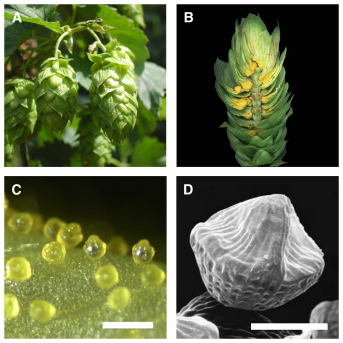
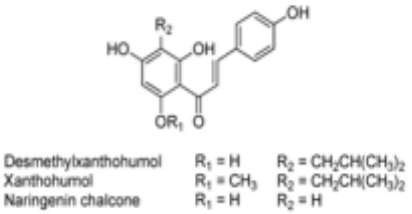
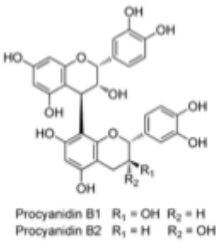
Terpenophenolics - Hop and Cannabis (Cannabinaceae)
(and why beer should be stored in dark bottles)

1. Introduction to Hop (*Humulus lupulus*)

- used to flavor and stabilize beer (since 700 AD)
- inflorescence bracts are rich in phenolics, terpenoids, and **terpenophenolics**
- many bioactive secondary plant metabolites
(flavor, antimicrobial, phytoestrogens)







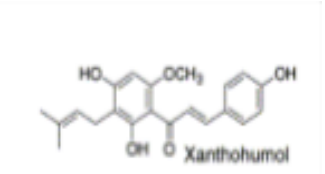
2. The diversity of secondary plant metabolites of hop. *Many of these you have seen already.*

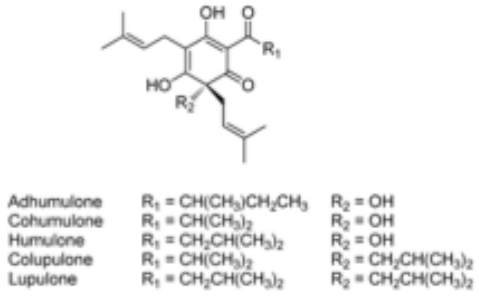
- flavonoids (quercetin, kaempferol)
- phenolic acids (ferulic, chlorogenic)
- proanthocyanidins and catechins (flavan 3-ols)
- monoterpenes: myrcene; sequiterpenes: humulene

Terpenophenolics:

i) **xanthohumol** and derivatives

ii) **prenylated acylphloroglucinols**
= **alpha-acids** (humulones) and **beta-acids (lupulones)**





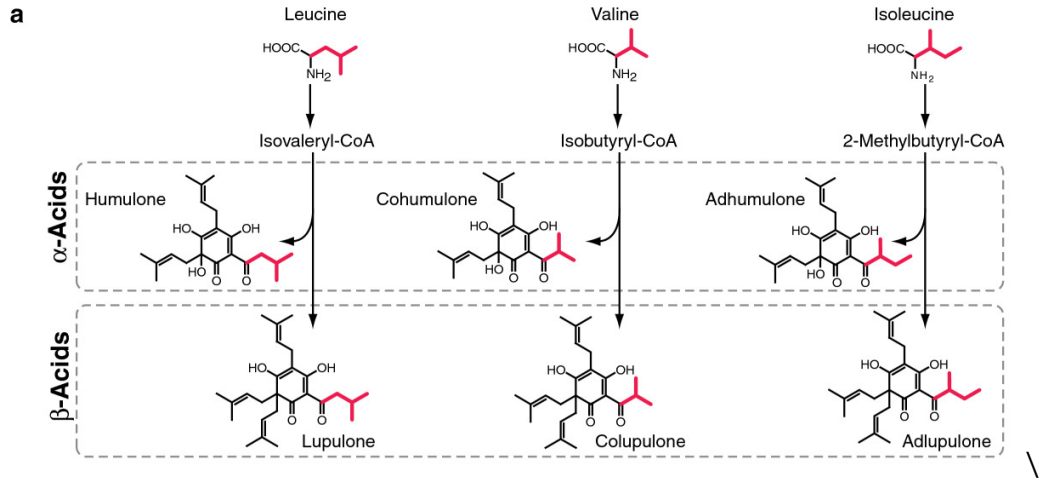
3. Localization of chemicals in **peltate** glands on the bracts of female inflorescence (**lupulin** glands)

