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Upcoming ACS Webinars

www.acs.org/acswebinars

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, University of Illinois Urbana-Champaign

Thursday, May 15, 2014

"From Batteries to Biological Machines – Crystallography Frontiers"

Cora Lind-Kovacs, American Crystallographic Association
Jim Kaduk, American Crystallographic Association

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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

12

History of Cannabis

13

- 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

14

- 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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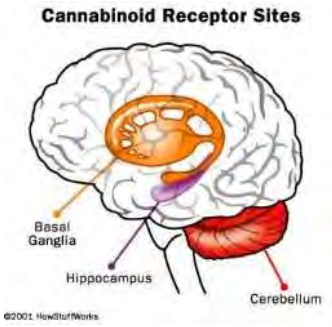
History of Cannabis

15

- 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.



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

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Audience Poll

16

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).**

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Role of Analytical Chemistry

17

- **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

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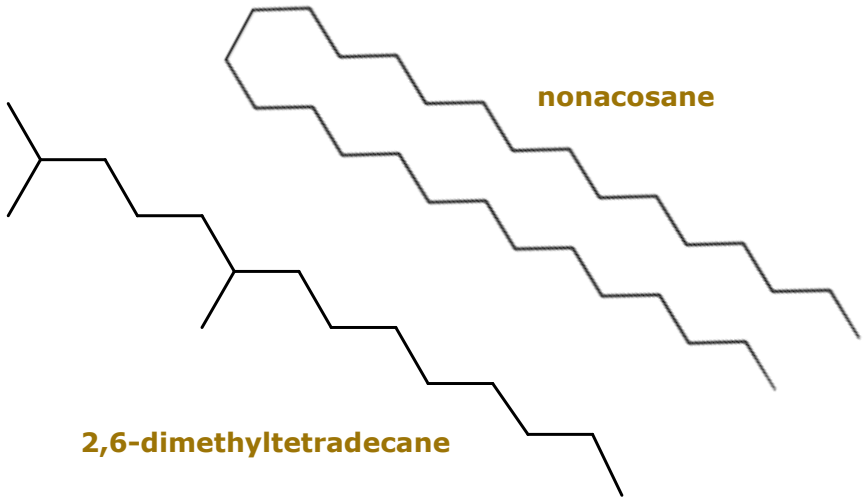
Chemical Complexity

18

Phytochemistry

- **Hydrocarbons**



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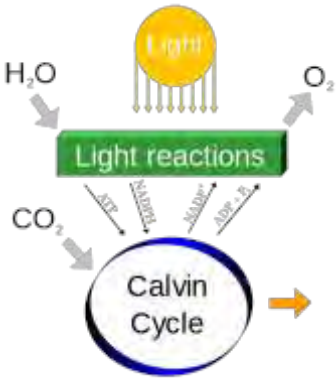
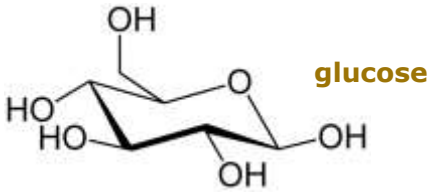
Chemical Complexity

19

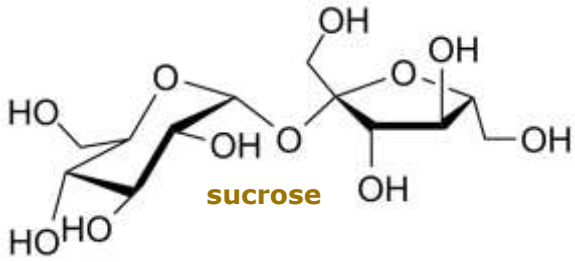
Phytochemistry

- Hydrocarbons
- Sugars





glucose



sucrose

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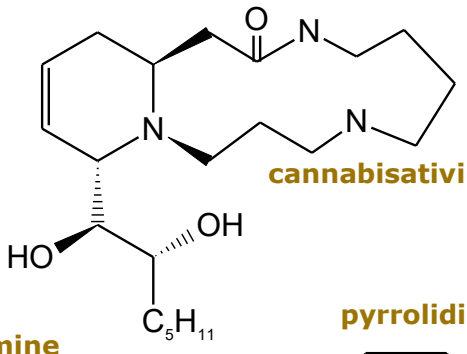
Chemical Complexity

