannabinoids and the ones detected in our herbal samples are listed in Figures 1 and 2. The numbering system on the cannabinoid chemical structures is similar to that of Lindigkeit et al. (1) All of the powders were stored in a desiccator at 4°C. Deuterated chloroform ($CDCl_3$) was purchased from Sigma Aldrich (St. Louis, MO, USA). Several pure herbs such as damiana, mullein, and mugwort (from Amazon.com)

were used to serve as a background or as blank samples for MS and NMR analyses. These herbs were popular choices as indicated on online drug-user forums and Youtube videos.

The herbal samples were purchased through several popular online vendors, all labeled with “not for human consumption”. One package branded “K-2201” was labeled with the identity and concentration of the synthetic compound (12.5 mg/g herb of AM-2201). All of the other Spice herb packages were neither labeled with the content nor the amount of synthetic cannabinoid present. After opening each package for inspection, the Mylar® sample bags were closed and sealed with tape to prevent sample evaporation and cross contamination. The sample packages are displayed in Figure 3 along with a microscopic image of an herb and a plastic vial containing one of the Mountain Industry powders. Figure 3b shows a close-up image of the leafy material in a product called “Moon Spice”.

DART-MS methods:

An AccuTOF-DART (JEOL USA, Inc., Peabody, MA, USA) time-of-flight mass spectrometer (TOF-MS) was used for all exact mass measurements (resolving power = 6000, FWHM definition). A mass spectrum of polyethylene glycol (PEG), with an average molecular weight of 600 g/mol, was included in each data set as a reference standard for the exact mass measurements. The atmospheric pressure interface was operated with the potential settings for Orifice 1 = 20 V, Orifice 2 = 5 V, and Ring Lens = 3 V. At these potentials, little to no collision-induced dissociation (CID) occurs and the resulting mass spectra are dominated by protonated molecule ions ($[M+H]^+$). Fragmentation spectra were obtained via in-source CID with Orifice 1 voltages at 30, 60, 90 and 120 V, respectively. The RF ion guide voltage was set to 600 V to allow the detection of ions greater than m/z 60. The DART-SVP ion source (IonSense Inc., Saugus, MA) was operated with a helium gas heater temperature of 300°C and exit grid voltage of 250 V. TSSPro3 software (Shrader Analytical, Detroit, MI) and Mass Spec Tools software (ChemSW Inc., Fairfield, CA) were used for data processing and data interpretation. For standard analysis, the powdered sample was introduced directly into the DART stream on the closed end of a melting point tube. For plant material analysis, three random pieces were selected from a given sample bag and each piece was held in the DART gas stream with forceps for 10 seconds. For each data file, PEG 600 was measured within the same data file for the exact mass calibration. Prior to DART-MS

analyses of the herbal blends with cannabinoids, the base herbs were also tested, which yielded no molecular ion peaks comparable to the synthetic cannabinoids. Most of the synthetic compounds possess molecular weights higher than 320 g/mol, and they produce strong, dominating, and distinctive peaks corresponding to protonated molecules.

NMR procedures:

H-1 NMR spectra were obtained on a JEOL ECS 400 MHz spectrometer (Peabody, MA, USA) with a JEOL 40 th5AT/FG2 5-mm proton/multi-frequency auto-tunable broadband probe and with $CDCl_3$ as the solvent. Chemical shifts were referenced to residual $CHCl_3$ at 7.25 ppm (1H). The proton sensitivity of the NMR instrument is >=280:1 using 0.1% ethylbenzene in $CDCl_3$ when methyl quartet signal region was evaluated with measured 200 Hz noise width between 3 ppm and 7 ppm. Typically one to five milligrams of the standard powder samples were weighed, dissolved in 1 mL $CDCl_3$, and transferred to NMR sample tubes. Mountain Industry sample concentrations were roughly 5 mg/mL, and Cayman samples 1 mg/mL. The proton spectra were scanned 128 times (18 minutes) in the 0-10 ppm range, unless 512 scans (one hour) was necessary to obtain sufficient signal-to-noise ratio (S/N) for sample amounts less than 1 mg.

For “Spice” plant material sample analysis, ~50 mg of each herbal product was placed into ~1 mL of $CDCl_3$ and vortexed for one minute. The liquid solution was then transferred with a glass pipette to an NMR sample tube. The proton NMR spectrum of each herbal extract was obtained after 32 scans (4 minutes) with a 4-second relaxation delay and chemical shift ranging from 0-10 ppm. The data were compared with the chemical shifts observed in the spectra of the standards to confirm the presence of the synthetic compounds.

With the powder sample, H-1 NMR was employed to elucidate the structures of synthetic cannabinoids. In most cases when a pure standard was available, matches of all chemical shift values were used to confirm its identity; for herbal samples, the standard chemical shift value ±0.1ppm range was used to account for peak marking deviation when the DELTA software (JEOL USA) was utilized. The H-1 NMR spectra of the herbal extracts were compared with their standard counterparts, particularly in the aromatic chemical shift region (6.5-

9 ppm) and the mid-field region (4-5 ppm) where overlapping signals from both the base herb and the synthetic components were avoided.

Results

The DART-MS spectra of JWH-019 and "Moon Spice" herbal sample are presented in Figures 4a and 4b, respectively and are typical of the mass spectra observed for DART analyses. Figure 4c shows the comparison between the 90V fragmentation mass spectrum from the Moon Spice sample and the pure JWH-018 standard. The exact masses for the matching ions within each spectrum were within 5mmu of each other, thus indicating that they have the same elemental compositions. The other ions depicted in the Moon Spice 90V spectrum (Figure 4c) were produced from the fragmentation of the other cannabinoid compound present in the sample, RCS-04. The identification results on all of the other standards and herbal blends along with their NMR confirmations are presented in Table 1.

Three of the Mountain Industry powders were mislabeled synthetic cannabinoids and three contained other cannabinoids as contaminants (Table 1). The H-1 NMR chemical shift values of the standards are listed in Table 2, in which the Cayman standards had been correctly labeled and their spectra compared with those from Mountain Industry powders and the herbal extracts (Tables 2 and 3).

Figure 5a is an H-1 NMR spectrum for the $CDCl_3$ extract of 50 mg of cannabinoid-free mugwort leaf. As indicated in the spectrum, most of the signals from the leaf are below 3 ppm. Besides the residual solvent peak, the $CDCl_3$ extraction method did not produce any strong or noticeable signal above 3 ppm. The same phenomena were observed with mullein and damiana leafs, two popular choices for the base herb in incense products as indicated in online discussions among drug users.

Figure 5b is the H-1 NMR spectrum of 1.0 mg RCS-04 cannabinoid standard purchased from Cayman Chemical. As the spectrum indicates, the signals within 3.5-9ppm do not overlap with blank herbal signals shown in the top panel. The bottom panel is from the $CDCl_3$ extracts of "Moon Spice" herbal incense. The signals for RCS-04 were found at seven locations. The remaining signals from 4-9 ppm are from JWH-018 according to literature values (1, 8) and the correlating chemical shift values are listed in Table 3. JWH-018

and RCS-04 were detected by both DART-MS and NMR (Table 1). Occasionally a proton signal for water (a broad singlet anywhere from 1.2 to 1.8 ppm) is present in the resulting spectra, but has not interfered with our region of interest: 3.5-9 ppm.

As Table 2 indicates, the "AM-1221" compound from Mountain Industry is indeed a mislabeled and actually contains AM-2201 (Figure 1). The herbal extract NMR data (Figure 5 and Table 3) confirmed the results obtained in the DART-MS experiments (Figure 4b and 4c). HPLC-DAD and conventional GC-MS methods were utilized to confirm all positive identifications indicated in Table 1.

