Streamlining Cannabis Testing Using GC-MS and GCxGC-MS

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Background

- The composition of cannabis is very important in determining its utility, potency, and medicinal effectiveness
- Cannabis is difficult to analyze because of its chemical diversity, but more importantly the wide concentration ranges of its constituents
- Analysis often requires:
  - Tedious sample preparation
  - Specialized (targeted) instrumental analysis

Objectives

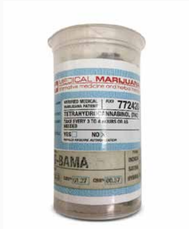
- Reduce sample manipulation & shorten preparation times
- Explore the possibility of streamlining cannabis screening
- Maximize the information obtained per analysis
- Implement the use of GC-TOFMS and GCxGC-TOFMS to effectively profile cannabis samples
- Use automated data processing software to quickly and confidently identify compounds
- Ultimately, the question to be answered… ***Is the product safe?***

Moisture | Potency | Terpenes (Flavor/Fragrance) | Residual Solvents | Pesticides | Microbials | Metals

One Analytical Platform

Samples

Terpene Oils and HEMP



Medical Marijuana

Recreational Marijuana

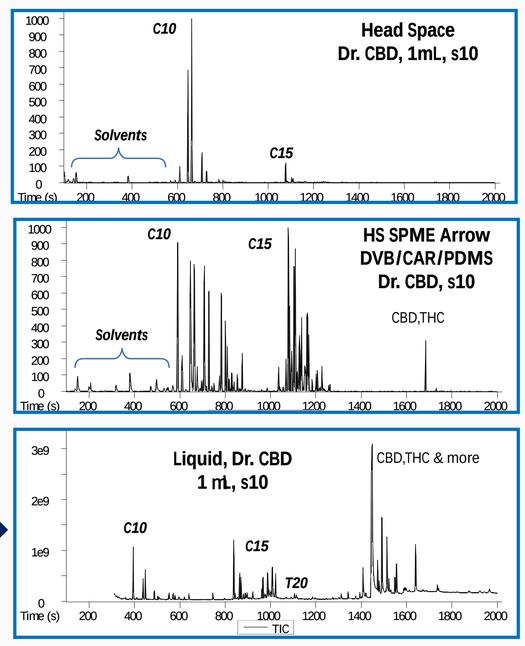
Instrument Parameters

Gas Chromatograph	Agilent 7890, LECO Dual Stage Quad Jet Modulator & L-PAL 3 Autosampler	
Injection	Variable (250 °C)	
Carrier Gas	He @ 1.0 mL/min, Constant Flow	
Columns (1st Dimension) (2nd Dimension)	Rxi-5 MS, 30 m x 0.25 mm i.d. x 0.25 µm (Restek, Bellefonte, PA, USA) Rxi-17 Sil MS 0.6 m x 0.25 mm i.d. x 0.25 µm (Restek, Bellefonte, PA, USA)	GCxGC-TOFMS
Temperature Program	40 °C (5 min), ramped 10 °C/min to 300 °C (2 min) Secondary oven maintained +5 °C relative to primary oven	GCxGC-TOFMS
Modulation	2s with temperature maintained +15 °C relative to secondary oven	GCxGC-TOFMS
Mass Spectrometer	**LECO Pegasus® BT 4D**	
Ion Source Temperature	250 °C	
Ionization Mode	EI	
Mass Range (m/z)	45-600	
Acquisition Rate	10 spectra/s (1D), 200 spectra/s (2D)	

Sample Preparation Methods

- Solvents
- Monoterpenes (C_{10})
- Sesquiterpenes (C_{15})
- Diterpenes (C_{20})
- Cannabinoids

