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Thursday, May 8, 2014

“Surviving and Succeeding in Grad School”

Sam Pazicni, Assistant Professor of Chemistry, University of New Hampshire
Patricia Simpson, Director of Academic Advising and Career Services,
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Cannabis Chemistry 101



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Cannabis Chemistry 101



ACS Webinar
May 1st, 2014

Christopher J. Hudalla, Ph. D.

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Cannabis Chemistry 101

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Joint Ditch Weed Doobie Bunk Dope Weed Hooch Stash Lid Jay
 Sticky-Icky Kush SKUNK Marijuana Ganja Hooch Stash Ganja
 Toke Reefer MJ Ganja Haze 420 Spliff
 Grass Cheeba Pot Maui Wauie Chronic
 HERB Roach Kief
 Dro Mary Jane Hash Smoke

History of Cannabis

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- ✦ 10,000 years ago – Hemp used to produce cord
- ✦ 5,000 years ago – First Chinese references to medicinal use of cannabis
- ✦ 3,000 years ago – Egyptians used cannabis to treat glaucoma, inflammation and other conditions
- ✦ 1611 – Hemp brought to America
- ✦ 1800's – Marijuana used in mainstream medicine
 - ✦ Marijuana added to the US Pharmacopeia



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History of Cannabis

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- ✦ 1910's – States begin to prohibit marijuana
- ✦ 1930's – American pharmaceutical firms sell cannabis extracts
- ✦ 1937 – Marijuana Tax Act leads to decline in marijuana prescriptions
- ✦ 1970 – Controlled Substance Act (CSA) classifies marijuana as a Schedule I drug, with "No Accepted Medical Use" (along with heroin and LSD)
- ✦ 1973 – Drug Enforcement Agency (DEA) established

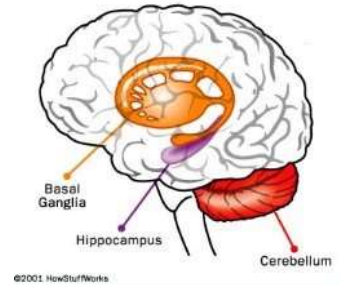


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History of Cannabis

- ✦ 1990 – Researchers at NIH discover cannabinoid receptor system.
- ✦ 1996 – California is the first state to legalize medical marijuana
- ✦ 2001 – US patent filed by US Health and Human Services for the use of cannabis for certain neurodegenerative diseases
- ✦ 2014 – 21 States + Washington DC have medical marijuana programs. 2 states permit adult use.

Cannabinoid Receptor Sites



United States Patent 6,630,507
 Hampson, et al. October 7, 2003
 Assignee: United States Department of
 Health and Human Services



Audience Poll

What is the status of marijuana legalization in the state in which you reside?

- Illegal for all use.
- Illegal, but expect it to be legalized here soon.
- Legal for medical use only.
- Legal for adult use (similar to alcohol).



Role of Analytical Chemistry

- ✦ **Ensuring Consumer Safety**
 - ✦ Confirm products are free from contamination
 - ✦ Assist in determining proper dosage
- ✦ **Optimization of Cultivation Practices**
 - ✦ Monitoring nutrient uptake
 - ✦ Early identification of phenotypes
- ✦ **Design and Development of Marijuana Infused Products (MIPs)**
 - ✦ Optimization of extractions and processes
 - ✦ Quantitation required for product labeling



Chemical Complexity

Phytochemistry

✦ Hydrocarbons

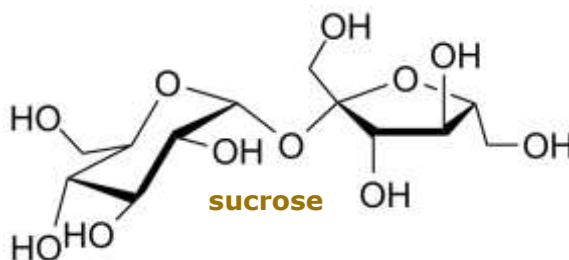
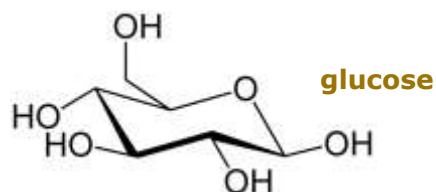
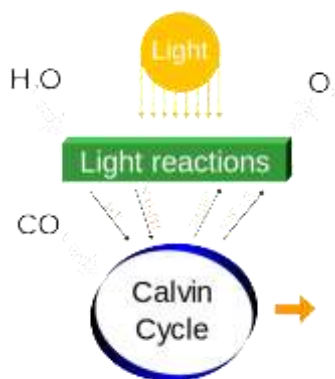