Discussion

The selected blank herbal leaves are popular base-herb choices among makers of synthetic marijuana because they have pleasant aromas, low prices and are readily available. These leaf samples were analyzed through DART-MS as blanks and showed no mass spectral peaks that could be associated with synthetic cannabinoids. For the NMR experiments, the blank leaves were prepared using the same extraction method utilized for the herbal spice samples prior to their NMR analyses. Peaks were not found between 6.5-9 ppm or from 3.5-5 ppm, which is where most synthetic cannabinoids demonstrate strong signals. These results confirmed that the detected signals in the spice samples all originated from the synthetic compounds rather than natural herbal constituents.

The combination of DART-TOF-MS and NMR, used in conjunction with the standards, quickly identified the synthetic cannabinoids in their powder form and as an additive in the herbal products. Total analysis time was under one hour including about five minutes for DART-MS analysis and under 10 minutes for NMR analysis. The NMR analytical time can be further reduced if a more sensitive probe is used to increase S/N. According to our study, the four-minute 32-NMR scans generated a S/N of 4 to 1 for as little as 50 μg (slightly above LOD) of a cannabinoid sample with successful identification. Our HPLC-Diode Array Detection (DAD) quantification on all the herbs (in supplemental Table S3) revealed that the concentration of cannabinoid on herbal base ranges from 1-50mg/g of herb. 50 μg is usually below the amount we found on 50 mg herbal product. When the sample concentration falls below 0.05mg/mL comparable to DART-MS LOD (11), the NMR scan times have to be increased to four hours or more in order to obtain a spectrum with a S/N higher than 5. The

adoption of 50 mg of herbal sample size for NMR investigation implies that at least 50 μg was placed in an NMR tube along with 0.5-1mL $CDCl_3$. The concentration of a cannabinoid was much higher than the detection limit of 1 part per million or 1ug/g for H1-NMR. Mixtures of two or three cannabinoids were readily identified by using the combined NMR and MS methods (Table 1).

As Table 1 demonstrates, NMR and DART-MS complement each other in the analysis of herbal blends, especially when more than one synthetic cannabinoid is present. Out of four "Mountain Industry" powder samples, three were found to be mislabeled: "AM-1221" was indeed AM-2201 (Figure 1); "AM-2201" is actually JWH-019; "JWH-122" is mislabeled "JWH-200". The mislabeling indicates that there is no quality control from these rogue vendors of cannabinoid powders or there might be intentional mislabeling to avoid law enforcement as the true contents tended to be quickly banned by authorities. In the seven herbal products tested by the NMR and DART-MS methods, one to three cannabinoids were detected. For product with very low concentration of cannabinoids (e.g. Sweet Leaf), the NMR signal from the minor ingredient JWH-250 is approaching the LOD as indicated in supplemental Figure S1 and supplemental Table S3.

If one minor component is missed by one method, the other method usually detects it. The minor ingredient in the NMR spectrum often produces peaks with poor S/Ns so either more scans need to be acquired, which increases experiment time, or an increased sample amount (e.g. 200 mg) is necessary. Additionally, increased sampling with more sample batches is sometimes necessary to get a better representation of the whole package. The herbal sample is not homogenized to demonstrate the variation in concentrations for "hot" and "cold" spots, which could cause great harm for unaware users. DART-MS produces a spectrum of the molecular ions (30V on Orifice 1), indicating how many species are in the sample and their molecular formula via exact mass. Mixtures were detected with DART-MS spectra as signals of various heights, which further confirmed the non-uniformity of the synthetic compound distribution among the herbal bases. Sometimes only one compound was discovered on one piece of leaf while another piece from the same bag at a different location produced peaks responsible for two synthetic compounds in the mass spectrum. These results show that it is important to perform at least three different measurements using different leafs from a particular herbal sample to comprehensively identify all of the components in an herbal mixture. And this also made NMR confirmation very important as the 50-mg sample size usually contains more than a dozen pieces of leafs.

Furthermore, care must be taken during the analysis of the MS data as isomers are often identified after matching an unknown elemental composition with the library results. As pointed out by Steiner (11), TOF-MS cannot differentiate isomers by accurate mass measurements alone. Therefore, it is necessary to do in-source CID at different cone voltages (e.g. 90 and 120V) to produce the complementary fragmentation data for any given analyte. This data must then be carefully analyzed to help identify the compound. After preliminary identification through this fragmentation data, the identity can be further strengthened through subsequent NMR experiments. Figure 6 demonstrates the powerful capability of NMR in differentiating two close isomers of AM-2201. The only difference between the two isomers is the connection location of the naphthyl ring to the carbonyl group. Most MS techniques would have a hard time differentiating the two isomers because they would produce identical fragments with similar peak height ratios. The subtle change in structure also makes the GC-MS library search difficult, as region-isomeric MS spectra are extremely close. Many MS spectra and NMR spectra for the cannabinoid standards can be obtained from expanding forensic databases, such as the one funded by NIJ and developed by RTI international at the Research Triangle Park in North Carolina, USA (17). This database provides free access to drug compound spectra using multiple instrumental methods such as MS, Fourier-Transform infrared spectroscopy (FTIR), and NMR. A free DART-MS library was compiled by Virginia State department of Forensic Science (18). SWG-DRUG also has monographs of synthetic cannabinoids and spectral libraries (19). These standard spectra can provide conclusive and decisive identifications of emerging cannabinoids from DART-MS and NMR screenings. With the banning of more synthetic compounds, the “Spice” producers are still pursuing even more novel compounds to evade the ban list. Therefore, careful analysis of the fragmentation MS spectra along with NMR confirmation will be required to provide concrete identification in the future.

Analytical challenges still remain with the detection of these synthetic cannabinoids due to the difficulty in obtaining all possible standards and in deconvoluting the interference signals from the background matrix. When the cannabinoids are not fully separated on GC-MS chromatogram, spectral deconvolution is also necessary (20). The ionization and fragmentation steps used during MS analysis are not always adequate to differentiate isomers, especially those structural isomers with identical fragments. When the isotope ratio data and accurate masses are obtained, DART-MS spectra can be used to confirm their molecular formulae.

Additionally, the fragment elemental compositions obtained from the accurate mass data can be used to confirm the presence of aromatic ring structures within the molecules. With NMR confirmation, the position of the substitution group on an aromatic ring can be determined (when compared to standard spectrum) as each proton in a unique chemical environment produces a unique signal that remains the same even in an herbal mixture. NMR analysis on herbal extracts occasionally omits the synthetic components with lower abundance in the mixture and some of the signals are masked by the botanical matrix as well as flavor and dye additives.

Illicit drug users and vendors, however, will continue to develop new analogous synthetic compounds for their herbal products. The accelerated analytical techniques introduced in our work can be deployed to obtain quick identification, providing useful alternatives to other separation and spectroscopic methods such as TLC, LC-MS or GC-MS. The amount of herb needed is only 50 mg, which largely reduced the need to consume and destroy large amounts of sample and also minimized the usage of organic solvents and reduced waste associated with LC mobile phases or conventional SPE or solvent extractions.