Best Coverage



Name	Formula	R.T. (s)	Mass Δ (Da)	Similarity
Ethylbenzene	C_8H_{10}	323	0.00	946
o-Xylene	C_8H_{10}	331	0.00	939
2-Heptanone	$C_7H_{14}O$	349	0.00	813
p-Xylene	C_8H_{10}	354	0.00	956
Heptanal	$C_7H_{14}O$	359	0.00	926
Benzene, (1-methylethyl)-	C_9H_{12}	421	0.00	824
Benzene, 1,2,3-trimethyl-	C_9H_{12}	453	0.00	809
Octanal	$C_8H_{16}O$	459	0.02	937
Heptanoic acid	$C_7H_{14}O_2$	520	-0.01	873
3-Methylcoumaran	$C_9H_{10}O$	582	0.04	872
Octanoic acid	$C_8H_{16}O_2$	610	-0.01	911
2-Decanone	$C_{10}H_{20}O$	636	0.01	812
Dec-(5E)-en-1-ol	$C_{10}H_{20}O$	692	0.03	878
Nonanoic acid	$C_9H_{18}O_2$	695	0.00	839
Hexanoic acid, hexyl ester	$C_{12}H_{24}O_2$	797	-0.04	821
4-Chloro-4'-methoxybiphenyl	$C_{13}H_{11}ClO$	869	0.12	779
n-Hexadecanoic acid	$C_{16}H_{32}O_2$	1185	-0.01	923
Linoelaidic acid	$C_{18}H_{32}O_2$	1284	0.01	888
Stearic acid	$C_{18}H_{36}O_2$	1297	0.01	824
γ-Tocopherol	$C_{28}H_{48}O_2$	1727	0.04	828
dl-α-Tocopherol	$C_{29}H_{50}O_2$	1774	0.04	866
Phytosterol	$C_{29}H_{50}O$	1923	0.04	893
α-Amyrin	$C_{30}H_{50}O$	2010	0.03	887

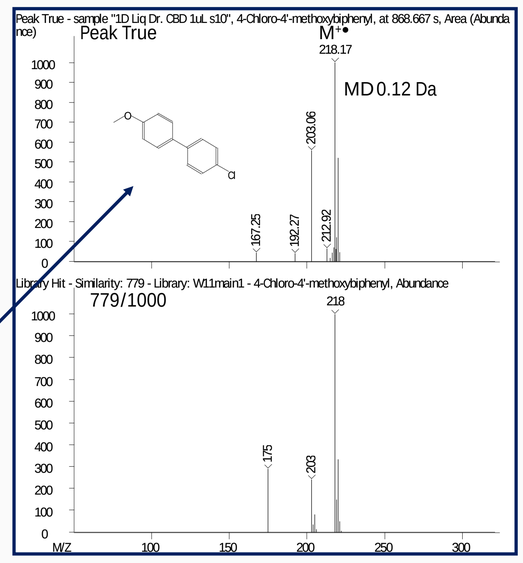


Figure 1: List of miscellaneous compounds in cannabis with deconvoluted (top) and NIST library (bottom) spectra shown for 4-Chloro-4'-methoxybiphenyl.