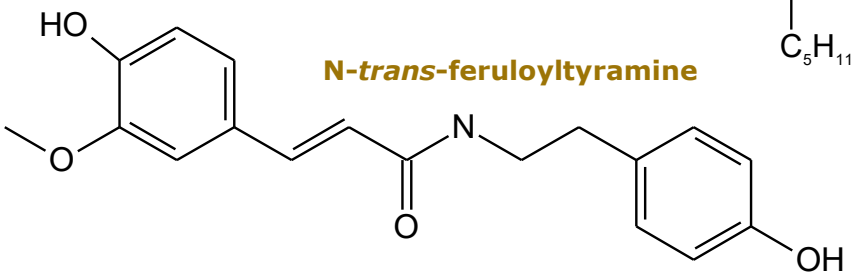
20

Phytochemistry

- Hydrocarbons
- Sugars
- Amine/Amide Functionality

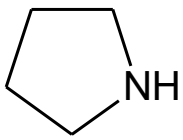


cannabisativine



N-*trans*-feruloyltyramine

pyrrolidine



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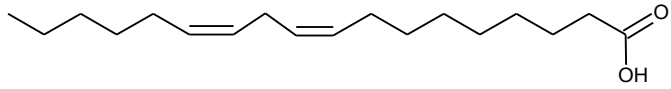
Chemical Complexity

21

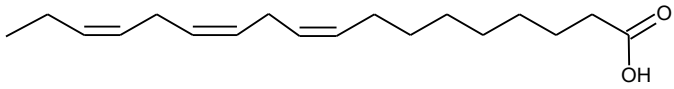
Phytochemistry

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

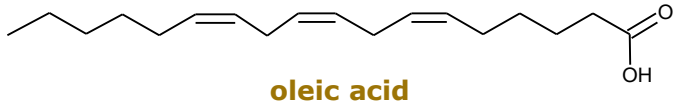
linoleic acid



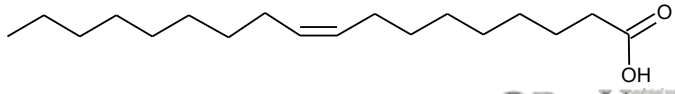
α-linolenic acid



γ-linolenic acid



oleic acid



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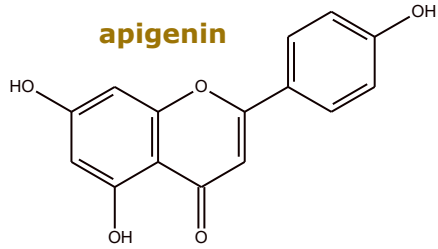
Chemical Complexity