With the combination of DART-MS and NMR, the identification of synthetic cannabinoids can be completed within an hour with simple extraction and minimal sample preparation effort with little involvement of organic solvents and no derivatization step. All synthetic cannabinoids, even on herbal products, were successfully ionized with the DART source and produced distinctive “molecular fingerprints” of H-1 NMR spectra. Our NMR method does not involve any heating while GC-based methods use high temperatures (usually above 250 ºC), sometimes decomposing or changing the nature of, the synthetic cannabinoids (21). Our methods also circumvent the difficulties of isomer differentiation from other MS-based detection methods (LC-MS, GC-MS) as used in conventional forensic drug analysis labs (22).The non-destructive nature of NMR facilitates the alternative analyses considering that the cannabinoids are preserved after NMR scanning and can be recovered for other testing. There is also an absence of “ghost peaks” (peaks from previous injections which could be higher molecular-weight and herbal component) as sometimes experienced in GC chromatograms for drug analyses (23). Although few forensic laboratories have access to DART-MS and NMR due to funding constraints and lack of expertise, our methodologies possess unique benefits that can potentially be used in contract organizations to provide evidence analysis service for law enforcement agencies.

Compared to conventional NMR methods (1, 7-10) in which analyze a milligram or more of each pure compound is extracted and separated prior to NMR scanning, our NMR method only requires 50 mg of herbal sample containing as little as 50 μg of synthetic cannabinoid with virtually no sample clean-up steps or chromatographic separation. We focused our analysis on the non-overlapping "fingerprint" regions of proton-NMR spectra for identification, taking advantage of the power of NMR spectral separation. The herbal matrix peaks (usually in 0-3ppm) were ignored to accelerate the analytical time. This approach dramatically shortened the analytical time and decreased sample consumption, which are crucial benefits for backlog reduction efforts. The reduced organic solvent usage and bypassing any filters, extraction or separation columns or TLC plates achieved simple sample preparation and saved analytical cost, which are highly desired in forensic labs.

In summary, the combination of simple NMR and DART-MS methods can used to successfully screen synthetic cannabinoids rapidly and without ambiguity, providing a helpful alternative to conventional GC-MS or LC-MS methods for designer drug detection. The combined method also maximizes the potential of instrumental detection and signal separation power that is inherent in DART-MS and NMR while minimizing cumbersome wet chemistry processing and organic solvent usage. Up to a three-component mixture from herbal Spice sample was detected with the correct isomer identifications (Table 1). The DART-MS+NMR method will hopefully accelerate the drug detection process in the enforcement of current laws and regulations, as well as the detection of future blends sold as "herbal potpourri" or "legal highs".

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Two supplemental NMR data tables containing all standard and herbal NMR signal assignments can be accessed online. One additional supplemental LC-DAD data table can be used as confirmation of the presence of detected cannabinoids in the analyzed herbal products. One supplemental H-1 NMR spectrum for Sweet Leaf herbal extract is given.

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Table 1 Identification results for synthetic cannabinoid powder samples and herbs

Product	Label/Matrix	AM-2201	JWH-122	JWH-203	RCS-04	Other
“AM-1221”	Mountain Industry Powder	DART-MS + NMR +	-	-	-	-
“AM-2201”	Mountain Industry Powder	-	-	-	-	JWH-019 (DART-MS +, NMR +)
“JWH-122”	Mountain Industry Powder	-	-	-	-	JWH-200 (DART-MS +, NMR +)
“JWH-203”	Mountain Industry Powder	-	-	DART-MS + NMR +	-	-
Barely Legal	Botanical	DART-MS + NMR +	-	-	DART-MS + NMR +	-
Funky Monkey	Botanical	-	DART-MS + NMR +	-	-	-
Ion Lab	Botanical	DART-MS + NMR +	-	-	DART-MS + NMR +	-
Melon Code Black	Botanical	-	DART-MS + NMR +	DART-MS + NMR +	-	-
Moon Spice	Botanical	-	-	-	DART-MS + NMR +	JWH-018 (DART-MS +, NMR +)
Mr. Nice Guy	Botanical	DART-MS + NMR +	DART-MS + NMR +	-	-	-
Sweet Leaf	Botanical		DART-MS + NMR +			JWH-210 (DART-MS +, NMR +) JWH-250 (DART-MS +, NMR +)

Table 2 H-1 NMR chemical shift values of the standards used for the confirmation of their presence in herbal extracts

Label	MI "AM-1221"	Cayman AM-2201	MI "AM-2201"	Reference JWH-018 (1,7)	MI "JWH-081"	Cayman JWH-122	MI"JWH-122"	MI"JWH -203"	Cayman JWH-210	MI "JWH-250"	Cayman RCS-04	Label
Actual	AM-2201	A.L.	JWH-19	JWH-018	A.L.	A.L.	JWH-200	A.L.	A.L.	A.L.	A.L.	**Actual**
H-2	7.30-7.41	7.34 S	7.34 S	7.34	7.35 M	7.32-7.38	7.44 M	7.87 S	7.36 M	7.86 S	7.57 S	**H-2**
H-4	8.49 M	8.49 M	8.48 M	8.49	8.46 M	8.48 M	8.52 M	8.39 M	8.48 M	8.40 M	8.36 M	**H-4**
H-5	7.34-7.40	7.34-7.37	7.35 M	7.33-7.39	7.35 M	7.34	7.36 M	7.28 M	7.32-7.40	7.25 M	7.28 M	**H-5**
H-6	7.34-7.40	7.34-7.37	7.33 M	7.33-7.39	7.31-7.41	7.32-7.38	7.33-7.42	7.33 M	7.32-7.40	7.25-7.32	7.31 M	**H-6**
H-7	7.34-7.40	7.34-7.37	7.37 M	7.33-7.39	7.31-7.41	7.32-7.38	7.33-7.42	7.36 M	7.32-7.40	7.25-7.32	7.38 M	**H-7**
H-2"	7.65 M	7.65 D	7.65 dD	7.64	7.65 D	7.55 M	7.65 D	-	7.55 M	-	7.84 D	**H-2"**
H-3"	7.51 M	7.50 M	7.50 M	7.51	6.82 D	7.36 M	7.51 M	7.38 M	7.32-7.40	6.87 D	6.98 D	**H-3"**
H-4"	7.96 D	7.96 D	7.96 D	7.95	-	-	7.96 D	7.19 M	-	7.21 M	-	**H-4"**
H-5"	7.90 D	7.90 D	7.90 D	7.89	8.30 M	8.06 D	7.90 D	7.23 M	8.12 D	6.91 T	6.98 D	**H-5"**
H-6"	7.50 M	7.49 M	7.51 M	7.5	7.49 M	7.54 M	7.50 M	7.29 M	7.55 M	7.29 M	7.84 D	**H-6"**
H-7"	7.46 M	7.45 M	7.45 M	7.45	7.50 M	7.47 T	7.45 M	-	7.46 T	-	-	**H-7"**
H-8"	8.18 D	8.18 D	8.18 D	8.19	8.33 M	8.24 D	8.17 D	-	8.24 D	-	-	**H-8"**
H-1'	4.09 T	4.09 T	4.06 T	4.03	4.07 M	4.06 T	4.14 T	4.15 T	4.06 T	4.12 M	4.14 T	**H-1'**
H-5'	4.37 dT	4.37 dT	<3	<3	<3	<3	<3	<3	<3	<3	<3	**H-5'**
H-4"C1	-	-	-	-	-	<3	-	-	3.17 Q	-	-	**H-4"C1**
H-2"O	-	-	-	-	-	-	-	-	-	3.81 S	-	**H-2"O**
H-4"O	-	-	-	-	4.05 S	-	-	-	-	-	3.88 S	**H-4"O**
H-2*	-	-	-	-	-	-	-	4.31 S	-	4.16 S	-	**H-2***

MI= Mountain Industry. A.L.= as labeled, S=singlet, D=doublet, T=triplet, Q=quadruplet, M=multiplet, dD=doublet of doublets, dT=doublet of triplets