Chemical Complexity

Phytochemistry

+ Hydrocarbons

+ Sugars



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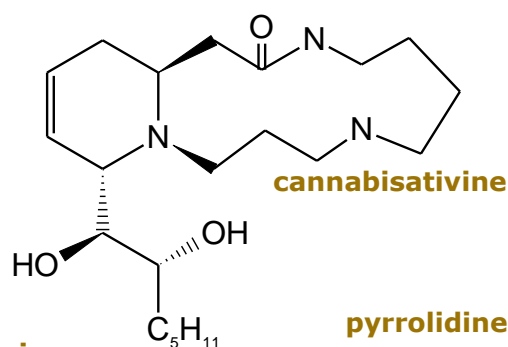
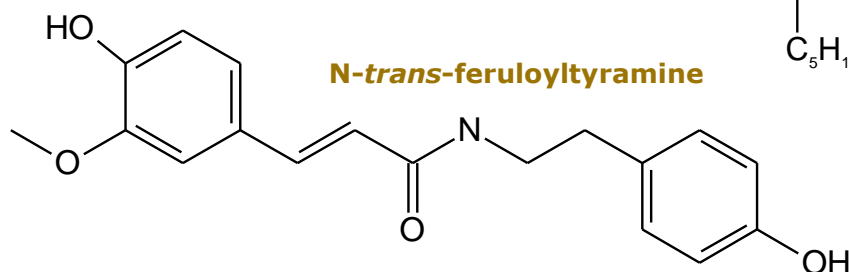
Chemical Complexity

Phytochemistry

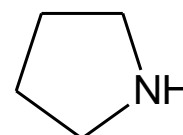
+ Hydrocarbons

+ Sugars

+ Amine/Amide Functionality



pyrrolidine



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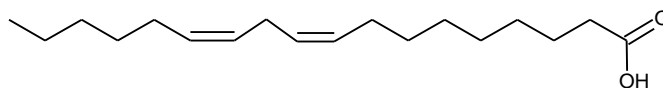
Chemical Complexity

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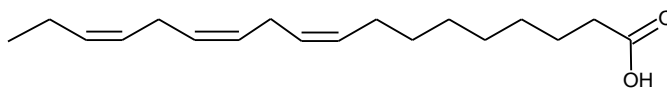
Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids

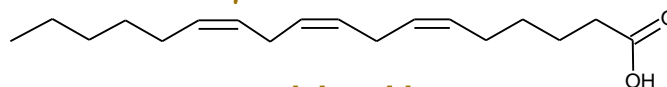
linoleic acid



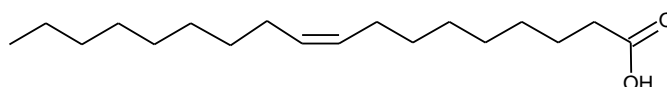
α -linolenic acid



γ -linolenic acid



oleic acid



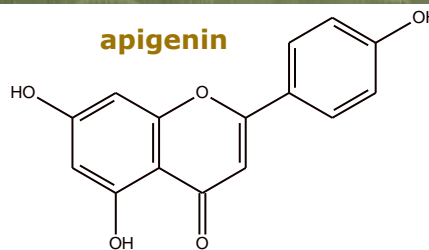
Chemical Complexity

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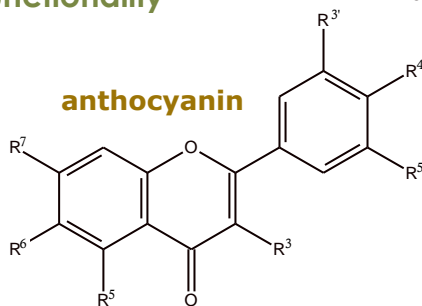
Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids
- ✦ Flavonoids

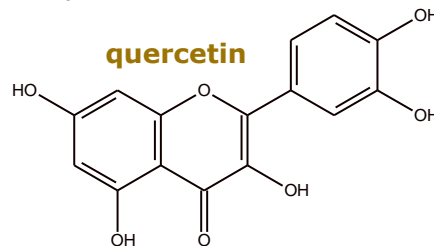
apigenin



anthocyanin



quercetin

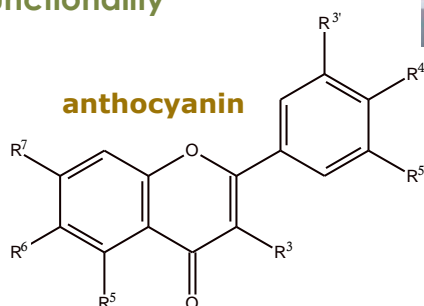


Chemical Complexity

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Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids
- ✦ Flavonoids



Low pH ← → High pH

Purple Kush
Purple Urkel
Grand Daddy Purple
Grape Ape



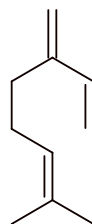
Chemical Complexity

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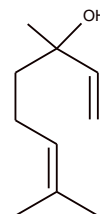
Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids
- ✦ Flavonoids
- ✦ Terpenes

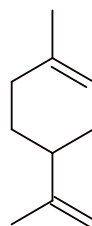
myrcene



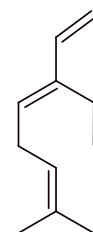
linalool



limonene



trans-ocimene



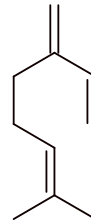
Chemical Complexity

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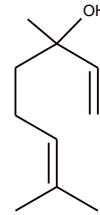
Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids
- ✦ Flavonoids
- ✦ Terpenes