22

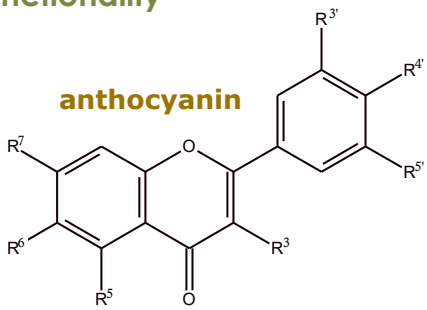
Phytochemistry

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

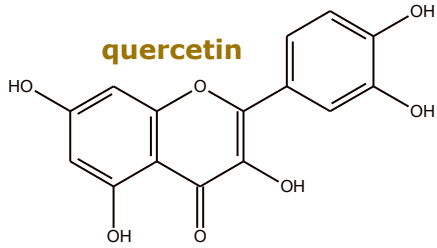
apigenin



anthocyanin



quercetin



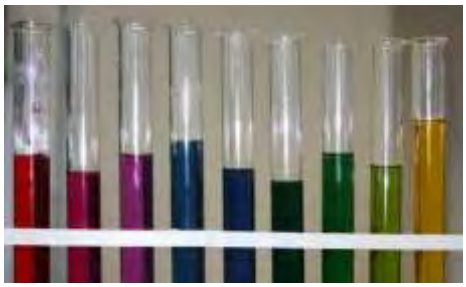
PROVERDE LABORATORIES

Chemical Complexity

23

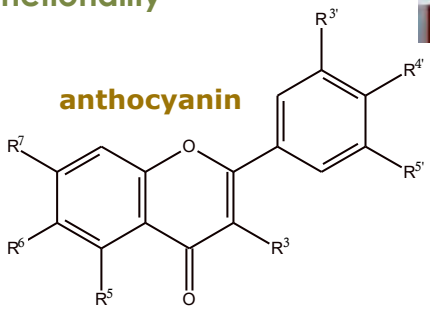
Phytochemistry

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



Low pH ⟷ High pH

anthocyanin



Purple Kush
Purple Urkel
Grand Daddy Purp
Grape Ape

PROVERDE LABORATORIES

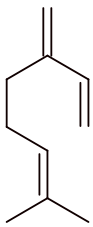
Chemical Complexity

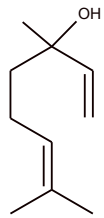
24

Phytochemistry

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

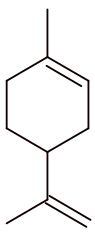
myrcene

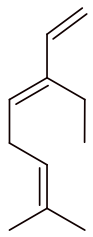




linalool

limonene





***trans*-ocimene**

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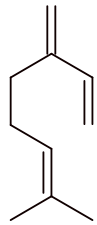
Chemical Complexity

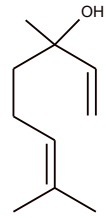
25

Phytochemistry

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

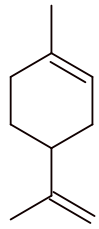
myrcene





linalool

limonene



Pineapple Diesel
Super Lemon Haze
Strawberry Kush
Lemon Wreck

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Chemical Complexity

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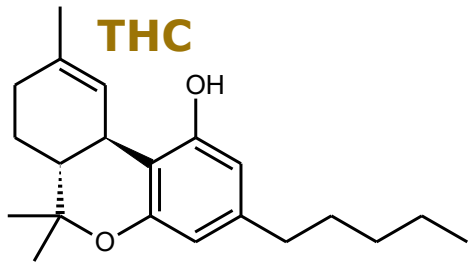
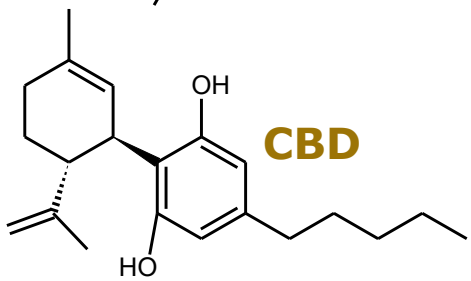
Phytochemistry

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

THC





CBD

Charlotte's Web
Harlequin
CBD Crew
Cannatonic

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Chemical Complexity

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Contaminants

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

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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

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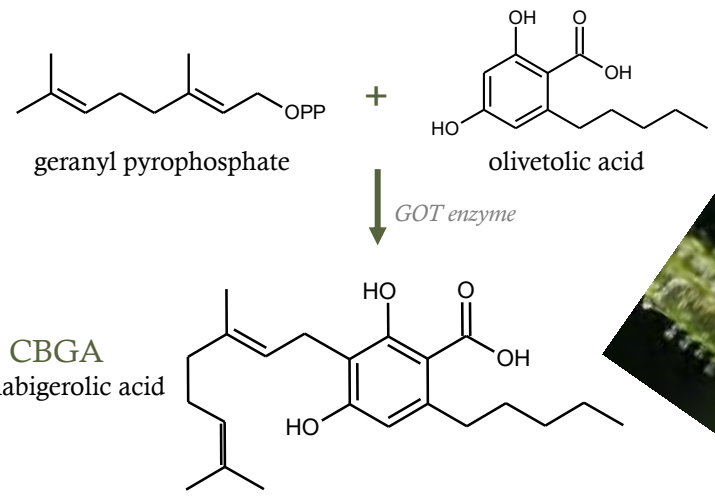
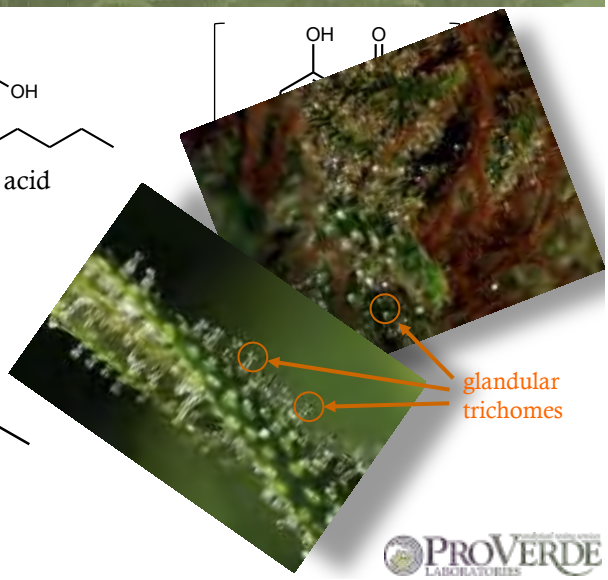
Cannabinoid Alphabet Soup

