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- Presenter: Jonathan Page
- Relationships with commercial interests:
  - Chief Science Officer of Aurora Cannabis Inc, a licensed cultivator and processor of medical and adult use cannabis
  - Shareholder of Aurora Cannabis Inc
  - Director of Trichome Financial Inc, a private funder of cannabis ventures
- Relationships with non-commercial interests
  - Adjunct Professor, UBC
  - Director of CCIC

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### Cannabis Botany

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### Cannabis has been used for millennia

Food and oil (seeds)



Fibre (stems)



Drug /  
Medicine  
(flowers)



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Basic botany

- Botanical Family: Cannabaceae
- Genus: *Cannabis*
- Species: *sativa*
- Closest relative is *Humulus*  
(hop plant used in beer)
- Origin in Central Asia
- Annual herb
- Dioecious = separate female and male plants
- The dried female flowers ("buds") are "marijuana"
- Male plants are rarely grown or consumed



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Female cannabis flowers



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Cannabis cultivar diversity



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What is a "strain" and a cultivar?

**strain**<sup>2</sup>  
/s'traɪn/ ⓘ

*noun*  
noun: strain; plural noun: strains

1. a breed, stock, or variety of an animal or plant developed by breeding.  
synonyms: variety, kind, type, sort, breed, genus  
"a different strain of flu"

- a natural or cultured variety of a microorganism with a distinct form, biochemistry, or virulence.

- The term "strain" has been used for different cannabis types because the plant has (mostly) been ignored by formal horticultural naming conventions
- Cultivar (Cultivated Variety) is used for most other crop plants
- Chemovar (Chemical Variety) has been suggested for some cannabis types

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### “Indica” vs “Sativa”

Patients, growers, and retailers differentiate two types:

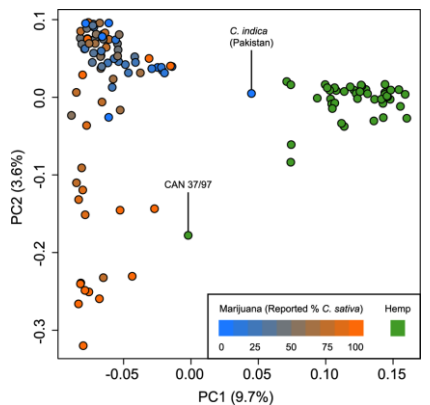
**“Indica”**

- short plant with broad leaves
- sedative and “body stone”

**“Sativa”**

- tall plant with narrow leaves
- stimulating and cerebral effects

### Cannabis genotyping: “Indica” vs “Sativa” plus hemp



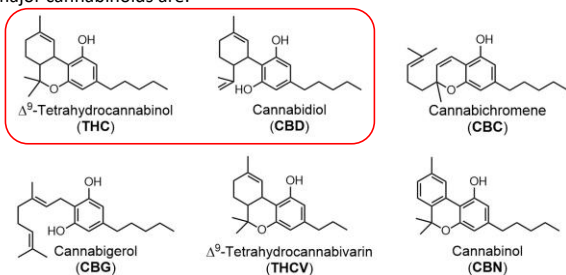
Sawler et al, PLOS ONE 2015

### Cannabis Chemistry

**Cannabis: The mixture is the medicine**

## The (phyto)cannabinoids

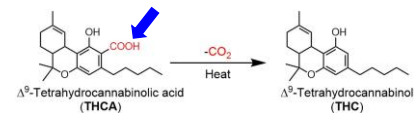
- THC and CBD are just two of a group of plant metabolites called the cannabinoids
- Present only in cannabis (with a few rare exceptions)
- There are more than 115 known cannabinoids
- The major cannabinoids are:



EISOHLY &amp; SLADE, 2005

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## Cannabinoid acids require decarboxylation to become active

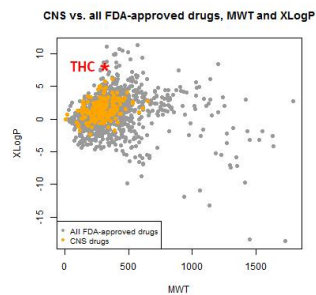


- Cannabis produces cannabinoid acids
- The acid forms lack the typical spectrum of pharmacological effects because they don't bind cannabinoid receptors
- **Cannabinoid acids** decarboxylate with heat (smoking or cooking) or prolonged storage to form **neutral cannabinoids**
- **Cannabis preparations must be heated to be active**
  - Juices and salads have minimal psychoactivity