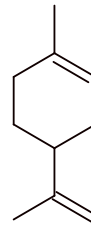
myrcene



linalool



limonene



Pineapple Diesel
Super Lemon Haze
Strawberry Kush
Lemon Wreck



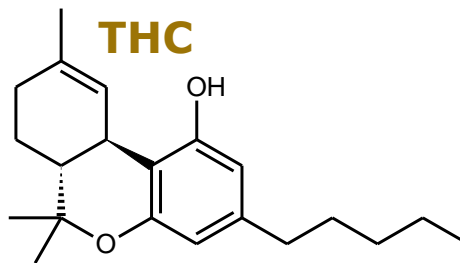
Chemical Complexity

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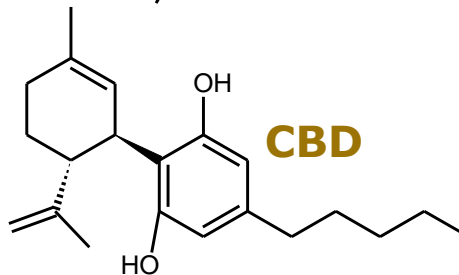
Phytochemistry

- ✦ Hydrocarbons
- ✦ Sugars
- ✦ Amine/Amide Functionality
- ✦ Fatty Acids
- ✦ Flavonoids
- ✦ Terpenes
- ✦ Cannabinoids

THC



CBD



Charlotte's Web
Harlequin
CBD Crew
Cannatonic

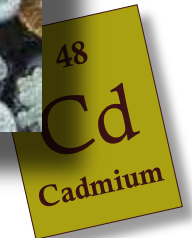
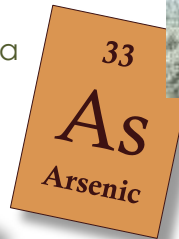
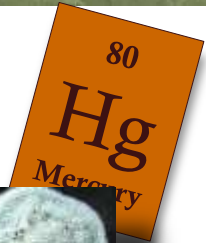
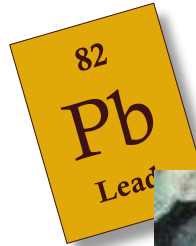


Chemical Complexity

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Contaminants

- ✦ Pesticides
- ✦ Plant Growth Regulators
- ✦ Heavy Metals
- ✦ Microbiological Contaminants
 - ✦ Mold, Fungus, Mycotoxins, Bacteria
- ✦ Process Solvents



Chemical Complexity

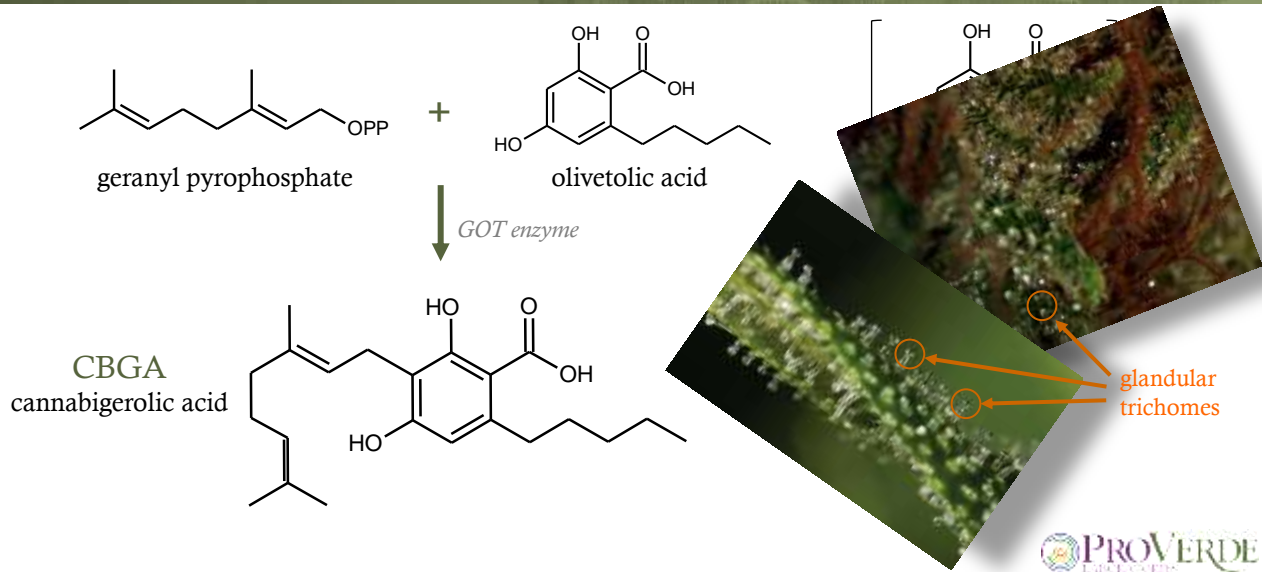
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Sample Matrices