29





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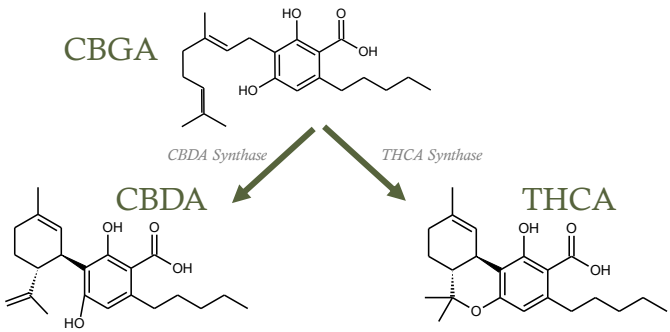
Cannabinoid Alphabet Soup

30



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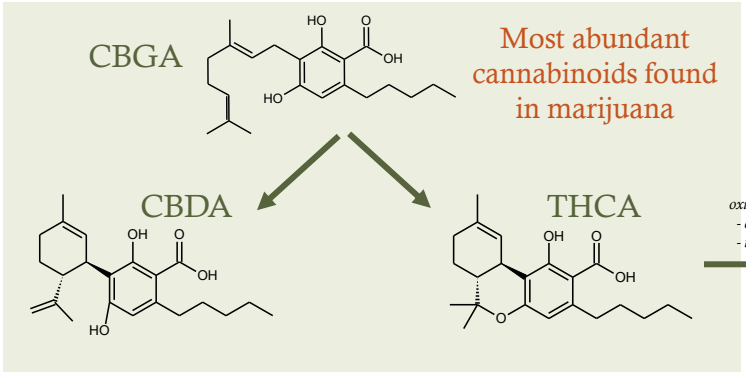
Cannabinoid Alphabet Soup

31



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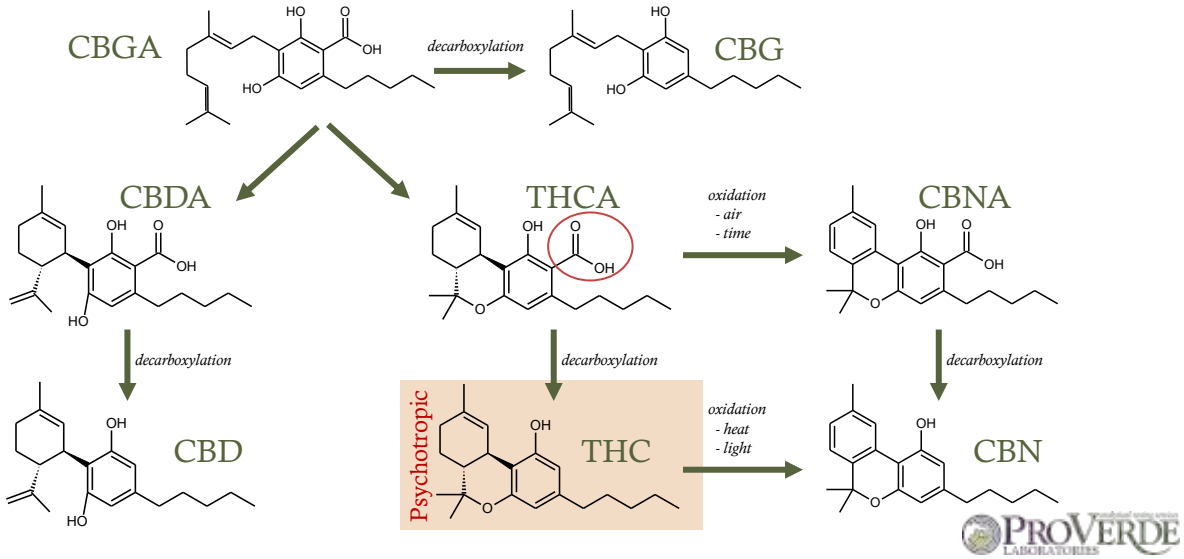
Cannabinoid Alphabet Soup