Table 3 Chemical shift values identified in 50mg herbal extracts

Label	Barely Legal		Melon Code Black		Moon Spice		Sweet Leaf		
ID	AM-2201	RCS-04	JWH-122	JWH-203	RCS-04	JWH-018	JWH-210	JWH-122	JWH-250
H-2	7.28-7.41	7.41-7.58	7.32-7.40	7.88 S	7.57 S	7.36 M	7.32-7.40	7.32-7.38	7.86 S
H-4	4.48 M	8.36 M	8.46 M	8.39 M	8.36 M	8.47 M	8.48 M	8.48 M	8.39 M
H-5	7.28-7.41	7.28-7.41	7.32-7.40	7.28 M	7.25-7.38	7.33-7.38	7.32-7.40	7.32-7.38	7.25-7.32
H-6	7.28-7.41	7.28-7.41	7.32-7.40	7.32-7.40	7.25-7.38	7.33-7.38	7.32-7.40	7.32-7.38	7.25-7.32
H-7	7.28-7.41	7.28-7.41	7.32-7.40	7.32-7.40	7.25-7.38	7.33-7.38	7.32-7.40	7.32-7.38	7.25-7.32
H-2"	7.64 M	7.83 M	7.55 M	-	7.84 D	7.64 M	7.55 M	7.55M	-
H-3"	7.41-7.58	6.98 M	7.32-7.40	7.32-7.40	6.98 D	7.52 M	7.32-7.40	7.32-7.38	6.87 D
H-4"	7.96 M	-	-	7.19-7.23	-	7.96 D	-	-	7.21 M
H-5"	7.90 M	6.98 M	8.05 M	7.19-7.23	6.98 D	7.90 D	8.12 D	8.06 D	6.91 T
H-6"	7.41-7.58	7.83 M	7.54 M	7.26-7.30	7.84 D	7.48 M	7.55 M	7.54 M	7.25-7.32
H-7"	7.41-7.58	-	7.47 T	-	-	7.48 M	7.46 T	7.47 T	-
H-8"	8.16 D	-	8.22 M	-	-	8.17 D	8.24 D	8.24 D	-
H-1'	4.09 M	4.15 M	4.06 T	4.15 T	4.15 T	4.05 T	4.06 T	4.06 T	4.12 T
H-4"O	-	3.88 S	-	-	3.88 S	-	-	-	3.81 S
H-5'	4.37 dM	-	-	-	-	-		-	-
H-4"C	-	-	-	-	-	-	3.17 Q	-	-
H-2*	-	-	-	4.31 S	-	-	-	-	4.16 S

S=singlet, D=doublet, T=triplet, Q=quadruplet, M=multiplet

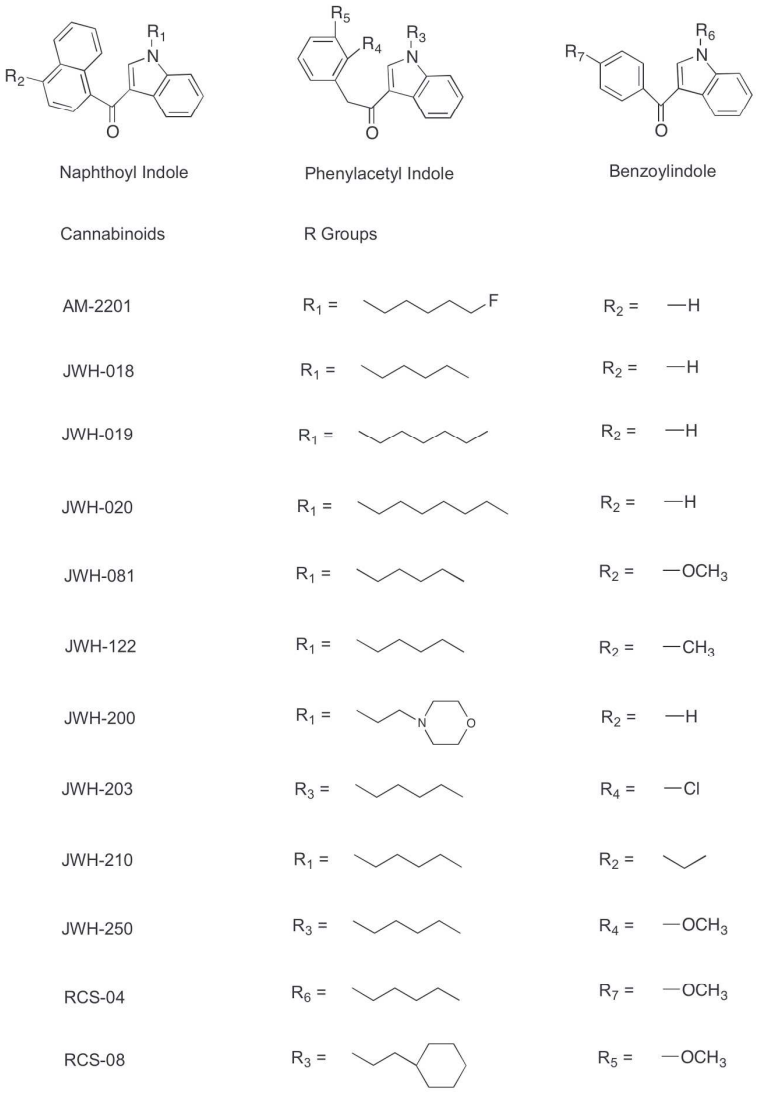

FIG. 1 Structures of synthetic indole cannabinoids
154x223mm (300 x 300 DPI)

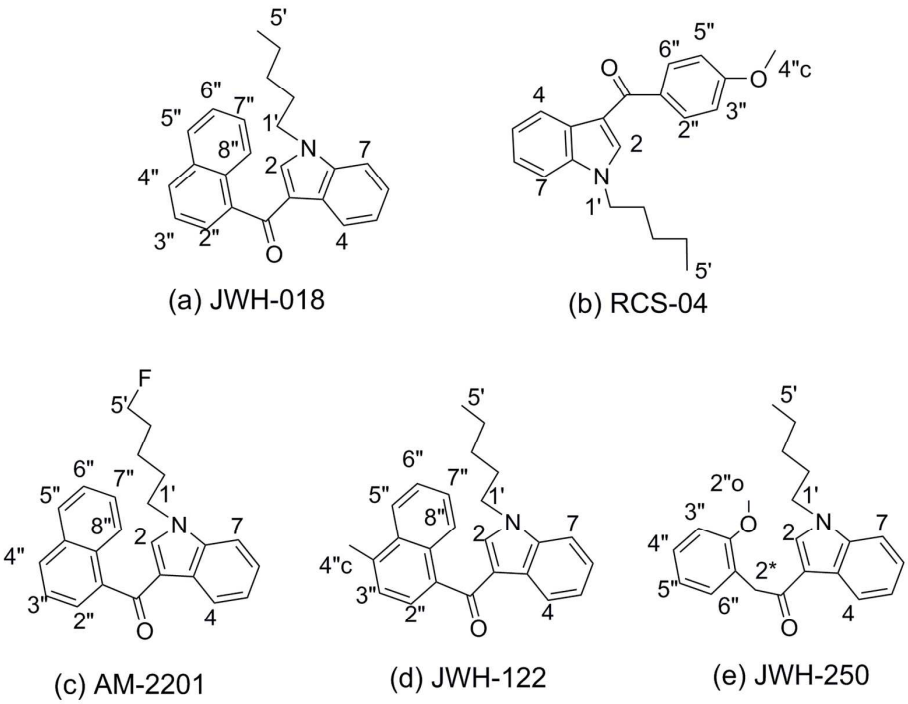

FIG. 2 Synthetic cannabinoid structures with numbering scheme: (a) JWH-018, (b) RCS-04, (c) AM-2201, (d) JWH-122, (e) JWH-250
138x107mm (300 x 300 DPI)