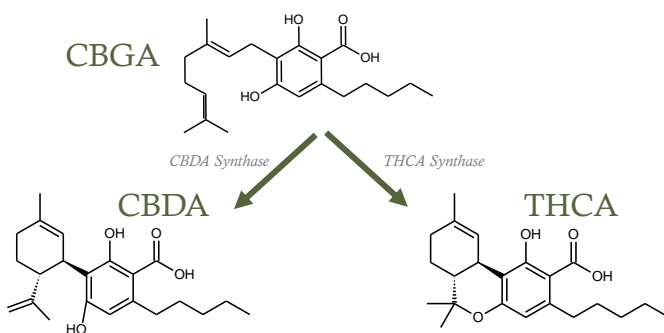
- ✦ Biological (Urine/Blood)
- ✦ Flower or Leaf (fresh or dried)
- ✦ Extracts/Concentrates
- ✦ Tinctures/Infusions
 - ✦ Glycerin, alcohol, or oil based
- ✦ Topical Salves or Lotions
- ✦ Consumables



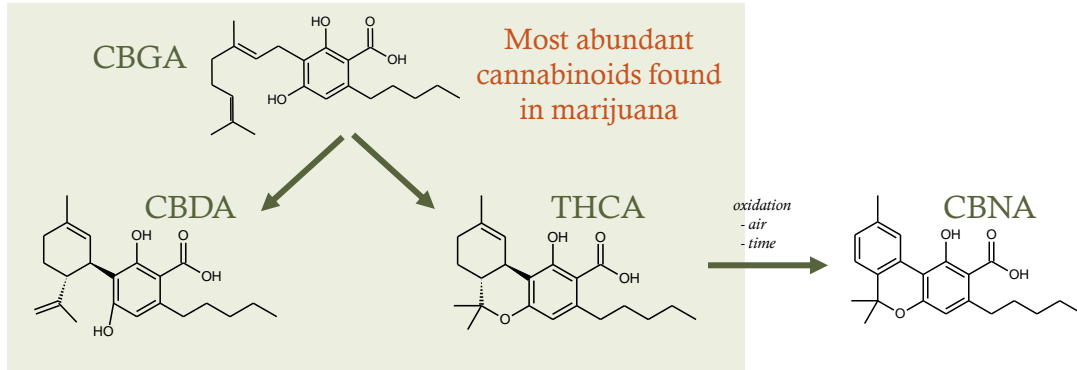
Cannabinoid Alphabet Soup



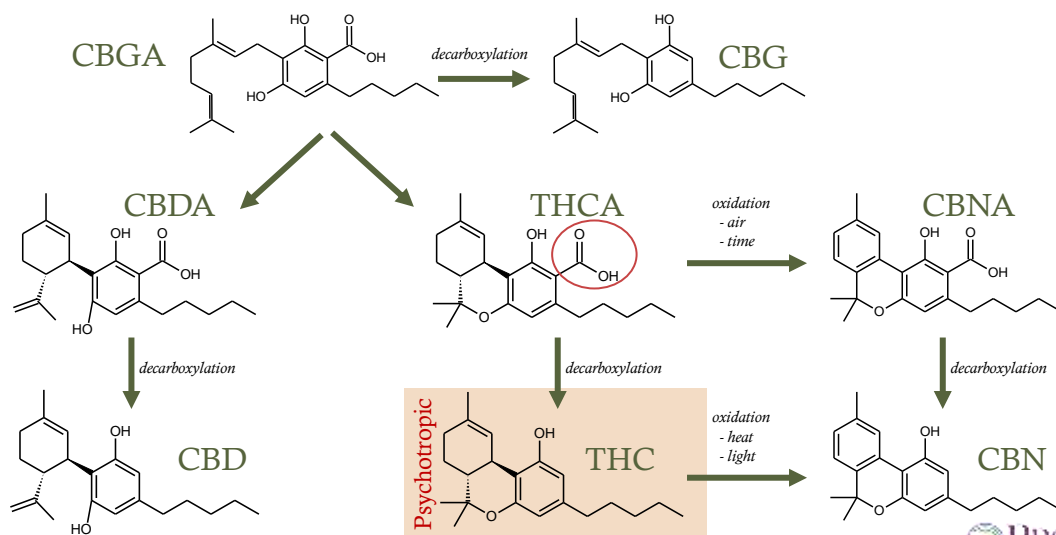
Cannabinoid Alphabet Soup



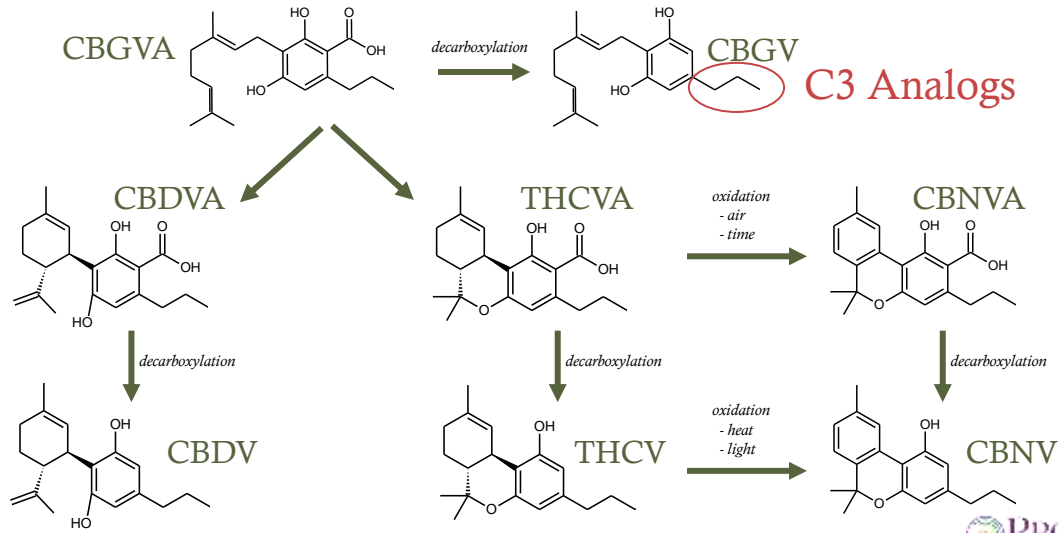
Cannabinoid Alphabet Soup



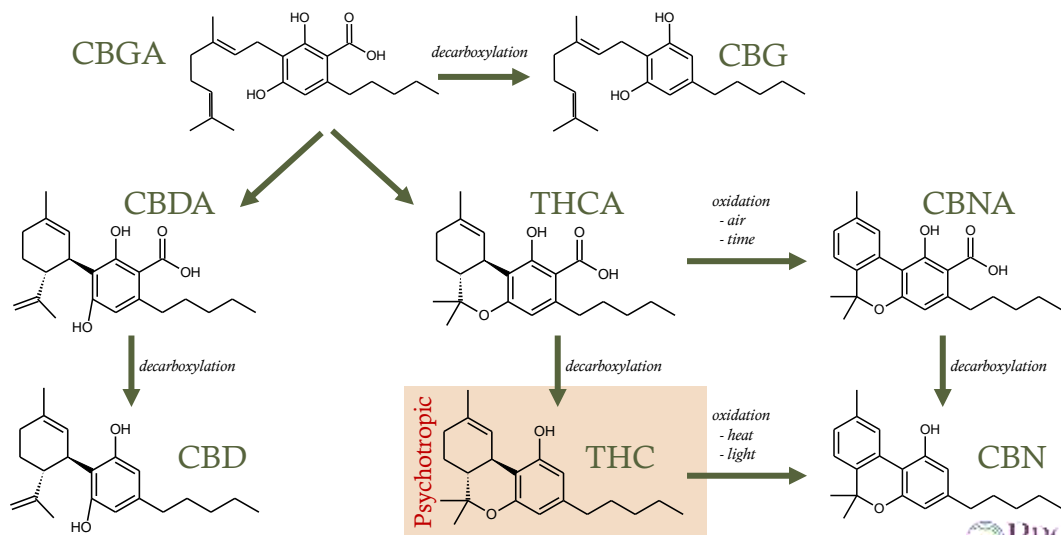
Cannabinoid Alphabet Soup



Cannabinoid Alphabet Soup

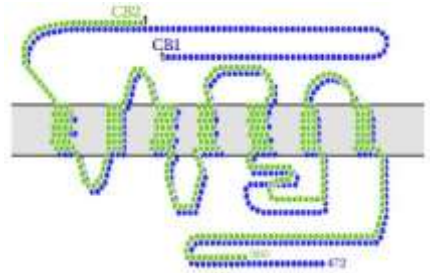


Cannabinoid Alphabet Soup