32



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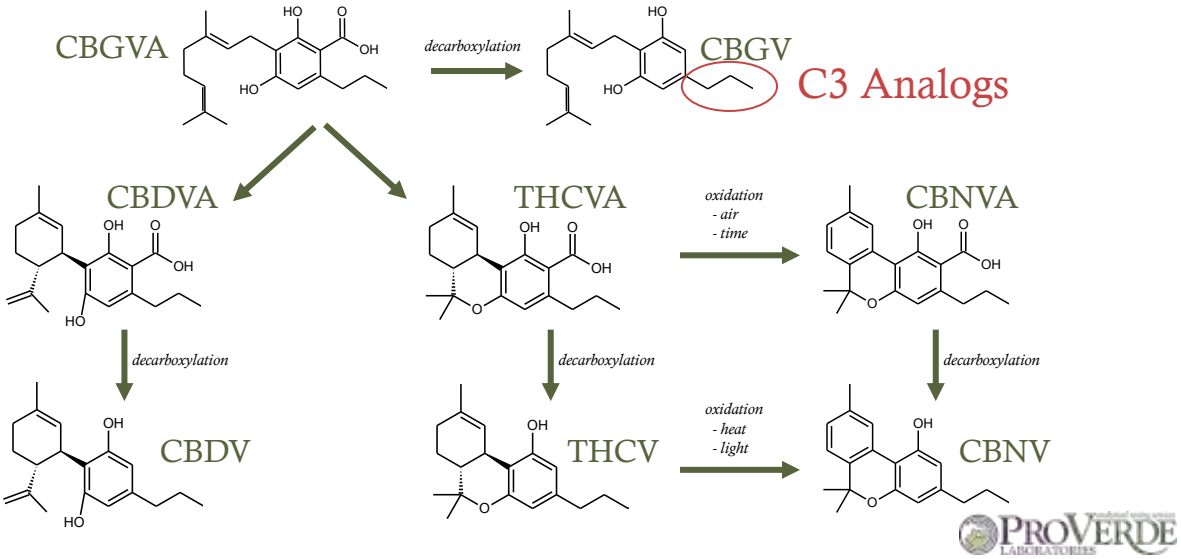
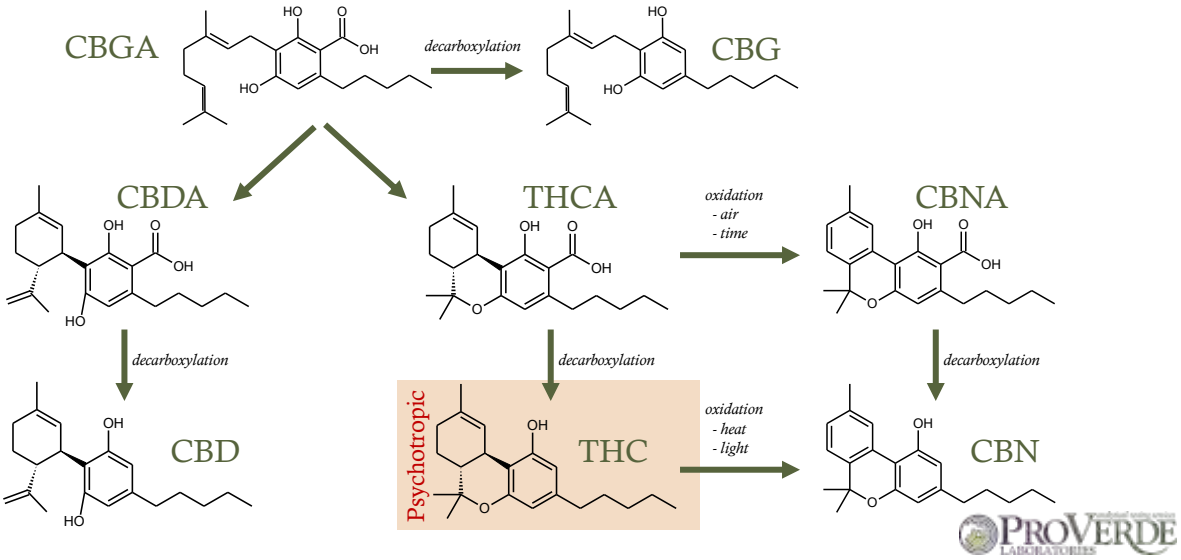
Cannabinoid Alphabet Soup