FIG. 3 Various Spice products: (a). "Mountain Industry" JWH-122 powder, (b) "Moon Spice" leaf, (c) "Barely Legal" "Spice" package, (d) "Melon: Code Black" "Spice" package.
152x139mm (300 x 300 DPI)

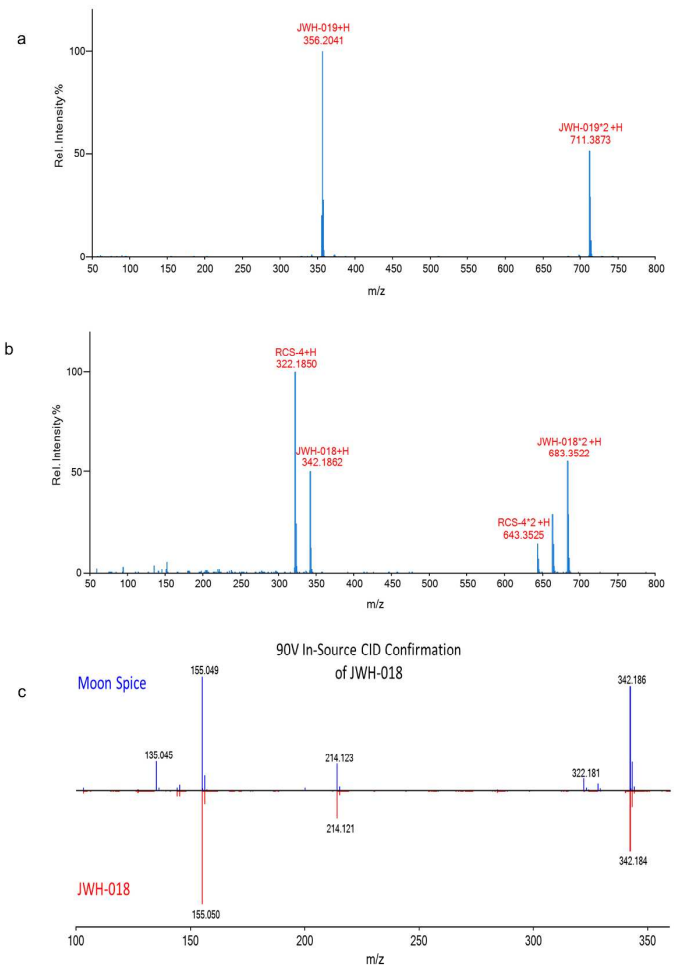

FIG. 4 DART-MS Spectra of (a) JWH-019 powder standard and (b) one piece of "Moon Spice" leaf, along with (c) the comparison of the 90V-spectra between "Moon Spice" leaf and JWH-018 standard powder.
381x508mm (300 x 300 DPI)

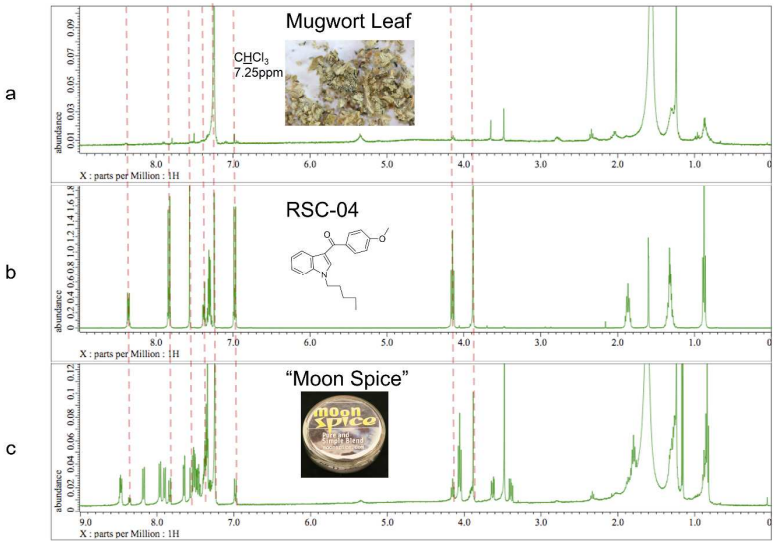

FIG. 5 Proton-NMR spectra of (a) 50 mg blank herb "Mugwort Leaf" extracted with CDCl3, (b) 5 mg RCS-04 standard powder in 1 mL CDCl3, and (c) 50 mg "Moon Spice" herbal sample extracted with 1 mL CDCl3.
558x431mm (300 x 300 DPI)

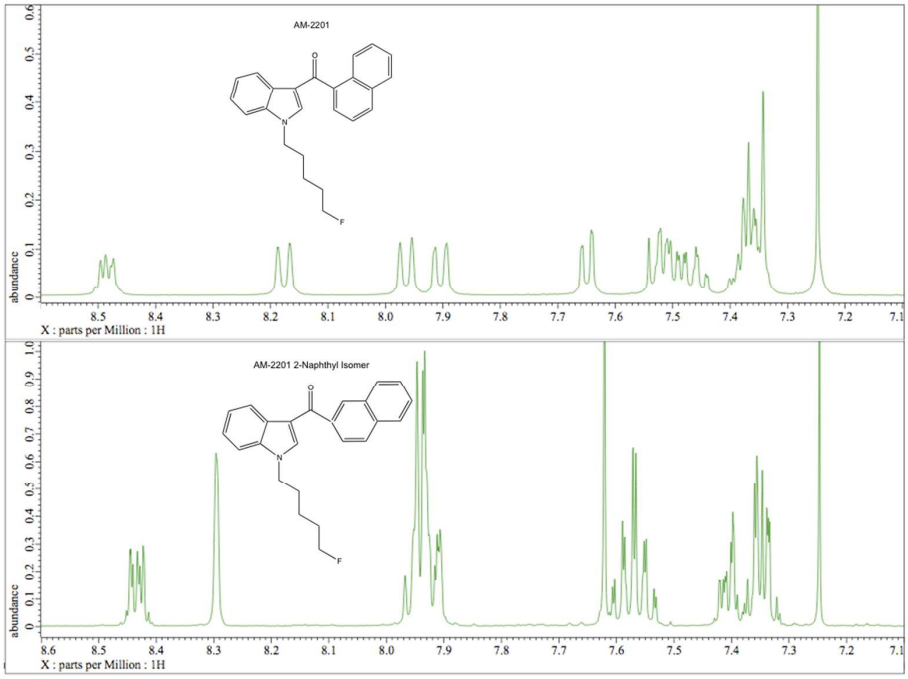

FIG. 6 Comparison of the H-1 NMR spectra of AM-2201 and the corresponding 2"-isomer
190x142mm (300 x 300 DPI)

$CDCl_3$ Proton STANDARDS (Avg. Method)