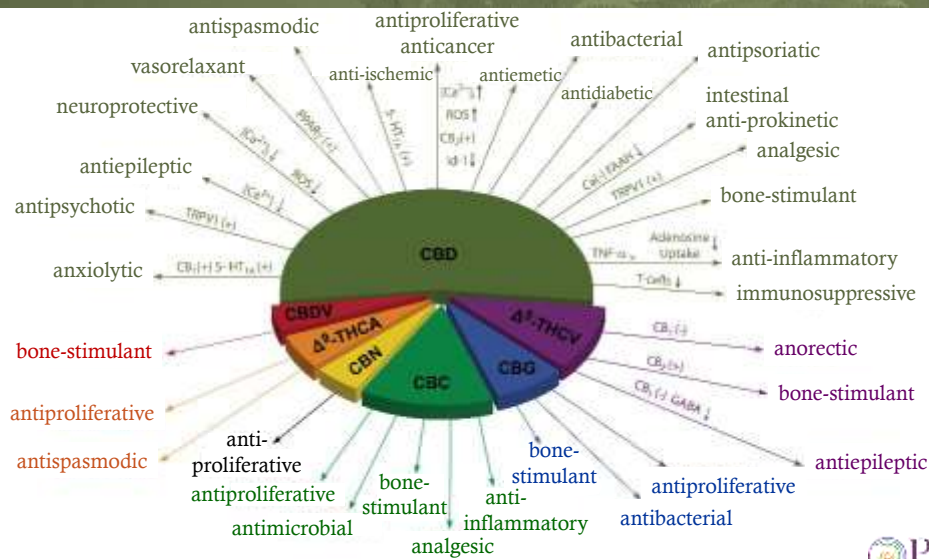


Cannabinoid Receptors

- ✦ **Cannabinoid receptors are a class of cell membrane receptors that are involved with a variety of physiological processes, including:**
 - ✦ Appetite, pain-sensation, mood, and memory
- ✦ **Cannabinoid receptors are activated by cannabinoids, generated naturally inside the body or introduced into the body.**
- ✦ **Two cannabinoid receptors have been identified to date, CB1 and CB2.**
 - ✦ CB1 receptors are found primarily in the Central Nervous System (CNS), as well as the lung, liver and kidneys
 - ✦ CB2 receptors are expressed mainly on T cells of the immune system