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## Cannabinoids are lipophilic (fat soluble)

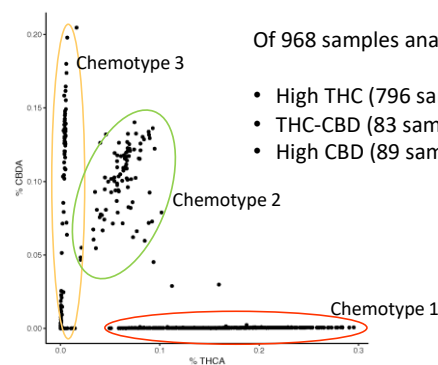
- Acidic and neutral cannabinoids are lipophilic / non-polar
- Very limited solubility in water
- Soluble in organic solvents and oils



<http://www.cureffi.org/2013/10/04/properties-of-cns-drugs-vs-all-fda-approved-drugs/>

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## THC and CBD levels in cannabis cultivars



Of 968 samples analyzed:

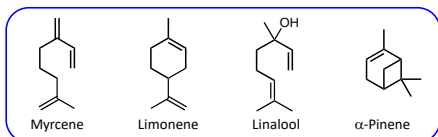
- High THC (796 samples): average 17.5% THC
- THC-CBD (83 samples): 10% THC: 7% CBD
- High CBD (89 samples): average 12% CBD

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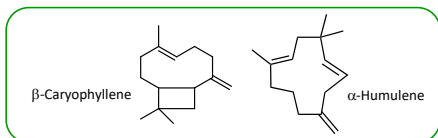
### The terpenes

- Group of 40,000+ metabolites; found in all plants
- Also called terpenoids or isoprenoids

Monoterpenes



Sesquiterpenes



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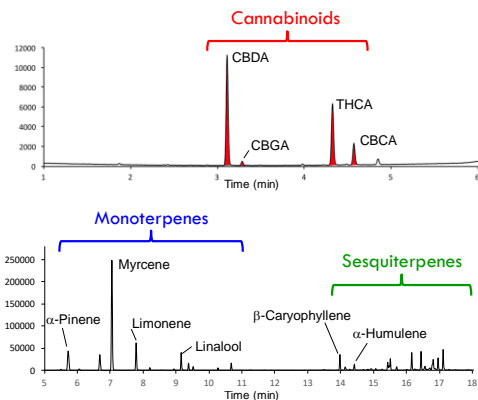
### Bioactive terpenes in cannabis

Compound	Structure	Activities
Myrcene		Sedative Anti-inflammatory Analgesic
Limonene		Anxiolytic
D-Linalool		Anxiolytic Sedative Analgesic
$\beta$ -Caryophyllene		CB <sub>2</sub> agonist Anti-inflammatory

Fischedick et al, 2010; Russo, 2011

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### Metabolite profiling: Cannabinoids + terpenes



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### Competing hypotheses about how cannabis metabolites affect pharmacology

The effects of cannabis are mediated by:

1. THC (dominant active principle)
2. THC and CBD (e.g. Health Canada's label)
3. The collective and interactive effects of THC, CBD and other compounds (minor cannabinoids and terpenes).

Decreasing support for the first hypothesis

- Patient reports of strain-specific effects
- Preclinical pharmacology

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## The “entourage effect”

**Why do patients and consumers report that cannabis cultivars differ in their effects, when they typically contain high levels of THC?**

- Minor cannabinoids?
- Terpenes?
- Other compounds?
- The complex mixture of cannabinoids and terpenes together *may* form a metabolic “entourage” that is responsible for the bioactivity of cannabis (Russo, 2011)
- Note: this remains a hypothesis that requires testing

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## Summary

### Botany

- Cannabis is food, fibre and drug/medicine
- Female flowers are rich in cannabinoids and terpenes
- Many cultivars with different potencies and cannabinoid profiles
- “Indica” and “Sativa” is an overused and inaccurate classification

### Chemistry

- The main active constituents are THC and CBD; 115 cannabinoids in total
- Other cannabinoids and terpenes have pharmacological activity
- Cannabinoid acids need to undergo decarboxylation
- Cannabinoids are fat soluble
- Survey and anecdotal evidence supports reports of cultivar-specific effects (but the “entourage effect” still needs more study)

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