Label Actual	Reference JWH-018	RCS-04 As Labeled (MI)	RCS-04 (in Acetone) (Cayman)	"AM-1221" AM-2201 (Impurities)	"AM-2201" JWH-019	JWH-081 As labeled	"JWH-122" JWH-200
H-2	7.34	7.58 S	7.88 S	7.36 M	7.34 S	7.35 M	7.37 M
H-4	8.49	8.36 M	8.32 D	8.48 M	8.48 M	8.46 M	8.52 M
H-5	7.33-7.39	7.30 M	7.18-7.27 M	7.35 M	7.35 M	7.34 M	7.36 M
H-6	7.33-7.39	7.32 M	7.18-7.27 M	7.36 M	7.33 M	7.32-7.39	7.44-7.54
H-7	7.33-7.39	7.38 M	7.52 D	7.40 M	7.37 M	7.32-7.39	7.44-7.54
H-1"	-	-	-	-	-	-	-
H-2"	7.64	7.84 D	7.80 D	7.64 M	7.65 Dd	7.64 D	7.65 D
H-3"	7.51	6.98 D	6.99 D	7.52 M	7.50 M	6.82 D	7.51 M
H-4"	7.95	-	-	7.97 D	7.96 D	-	7.96 D
H-5"	7.89	6.98 D	6.99 D	7.91 D	7.90 D	8.29 M	7.90 D
H-6"	7.5	7.84 D	7.80 D	7.50 M	7.51 M	7.50 M	7.49 M
H-7"	7.45	-	-	7.45 M	7.45 M	7.50 M	7.46 M
H-8"	8.19	-	-	8.17 D	8.18 D	8.34 M	8.16 D
H-1'	4.03	4.15 T	4.29 T	4.09 T	4.06 T	4.07 T	4.14 M
H-2'	1.78	1.87 M	1.86 M	1.84 M	1.79 M	1.80 M	2.69 S
H-3'	1.22	1.32 M	1.29 M	1.38 M	1.23 M	1.26 M	-
H-4'	1.27	1.33 M	1.29 M	1.63 M	1.25 M	1.30 M	-
H-5'	0.84	0.88 T	0.81 T	4.36 Dt	1.23 M	0.84 M	-
H-6'	-	-	-	-	0.82 T	-	-
H-7'	-	-	-	-	-	-	-
H-8'	-	-	-	-	-	-	-
H-2C	-	-	-	-	-	-	-
H-1"N	-	-	-	-	-	-	-
H-2"C(a/b)	-	-	-	-	-	-	-
H-3"C(a/b)	-	-	-	-	-	-	-
H-2"O	-	-	-	-	-	-	-
H-3"O	-	-	-	-	-	-	-
H-4"a	-	-	-	-	-	-	-
H-4"b	-	-	-	-	-	-	-
H-4"O	-	3.88 S	3.84 S	-	-	4.06 S	-
H-4"C	-	-	-	-	-	-	-
H-4"Ca	-	-	-	-	-	-	-
H-4"Cb	-	-	-	-	-	-	-
H-5"N	-	-	-	-	-	-	-
H-3'N	-	-	-	-	-	-	2.38 T
H-6'N	-	-	-	-	-	-	2.38 T
H-4'O	-	-	-	-	-	-	3.54 M
H-5'O	-	-	-	-	-	-	3.54 M
2*	-	-	-	-	-	-	-
MeOH	-	-	-	-	-	-	-
Acetone	-	-	2.00 S	-	-	-	-

$CDCl_3$ Proton STANDARDS

JWH-20 As labeled	Label Actual	JWH-203 As labeled (Impurities)	JWH-250 As labeled	JWH-122 Cayman	AM-2201 Cayman	JWH-210 Cayman	UR-144 Cayman	RCS-08 As labeled
7.36 M	H-2	7.87 S	7.86 S	7.35 M	7.34 S	7.36 M	7.65 S	7.87 S
8.47 M	H-4	8.39 M	8.40 M	8.47 M	8.48 M	8.49 M	8.39 M	8.39 M
7.34-7.40	H-5	7.28 M	7.25 M	7.34 M	7.34 M	7.34 M	7.27 M	7.23-7.34
7.34-7.40	H-6	7.33 M	7.25-7.32	7.37 M	7.37 M	7.40 M	7.33 M	7.23-7.34
7.34-7.40	H-7	7.36 M	7.25-7.32	7.40 M	7.40 M	7.32-7.41	7.38 M	7.23-7.34
-	H-1"	-	-	-	-	-	1.94 S	-
7.64 M	H-2"	-	-	7.55 T	7.65 D	7.58 D	-	-
7.52 M	H-3"	7.38 M	6.87 D	7.35 h	7.50 M	7.38 M	-	6.88 D
7.96 D	H-4"	7.19 M	7.21 M	-	7.96 D	-	-	
7.90 D	H-5"	7.23 M	6.91 T	8.06 D	7.90 D	8.12 D	-	6.91 T
7.52 M	H-6"	7.29 M	7.29 M	7.55 M	7.48 M	7.54 Td	-	7.29 M
7.52 M	H-7"	-	-	7.46 T	7.44 M	7.45 Td	-	-
8.17 D	H-8"	-	-	8.23 D	8.18 D	8.23 D	-	-
4.06 T	H-1'	4.15 T	4.12 M	4.06 T	4.09 T	4.06 T	4.15 M	4.15 T
1.79 M	H-2'	1.88 M	1.85 M	1.79 M	1.86 M	1.80 M	1.87 M	
1.24 M	H-3'	1.32 M	1.31 M	1.24 M	1.39 M	1.26 M	1.34 M	
1.24 M	H-4'	1.32 M	1.31 M	1.28 M	1.64 M	1.28 M	1.34 M	
0.83 T	H-5'	0.89 T	0.88 T	0.84 T	4.36 Dt	0.84 T	0.88 M	
1.55 S	H-6'	-	-	-	-	-	-	
1.55 S	H-7'	-	-	-	-	-	-	
-	H-8'	-	-	-	-	-	-	
-	H-2C	-	-	-	-	-	-	-
-	H-1"N	-	-	-	-	-	-	-
-	H-2"C(a/b)	-	-	-	-	-	1.33/1.29	-
-	H-3"C(a/b)	-	-	-	-	-	1.33/1.29	-
-	H-2"O	-	3.81 S	-	-	-	-	3.82 S
-	H-3"O	-	-	-	-	-	-	-
-	H-4"a	-	-	-	-	-	-	-
-	H-4"b	-	-	-	-	-	-	-
-	H-4"O	-	-	-	-	-	-	-
-	H-4"C	-	-	2.77 S	-	-	-	-
-	H-4"Ca	-	-	-	-	3.17 M	-	-
-	H-4"Cb	-	-	-	-	1.43 T	-	-
-	H-5"N	-	-	-	-	-	-	-
-	H-3'N	-	-	-	-	-	-	-
-	H-6'N	-	-	-	-	-	-	-
-	H-4'O	-	-	-	-	-	-	-
-	H-5'O	-	-	-	-	-	-	-
-	2*	4.31 S	4.16 S	-	-	-	-	4.16 S
-	MeOH	-	-	-	-	-	-	-
-	Acetone	-	-	-	-	-	-	-