Medicinal Marijuana



Reproduced with permission from the author, Angelo Izzo, Trends in Pharmacological Sciences, 2009 Oct; 30(10):515-27



Medicinal Marijuana

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- ✦ Epilepsy
- ✦ Multiple Sclerosis
- ✦ Glaucoma
- ✦ Post-Traumatic Stress Syndrome
- ✦ Cancer
- ✦ Alzheimer's Disease
- ✦ HIV/AIDS
- ✦ Fibromyalgia
- ✦ Spasticity
- ✦ Arthritis
- ✦ Anorexia
- ✦ Cachexia (Wasting Syndrome)
- ✦ Crohn's Disease
- ✦ Migraine
- ✦ Pain
- ✦ Nausea



Audience Poll

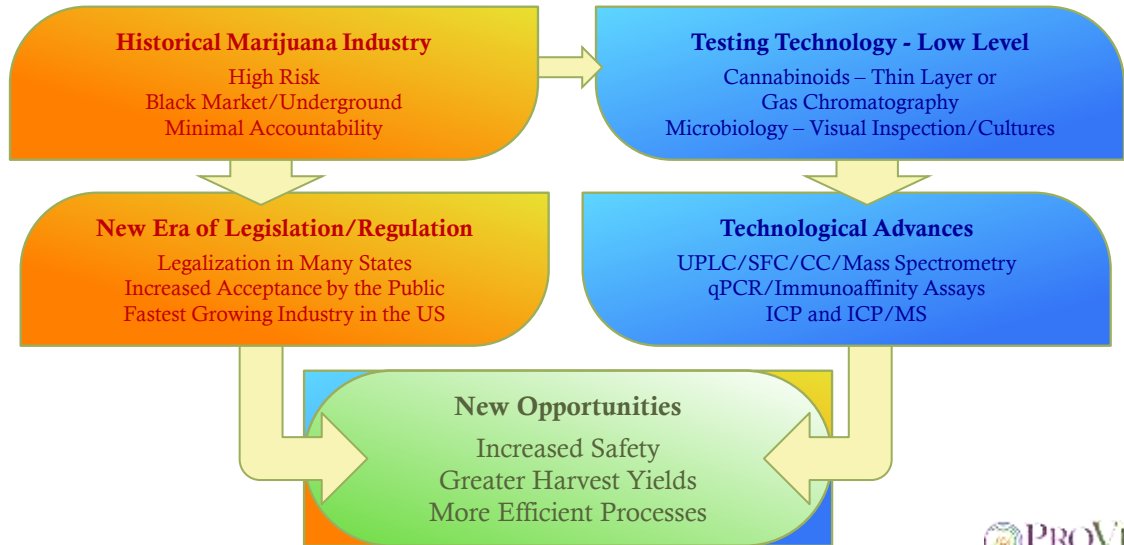
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Where do YOU stand on the issue of marijuana legalization?

- In favor of federal legalization, to be regulated like alcohol.
- Should be legalized federally for medicinal use only.
- Should be left to individual states to legislate and regulate.
- Medical marijuana is just an excuse to enable people to get stoned, and should remain illegal.



Analytical Testing Opportunities



Convergence Chromatography



- ✦ **UltraPerformance Convergence Chromatography System (UPC²)**
- ✦ **Based on the theory of Supercritical Fluid Chromatography (SFC)**
 - ✦ Uses liquid CO₂ as the primary mobile phase
- ✦ **Reduces the hazardous waste generated relative to conventional liquid chromatography**
- ✦ **Captures quantitative information on both acid and decarboxylated form of cannabinoids**
- ✦ **Amenable to non-polar solvents, ideal for analysis of analytes in lipid-rich matrices**