33



Cannabinoid Alphabet Soup

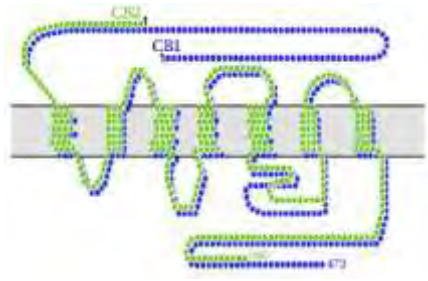
34



Cannabinoid Receptors

35

- **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

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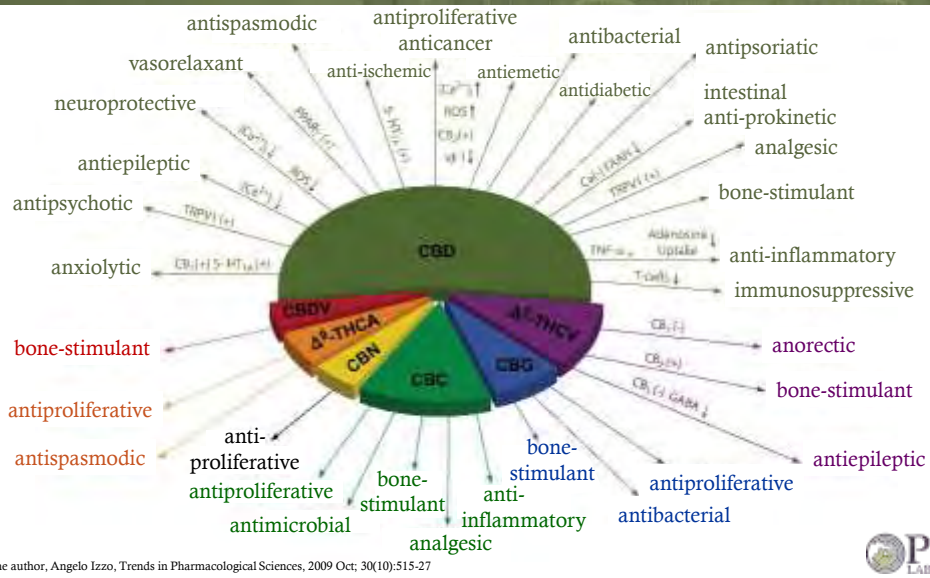
Medicinal Marijuana

36



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

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Medicinal Marijuana

37

- 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

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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.**

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Analytical Testing Opportunities

39

Historical Marijuana Industry
High Risk
Black Market/Underground
Minimal Accountability

Testing Technology - Low Level
Cannabinoids – Thin Layer or
Gas Chromatography
Microbiology – Visual Inspection/Cultures

New Era of Legislation/Regulation
Legalization in Many States
Increased Acceptance by the Public
Fastest Growing Industry in the US

Technological Advances
UPLC/SFC/CC/Mass Spectrometry
qPCR/Immunoaffinity Assays
ICP and ICP/MS

New Opportunities
Increased Safety
Greater Harvest Yields
More Efficient Processes

ProVerde Laboratories

Convergence Chromatography

40

- **UltraPerformance Convergence Chromatography System (UPC^2)**
- **Based on the theory of Supercritical Fluid Chromatography (SFC)**
  - Uses liquid CO_2 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**