GC-TOFMS Results: Terpenes

Name	Formula	R.T. (s)	M D (Da)	Similarity
3-Thujene	$C_{10}H_{16}$	386	0.00	896
2-Pinene	$C_{10}H_{16}$	394	0.00	967
Camphene	$C_{10}H_{16}$	410	0.00	952
4(10)-Thujene	$C_{10}H_{16}$	433	0.00	925
β-Myrcene	$C_{10}H_{16}$	448	0.00	954
α-Phellandrene	$C_{10}H_{16}$	463	0.00	865
δ 3-carene	$C_{10}H_{16}$	470	0.00	922
D-Limonene	$C_{10}H_{16}$	487	0.00	966
1,8-Cineole	$C_{10}H_{18}O$	491	0.00	879
β-Ocimene	$C_{10}H_{16}$	503	0.00	970
γ-Terpinene	$C_{10}H_{16}$	516	0.00	835
3,8-p-Menthadiene	$C_{10}H_{16}$	545	0.00	758
L-Fenchone	$C_{10}H_{16}O$	547	0.00	795
Linalool	$C_{10}H_{18}O$	552	0.01	941
1,3,8-p-Menthatriene	$C_{10}H_{14}$	567	0.00	814
Fenchol	$C_{10}H_{18}O$	570	0.00	964
Pinanol	$C_{10}H_{18}O$	579	0.00	885
cis-p-Mentha-2,8-dien-1-ol	$C_{10}H_{16}O$	588	0.06	797
Ipsdienol	$C_{10}H_{16}O$	595	0.00	889
(+)-2-Bornanone	$C_{10}H_{16}O$	601	0.01	850
Pinocarvone	$C_{10}H_{14}O$	617	0.00	813
endo-Borneol	$C_{10}H_{18}O$	620	0.00	963
Terpinen-4-ol	$C_{10}H_{18}O$	629	0.00	895
α-Terpineol	$C_{10}H_{18}O$	640	0.01	943
Perillal	$C_{10}H_{14}O$	654	0.00	773
Verbenone	$C_{10}H_{14}O$	660	0.00	896
Geraniol	$C_{10}H_{18}O$	690	0.07	814
3-Terpinolenone	$C_{10}H_{14}O$	772	0.00	805
α-Cubebene	$C_{15}H_{24}$	776	0.00	909
Ylangene	$C_{15}H_{24}$	796	0.00	926
Copaene	$C_{15}H_{24}$	800	0.00	904
β-Guaiene	$C_{15}H_{24}$	805	0.00	780
β-Yalangene	$C_{15}H_{24}$	808	0.00	749
β-Cubebene	$C_{15}H_{24}$	810	0.00	798
Selina-5,11-diene	$C_{15}H_{24}$	817	0.00	884
Cadinene	$C_{15}H_{26}$	828	-0.02	893
Santalene	$C_{15}H_{24}$	832	0.00	866
Isocaryophyllene	$C_{15}H_{24}$	837	0.00	960
α-Guaiene	$C_{15}H_{24}$	848	0.00	825
Aromandendrene	$C_{15}H_{24}$	852	0.00	930
(E)-β-Famesene	$C_{15}H_{24}$	854	0.02	884
Humulene	$C_{15}H_{24}$	864	0.00	955
Alloaromadendrene	$C_{15}H_{24}$	869	0.00	959
γ-Muurolene	$C_{15}H_{24}$	878	0.00	855
α-Selinene	$C_{15}H_{24}$	895	0.00	943
β-Bisabolene	$C_{15}H_{24}$	897	0.00	966
γ-Cadinene	$C_{15}H_{24}$	907	0.00	932
δ-Cadinene	$C_{15}H_{24}$	912	0.00	892
cis-Calamenene	$C_{15}H_{22}$	913	0.00	861
(E)-α-Bisabolene	$C_{15}H_{24}$	921	0.00	946
α-Calacorene	$C_{15}H_{20}$	929	0.00	878
Caryophyllene oxide	$C_{15}H_{24}O$	961	0.00	936
Guaiol	$C_{15}H_{26}O$	966	0.00	935
(-)-Globulol	$C_{15}H_{26}O$	975	0.00	918
Humulene epoxide 2	$C_{15}H_{24}O$	979	0.00	868
Selin-6-en-4α-ol	$C_{15}H_{26}O$	985	0.01	814
(-)-10-epiy-Eudsemol	$C_{15}H_{26}O$	987	0.00	928
Aristolene	$C_{15}H_{24}$	1002	0.00	756
(-)-α-Panasinsen	$C_{15}H_{24}$	1012	-0.24	767
α-Bisabolol	$C_{15}H_{26}O$	1022	0.01	922
Ledene	$C_{15}H_{24}$	1029	0.00	855
Junipercamphor	$C_{15}H_{26}O$	1038	0.01	853
Aromadendrane-4,10-diol	$C_{15}H_{26}O_2$	1101	0.01	824
Isoaromadendrene epoxide	$C_{15}H_{24}O$	1127	0.00	789
Spathulanol	$C_{15}H_{26}O$	1144	0.00	751
Corymbolone	$C_{15}H_{24}O_2$	1169	0.00	794
m-Camphorene	$C_{20}H_{32}$	1188	0.01	851
p-Camphorene	$C_{20}H_{32}$	1208	0.01	818
Phytol	$C_{20}H_{40}O$	1274	0.02	951
Neophytadiene	$C_{20}H_{38}$	2120	-0.02	887