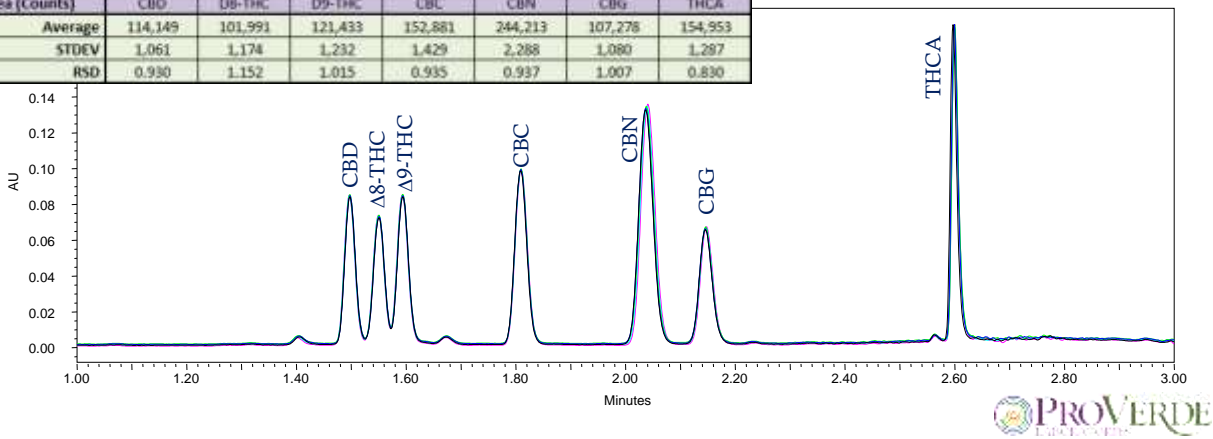
Injection Reproducibility

41

Retention Time (Min)	CBD	DB-THC	D9-THC	CBC	CBN	CBG	THCA
Average	1.497	1.550	1.594	1.809	2.038	2.146	2.599
STDEV	0.001	0.000	0.001	0.000	0.002	0.001	0.001
RSD	0.047	0.029	0.034	0.025	0.094	0.047	0.050

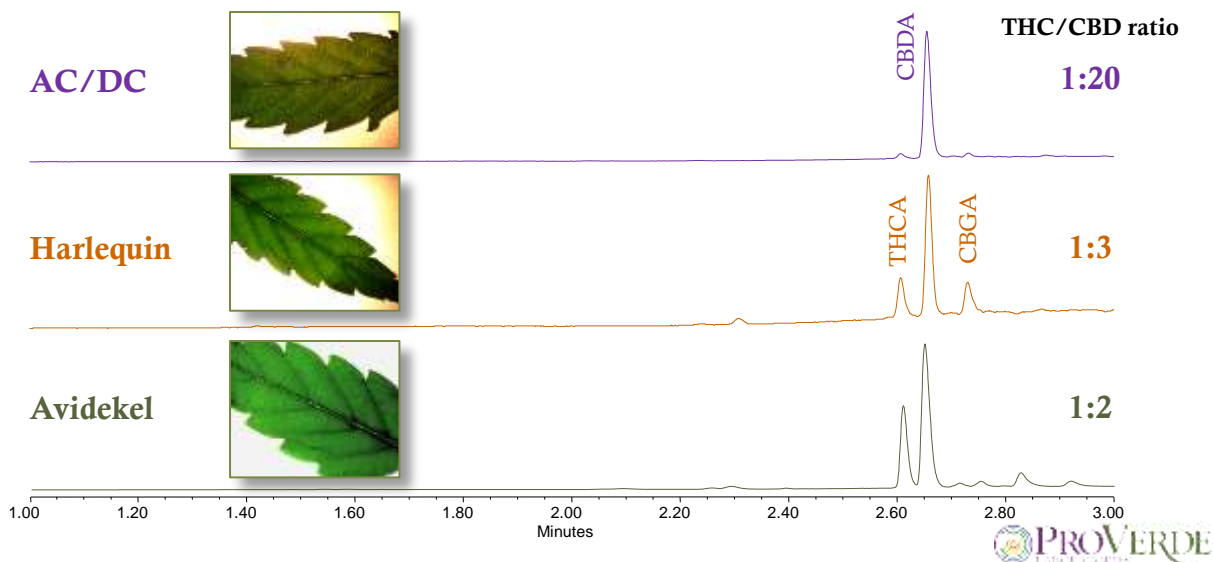
Area (Counts)	CBD	DB-THC	D9-THC	CBC	CBN	CBG	THCA
Average	114,149	101,991	121,433	152,881	244,213	107,276	154,953
STDEV	1,061	1,174	1,232	1,429	2,288	1,080	1,297
RSD	0.930	1.152	1.015	0.935	0.937	1.007	0.830