$CDCl_3$ Proton STANDARDS

RSC-08 Isomer (3-methoxy)	Label Actual	RCS-08 (4-methoxy)	JWH-019 Cayman	JWH-022 Cayman	AM-1220 Cayman	RCS-4 (C4 homolog) Cayman	RCS-4 (2-methoxy) Cayman
7.76 S	H-2	7.75 S	7.32-7.41	7.32-7.41	7.32-7.56	7.57 S	7.39-7.43
8.40 M	H-4	8.39 M	8.48 M	8.50 M	8.46 M	8.35 M	8.28 M
7.23-7.34	H-5	7.20-7.34	7.33 M	7.35 M	7.35 M	7.29 M	7.27 M
7.23-7.34	H-6	7.20-7.34	7.39 M	7.32-7.41	7.42 M	7.31 M	7.30-7.35
7.23-7.34	H-7	7.20-7.34	7.32-7.41	7.32-7.41	7.52 M	7.39 M	7.30-7.35
-	H-1"	-	-	-	-	-	-
6.88 S	H-2"	7.20-7.34	7.64 D	7.65 D	7.66 D	7.83 Dt	-
-	H-3"	6.85 D	7.50 M	7.51 M	7.52 M	6.98 Dt	6.98 T
6.77 D	H-4"	-	7.96 D	7.96 D	7.97 D	-	7.38 M
6.90 T	H-5"	6.85 D	7.90 D	7.90 D	7.91 D	6.98 Dt	7.26 M
7.28 M	H-6"	7.20-7.34	7.49 M	7.49 M	7.51 M	7.83 Dt	6.95 T
-	H-7"	-	7.44 M	7.46 M	7.47 M	-	-
-	H-8"	-	8.17 D	8.17 D	8.19 D	-	-
4.16 T	H-1'	4.15 T	4.06 T	4.08 T	4.53 and 3.84	4.16 T	4.05 T
1.60-1.79	H-2'	1.60-1.81	1.79 M	1.91 M	2.37 M	1.85 M	1.79 M
1.60-1.79	H-3'	1.60-1.81	1.23 M	2.03 M	-	1.35 M	1.26 M
1.60-1.79	H-4'	1.60-1.81	1.28 M	5.71 M	2.11 and 2.85	0.94 T	1.26 M
1.13-1.30	H-5'	1.12-1.34	1.22 M	4.96 M	1.61 and 1.58	-	0.82 T
0.90-1.04	H-6'	0.80-1.04	0.82 T	-	1.08 and 1.25	-	-
1.13-1.30	H-7'	1.12-1.34	-	-	1.08 and 1.50	-	-
1.60-1.79	H-8'	1.60-1.81	-	-	-	-	-
-	H-2C	-	-	-	-	-	-
-	H-1"N	-	-	-	-	-	-
-	H-2"C(a/b)	-	-	-	-	-	-
-	H-3"C(a/b)	-	-	-	-	-	-
-	H-2"O	-	-	-	-	-	3.74 S
3.77 S	H-3"O	-	-	-	-	-	-
-	H-4"a	-	-	-	-	-	-
-	H-4"b	-	-	-	-	-	-
-	H-4"O	3.77 S	-	-	-	3.88 S	-
-	H-4"C	-	-	-	-	-	-
-	H-4"Ca	-	-	-	-	-	-
-	H-4"Cb	-	-	-	-	-	-
-	H-5"N	-	-	-	-	-	-
-	H-3'N	-	-	-	2.41 S	-	-
-	H-6'N	-	-	-	-	-	-
-	H-4'O	-	-	-	-	-	-
-	H-5'O	-	-	-	-	-	-
4.11 S	2*	4.08 S	-	-	-	-	-
3.48	MeOH	-	-	-	3.48	-	-
-	Acetone	-	-	-	-	-	-

$CDCl_3$ Proton STANDARDS

RCS-4 (3-methoxy) Cayman	WIN 54461 Cayman	Label Actual	AM-679 Cayman	AB-Fubinaca Cayman	A-834735 Cayman	XLR-11 Cayman	AB-Pinaca Cayman
	-	H-2	7.29 S	-	7.61 S	7.66 S	-
8.29 M	7.74 Dm	H-4	8.32 M	8.33 D	8.39 M	8.39 M	8.31 M
7.25 M	7.72 Dm	H-5	7.33 M	7.27 M	7.25 M	7.26 M	7.27 M
	-	H-6	7.38 M	7.27-7.40	7.31 M	7.32 M	7.41 M
	7.48 S	H-7	7.40 M	7.27-7.40	7.34 M	7.34 M	7.44 M
-	-	H-1"	-	-	1.93 S	1.93 S	-
7.53 S	7.16 Dd	H-2"	-	4.50 M	-	-	4.49 M
-	6.91 Dm	H-3"	7.92 Dd	2.36 M	-	-	2.38 M
	-	H-4"	7.15 Td	-	-	-	-
	6.92 Dm	H-5"	7.42 M	-	-	-	-
	7.19 D	H-6"	7.37 M	-	-	-	-
-	-	H-7"	-	-	-	-	-
-	-	H-8"	-	-	-	-	-
4.08 T	4.21 T	H-1'	4.10 T	5.58 S	4.03 D	4.17 T	4.38 T
1.79 M	2.67 T	H-2'	1.84 M	-	2.14 M	1.95 M	1.94 M
1.25 M	-	H-3'	1.30 M	6.98 M	1.41 and 1.43	1.50 M	1.32 M
1.24 M	-	H-4'	1.31 M	7.18 Td	-	1.73 M	1.36 M
0.80 T	-	H-5'	0.87 T	-	-	4.43 Dt	0.88 T
-	-	H-6'	-	7.18 Td	1.41 and 1.43	-	-
-	-	H-7'	-	6.98 M	-	-	-
-	-	H-8'	-	-	-	-	-
-	2.58 S	H-2C	-	-	-	-	-
-	-	H-1"N	-	7.48 D	-	-	7.46 M
-	-	H-2"C(a/b)	-	-	1.30 and 1.33	1.29 and 1.34	-
-	-	H-3"C(a/b)	-	-	1.30 and 1.33	1.29 and 1.34	-
-	-	H-2"O	-	-	-	-	-
3.79 S	-	H-3"O	-	-	-	-	-
-	-	H-4"a	-	1.07 D	-		1.07 Dd
-	-	H-4"b	-	1.07 D	-	-	1.07 Dd
-	3.88 S	H-4"O	-	-	-	-	-
-	-	H-4"C	-	-	-	-	-
-	-	H-4"Ca	-	-	-	-	-
-	-	H-4"Cb	-	-	-	-	-
-	-	H-5"N	-	5.74 D	-	-	5.77 D
-	2.52 T	H-3'N	-	-	-	-	-
-	2.52 T	H-6'N	-	-	-	-	-
-	3.70 T	H-4'O	-	-	3.32 and 3.96	-	-
-	3.70 T	H-5'O	-	-	3.32 and 3.96	-	-
-	-	2*	-	-	-	-	-
-	3.48	MeOH	-	-	-	-	-
-	-	Acetone	-	-	-	-	-

JWH-007 Cayman	AKB-48 (A-Pinaca) Cayman
-	-
8.09 D	8.37 D
7.42 T	7.23 M
7.49 T	7.38 D
7.55 D	7.38 D
-	-
7.96 D	2.20 M
7.49 T	2.13 M
7.90 D	1.72 M
6.98 M	-
7.13 M	-
7.16 M	-
7.30 D	-
4.11 T	4.34 T
1.78 M	1.92 M
1.36 M	1.30 M
1.36 M	1.35 M
0.90 T	0.88 T
-	-
-	-
-	-
2.48 S	-
-	-
-	-
-	-
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CDCl Proton HERBS (Avg. Method)

Label Name	Sweet Leaf			Cloud Nine		Melon Code Black	
Possible ID	JWH-210	JWH-122	JWH-250	XLR-11	UR-144	JWH-122	JWH-203
H-2	7.33 M	7.33 M	7.87 S	7.65 S	7.65 S	7.35 M	7.86 M
H-4	8.48 M	8.48 M	8.40 M	8.39 M	8.39 M	8.46 M	8.39 M
H-5	7.35 M	7.35 M	7.26 M	7.26 M	7.26 M	7.31-7.39	7.19-7.30
H-6	7.24-7.38	7.24-7.38	7.24-7.38	7.33 M	7.33 M	7.31-7.39	7.19-7.30
H-7	7.24-7.38	7.24-7.38	7.24-7.38	7.30-7.35	7.30-7.35	7.31-7.39	7.19-7.30
H-1"	-	-	-	1.93 S	1.93 S	-	-
H-2"	7.58 D	7.55 M	-	-	-	7.55 M	-
H-3"	7.38 M	7.37 M	6.87 D	-	-	7.55 M	7.25 M
H-4"	-	-	7.33 M	-	-	-	7.25 M
H-5"	8.12 D	8.06 D	6.91 T	-	-	8.05 M	7.23 D
H-6"	7.51 M	7.51 M	-	-	-	7.46 M	7.35 M
H-7"	7.51 M	7.51 M	-	-	-	7.46 M	-
H-8"	8.23 M	8.23 M	-	-	-	8.23 M	-
H-1'	4.06 T	4.06 T	4.12 M	4.17 M	4.14 M	4.06 T	4.15 T