ProVerde Laboratories

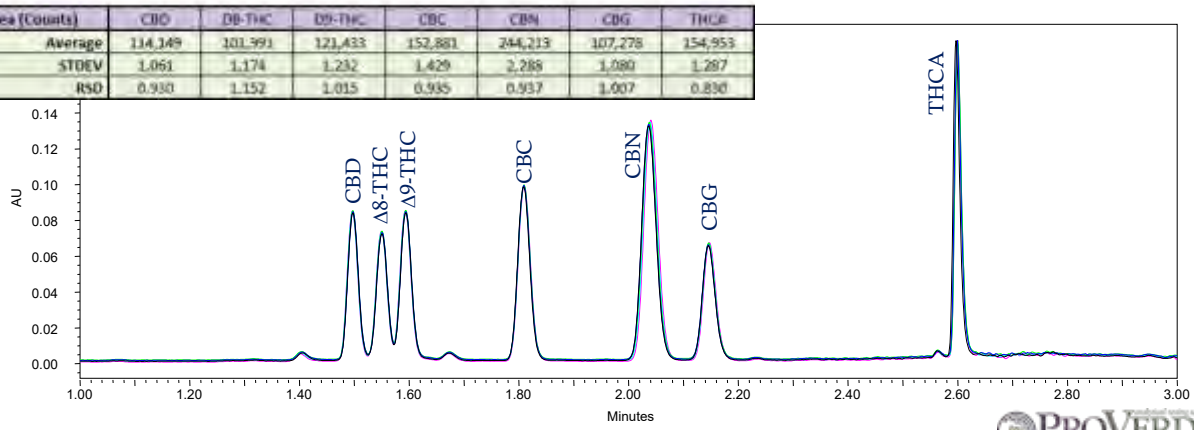
Injection Reproducibility

41

Retention Time (Min)	CBD	D8-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

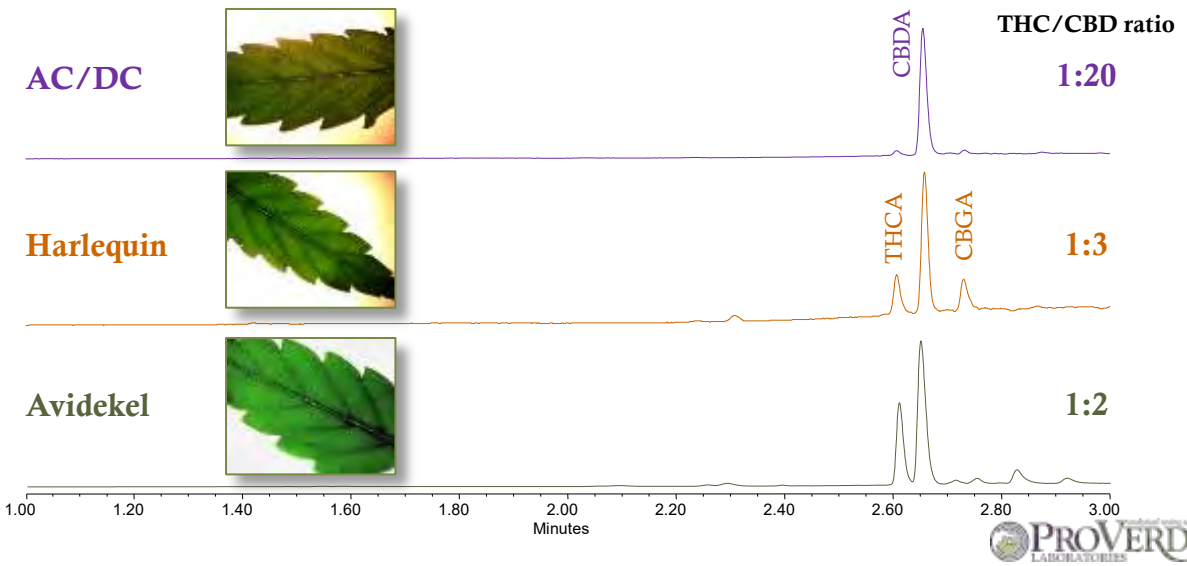
Area (Counts)	CBD	D8-THC	D9-THC	CBC	CBN	CBG	THCA
Average	114,149	101,991	121,433	152,881	244,213	107,278	154,953
STDEV	1,061	1,174	1,232	1,429	2,288	1,080	1,287
RSD	0.930	1.152	1.015	0.935	0.937	1.007	0.830