Overlay of 5 standard injections



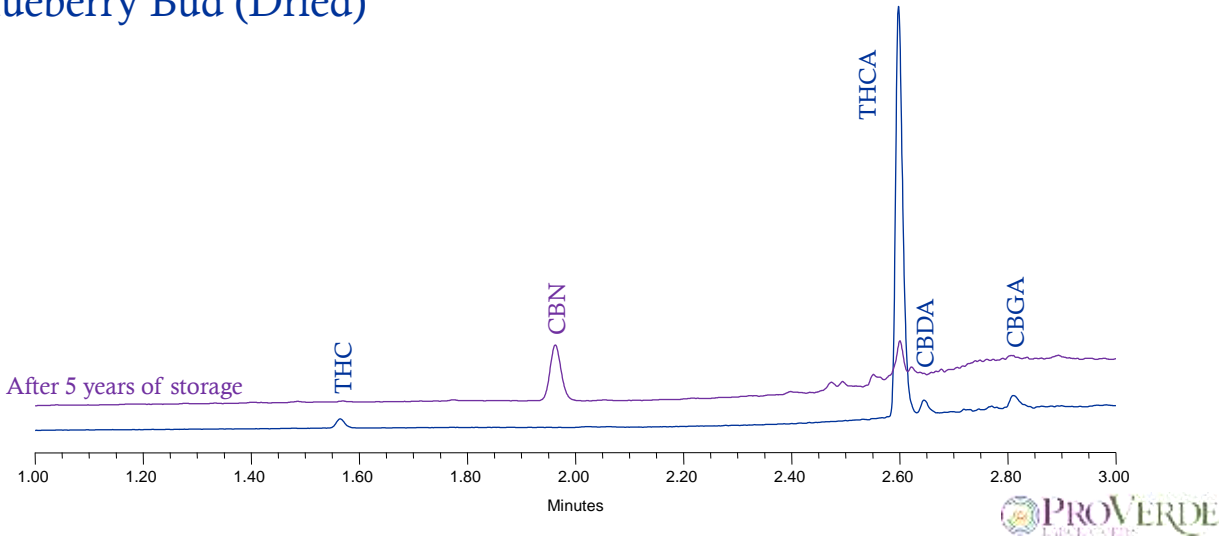
Vegetative Plant Tissue

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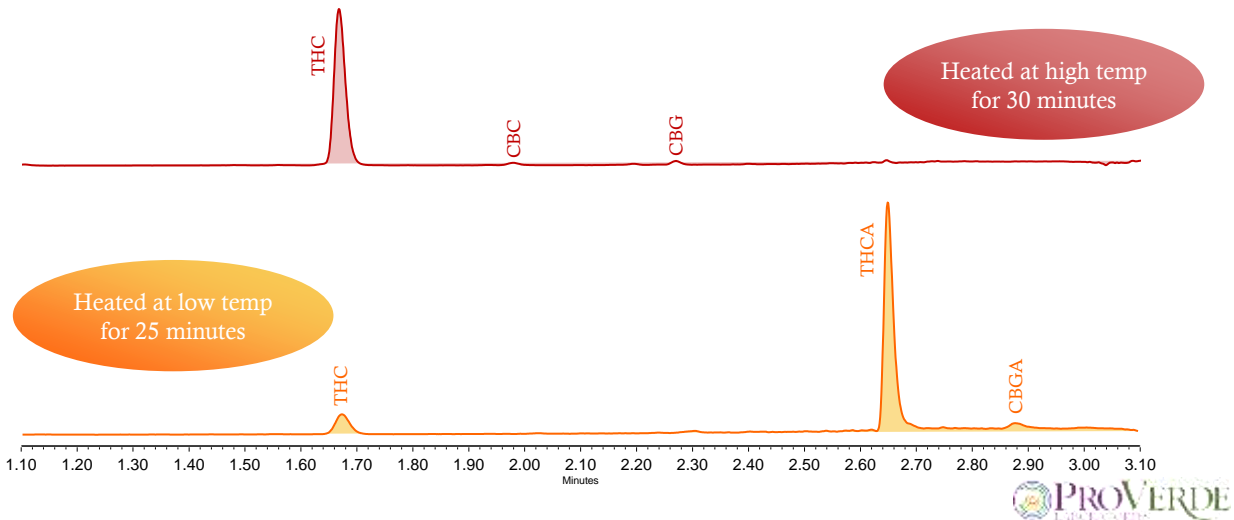
Understanding Chemical Processes

Blueberry Bud (Dried)



Optimization of Processes

Ethanol Extracts of Pineapple Kush



Summary

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- + Cannabis presents a complex system that has many challenges for a complete understanding
- + Cannabis has shown great promise for the treatment of many medical conditions
- + Chemical understanding is an essential element of the most rapidly growing sector in the US economy
 - ✦ Understanding the physiological effects, ensuring consumer/patient safety, optimization of cultivation, and development of consumer products
- + While increased acceptance has provided new opportunities for the application of current technologies, additional changes in legislation/regulation will be required to accelerate research in this promising industry



References for Additional Information

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- + ***Chemistry and Analysis of Phytocannabinoids and Other Cannabis Constituents***, Rudolf Brenneisen, Marijuana and the Cannabinoids (Chapter 2), **2007**, pp 17-49, ISBN 978-1-58829-456-2.
- + ***Taming THC: Potential Cannabis Synergy and Phytocannabinoid-Terpenoid Entourage Effects***, Ethan Russo, British Journal of Pharmacology, 2011, **163**, 1344-1364.
- + ***Non-Psychotropic Plant Cannabinoids: New Therapeutic Opportunities from an Ancient Herb***, Angelo Izzo, et al., Trends in Pharmacological Sciences, **2009**, 30(10), 515-527.
- + ***Naturally Occurring and Related Synthetic Cannabinoids and their Potential Therapeutic Applications***, Mahmoud Elsohly, et al., Recent Patents on CNS Drug Discovery, **2009**, 4, 112-136.



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Cannabis Chemistry 101



Dr. Jeff Kiplinger
Averca Discovery Services



Dr. Christopher Hudalla
ProVerde Laboratories

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