Ave.: |Mass Δ|=0.01, Similarity =878/1000

Characterization: Spectral Similarity Searches + Mass Delta + Retention Index Filtering

Increased confidence in compound IDs

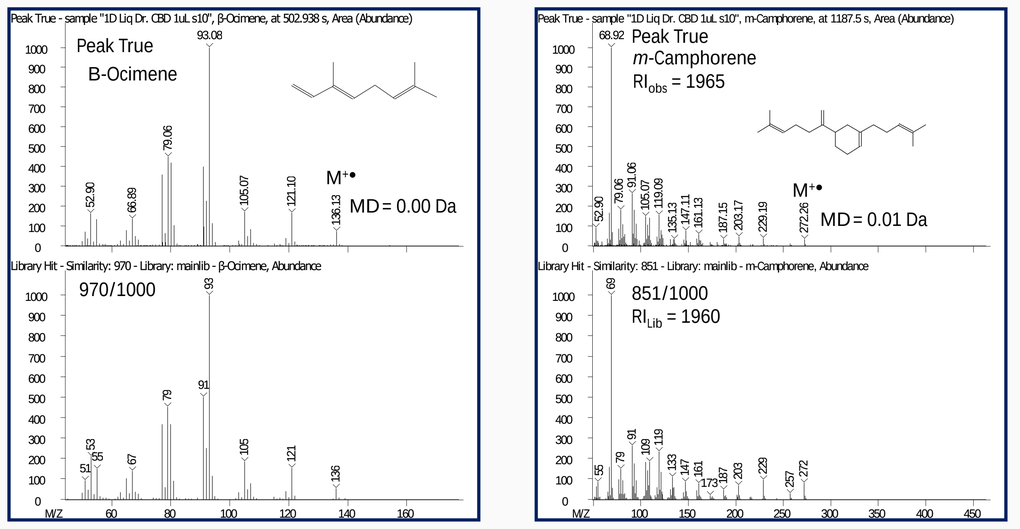


Figure 2. Deconvoluted (top) and NIST library spectra (bottom) for B-Ocimene and m-Camphorene.

GC-TOFMS: Cannabinoids

Name	Formula	R.T. (s)	Mass Delta (Da)	Similarity
Cannabidivarol	$C_{19}H_{26}O_2$	1342	0.01	882
Cannabidiol	$C_{21}H_{30}O_2$	1445	0.07	905
Delta 8-THC	$C_{21}H_{30}O_2$	1483	0.01	837
Delta 9-THC	$C_{21}H_{30}O_2$	1491	-0.01	928
Cannabigerol	$C_{21}H_{32}O_2$	1510	0.01	900
Cannabinol	$C_{21}H_{26}O_2$	1522	0.01	902
Cannabichromene	$C_{21}H_{30}O_2$	1578	N/A	873