Overlay of 5 standard injections



Vegetative Plant Tissue

42



Understanding Chemical Processes

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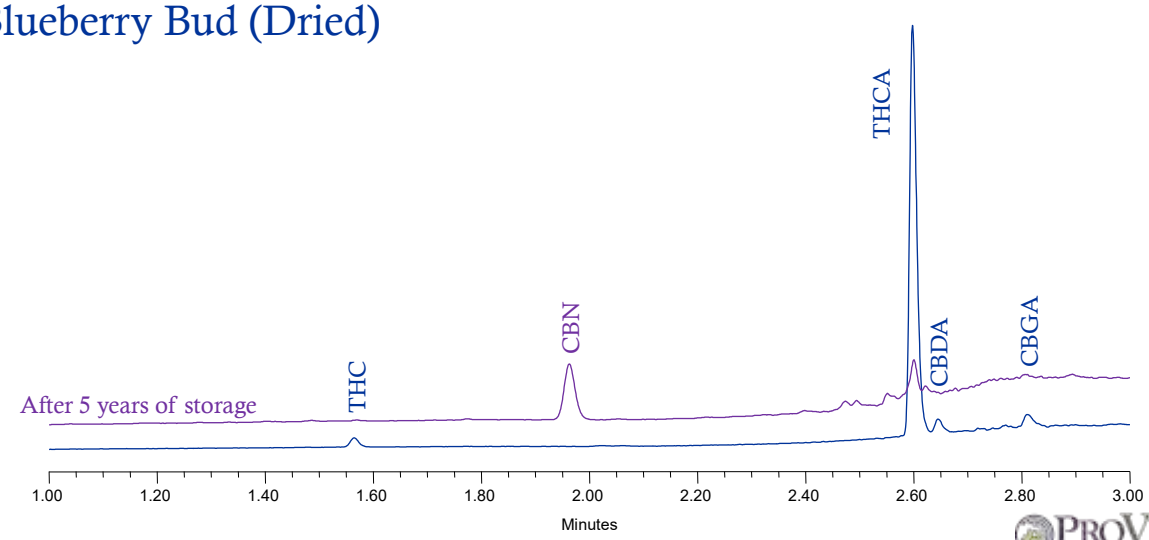
Blueberry Bud (Dried)



Optimization of Processes

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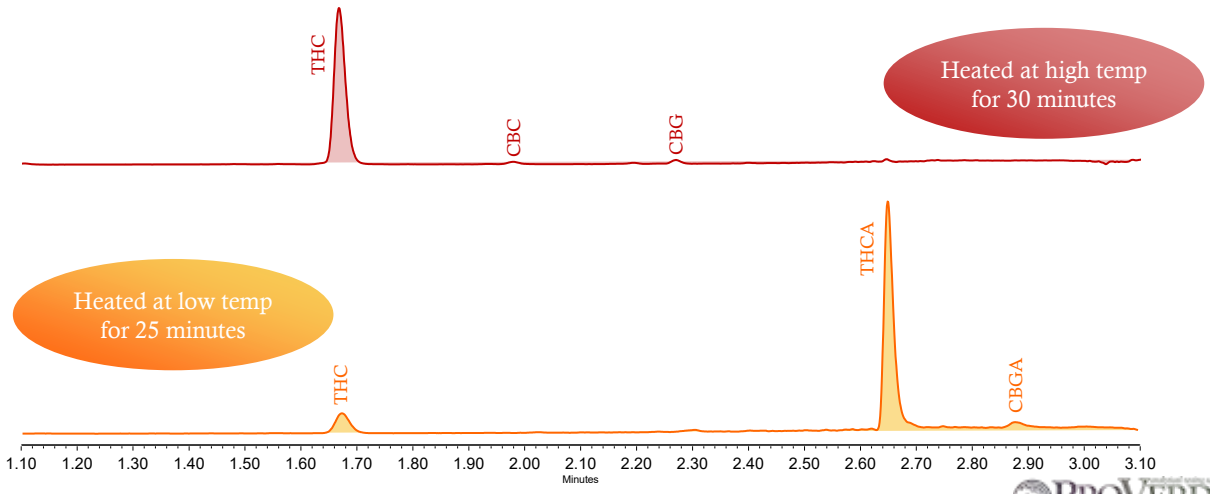
Ethanol Extracts of Pineapple Kush



Summary

- **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**

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References for Additional Information

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