CDCl Proton HERBS (Avg. Method)

Rack City	Label Name	Ion Source		K-250	Extremely Legal XXX	
XLR-11	Possible ID	JWH-203	RCS-08	JWH-250	JWH-122	JWH-210
7.65 S	H-2	7.31 M	7.31 M	7.27 M	7.36 M	7.36 M
8.39 M	H-4	8.39 M	8.39 M	8.39 M	8.47 M	8.47 M
7.26 M	H-5	7.23-7.39	7.23-7.39	7.20-7.33	7.33-7.40	7.33-7.40
7.32 M	H-6	7.23-7.39	7.23-7.39	7.20-7.33	7.33-7.40	7.33-7.40
7.34 M	H-7	7.23-7.39	7.23-7.39	7.20-7.33	7.33-7.40	7.33-7.40
1.93 S	H-1"	-	-	-	-	-
-	H-2"	-	6.89 M	-	7.56 M	7.56 M
-	H-3"	7.31 M	-	6.89 M	7.53 M	7.56 M
-	H-4"	7.31 M	6.89 M	7.27 M	8.06 D	8.12 D
-	H-5"	7.87 D	7.51 M	7.85 M	8.06 D	8.12 D
-	H-6"	7.31 M	7.31 M	-	7.47 M	7.47 M
-	H-7"	-	-	-	7.47 M	7.47 M
-	H-8"	-	-	-	8.23 D	8.23 D
4.17 T	H-1'	4.13 M	4.13 M	4.13 M	4.05 T	4.05 T

CDCl Proton HERBS (Avg. Method)

Head Trip	Nuclear Bomb	Label Name	Zombie Matter		Mr. Nice Guy	
JWH-210	JWH-122	Possible ID	AM-2201	JWH-210	AM-2201	JWH-122
7.34 M	7.34 M	H-2	7.31-7.40M	7.31-7.40M	7.35 M	7.35 M
8.46 M	8.43 M	H-4	8.48 M	8.48 M	8.48 M	8.48 M
7.29-7.39	7.32-7.35	H-5	7.32-7.40	7.32-7.40	7.34-7.37	7.34-7.37
7.29-7.39	7.32-7.35	H-6	7.32-7.40	7.32-7.40	7.34-7.37	7.34-7.37
7.29-7.39	7.32-7.35	H-7	7.32-7.40	7.32-7.40	7.34-7.37	7.34-7.37
-	-	H-1"	-	-	-	-
7.54 M	N/D	H-2"	7.65D	7.58 D	7.42-7.58	7.65 D
7.54 M	7.53 M	H-3"	7.42-7.56	7.32-7.40	7.51 M	7.56 M
8.12 D (small)	8.04 M	H-4"	7.96 D	-	7.97 D	-
8.12 D (small)	N/D	H-5"	7.90 D	8.12 D	7.90 D	8.06 D
7.46 T	7.46 M	H-6"	7.42-7.56	7.42-7.56	7.49 M	7.52 M
7.46 T	7.46 M	H-7"	7.42-7.56	7.42-7.56	7.45 M	7.45 M
8.22 D	8.19 M	H-8"	8.17 D	8.23 D	8.18 D	8.23 D
4.05 T	4.04 M	H-1'	4.09-4.03	4.09-4.03	4.09 M	4.07 M

Moon Spice	
RCS-04	JWH-018
7.36 M	7.36 M
8.36 M	8.47 M
7.25-7.38	7.33-7.38
7.25-7.38	7.33-7.38
7.25-7.38	7.33-7.38
-	-
7.84 D	7.64 M
6.98 D	7.52 M
-	7.96 D
6.98 D	7.90 D
7.84 D	7.48 M
-	7.48 M
-	8.17 D
4.15 T	4.05 T

Table S3 LC-DAD results for herbal extract

Separation conditions: Phenomenex Luna 5 u Phenyl-Hexyl column (150 * 4.6 mm),

70% Acetonitrile and 30% H2O isocratic separation, 1.5 mL/min flow rate, 1 uL injection, 210 nm and 280 nm detection

Herbal Incense	TR1 (min)	ID1	Conc1 (mg/g)	TR2(min)	ID2	Conc.2	TR3 (min)	ID3	Conc.3
Sweet Leaf	11.09	JWH-210	0.88±0.59	9.05	JWH-122	0.44±0.26	5.8	JWH-250	0.09±0.08
Cloud Nine	3.56	XLR-11	9.66±0.37	4.78	UR-144	10.6±0.32			
Melon Code Black	6.80	JWH-203	8.30±0.80	9.223	JWH-122	5.1±0.5			
Rack City	3.58	XLR-11	11.24±3.75						
Ion Source	8.86	RCS-8	2.57±0.46	6.70	JWH-203	1.16±0.05			
K-250	5.79	JWH-250	2.49±0.53						
Extremely Legal XXX	9.09	JWH-122	9.98±2.70	11.11	JWH-210	1.17±1.00			
Head Trip	9.11	JWH-122	12.6±0.53	11.12	JWH-210	2.48±0.44			
Nuclear Bomb	9.10	JWH-122	4.53±0.30						
Zombie Matter	5.55	AM-2201	6.53±0.17	11.15	JWH-210	5.8±0.8			
Mr. Nice Guy	7.08	AM-2201	47.0±3.18	12.02	RCS-8	12.8±2.33			
Moon Spice	7.79	JWH-018	6.6±0.8	5.21	RCS-4	2.44±0.60			

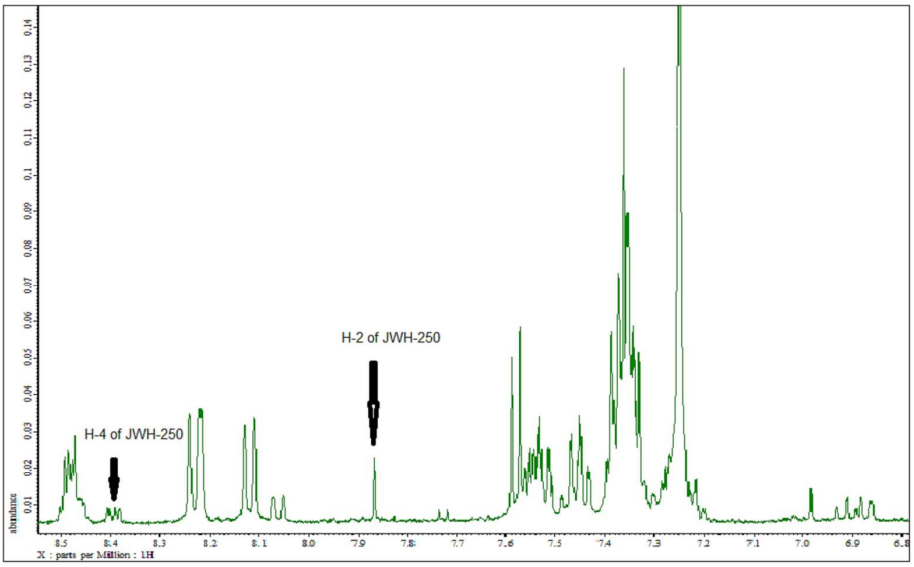

Fig. S1 H1-NMR spectrum Sweet Leaf herbal extract showing very low JWH-250 signals
406x250mm (300 x 300 DPI)