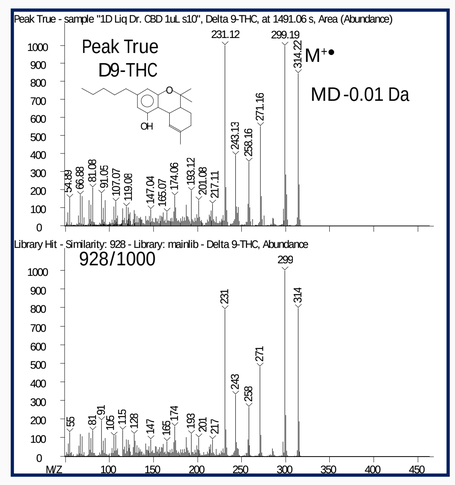
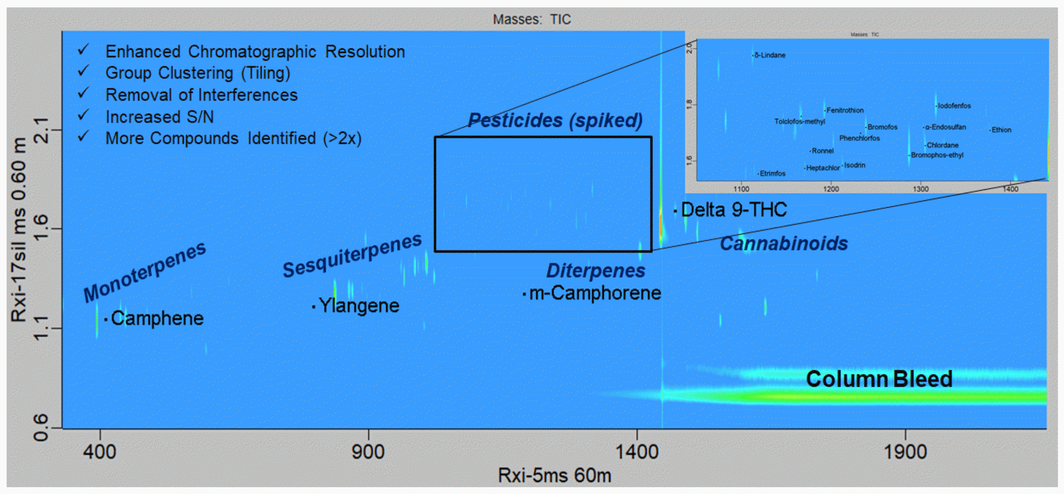
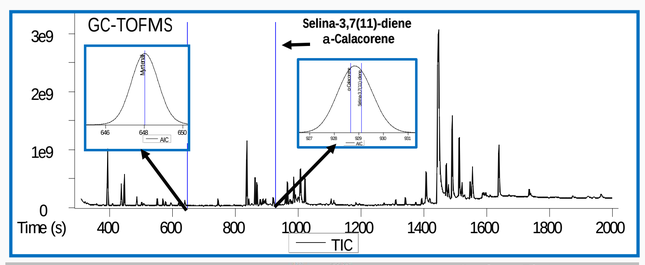


Figure 3. List of representative cannabinoids with deconvoluted (top) and NIST library (bottom) spectra shown for Delta 9-THC.

GCxGC-TOFMS Contour Plot Showing Separation of Several Compound Classes

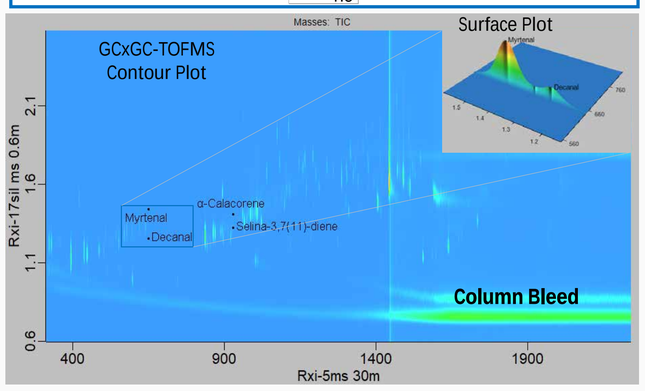


GCxGC-TOFMS – More Compounds Identified



GC-TOFMS

Name	Formula	R.T. (s)	Similarity
Decanal	$C_{10}H_{20}O$	Not Found	
Myrtenal	$C_{10}H_{14}O$	648	745
Selina-3,7(11)-diene	$C_{15}H_{24}$	929	805
α-Calacorene	$C_{15}H_{20}$	929	878



GCxGC-TOFMS

Name	R.T. (s)	Similarity
Decanal	648 s, 1.262 s	723
Myrtenal	648 s, 1.445 s	890
Selina-3,7(11)-diene	928 s, 1.323 s	869
α-Calacorene	928 s, 1.414 s	881

Summary

- A variety of sample introduction methods can be used to prepare cannabis products for analysis
- Comprehensive profiling of cannabis is an attractive alternative to targeted, panel-based methods
- GCxGC-TOFMS facilitates fast and confident cannabis profiling.
- Compound identification: Similarity searches, mass Δ calculations, and RI filtering