4. Biosynthetic highlights

i) **xanthohumol**: - chalcone (recall flavonoids) via chalcone synthase
- prenylation using dimethylallyl pyrophosphate (DMAPP) by an aromatic prenyltransferase

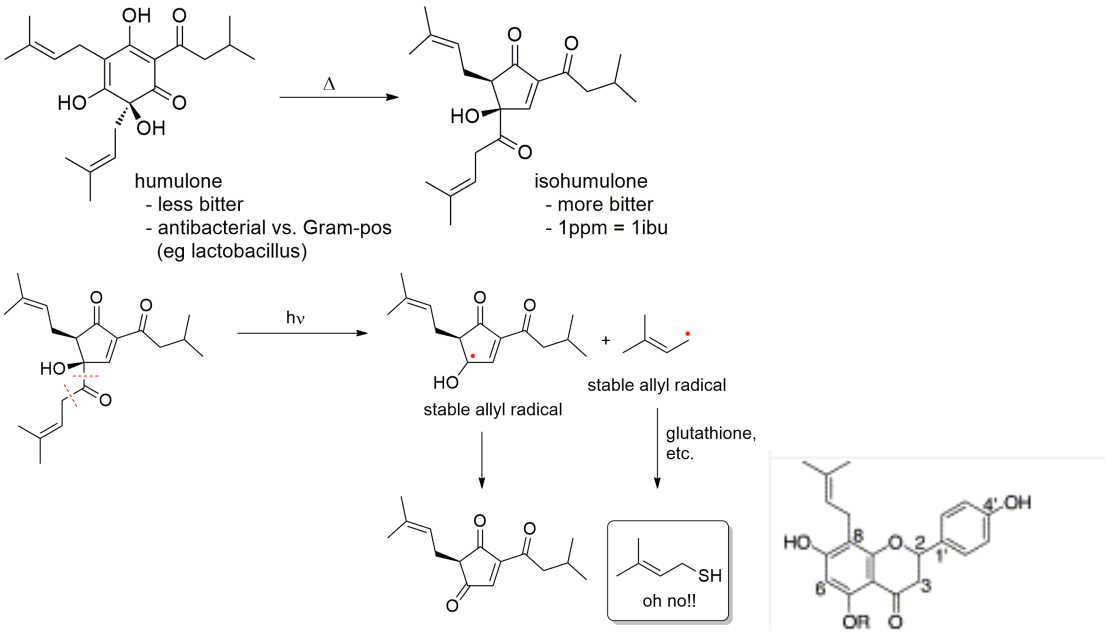
ii) **prenylated acylphloroglucinols (alpha- & beta-acids)**
- branched chain amino acids (Leu, Ile, Val)
- **polyketide synthases** to make **phloroglucinol** part from malonyl-CoA
- prenyltansferases decorate the phloroglucinol

Figure 1.



5. Human and chemical ecology of hops (why this should matter to us)

- **international bitterness units** (IBU) is defined as
  1 ppm of isohumulone
- bitter vs sweet hops (2-7% / 10-20 % alpha acids)
- boiling hops converts humulones to isohumulone, which is further degraded by light -> S compounds!
- *(why do they serve Corona beer with lemon??)*
- boiling hops volatilizes terpenes (less flavor)
- boiling converts desmethylxanthohumol to 8-prenylnarigenin (= potent phytoestrogen).



Cannabis sativa - Hemp and marijuana

1. History

- ancient domestication (6000 BP in China, Middle East 1700 BP)
- traditionally used for fiber, oil, medicine, psychoactive properties & spirituality
- medical marijuana is causing a "green rush" in Canada

2. Biology

- one or several species? (*C. sativa & C. indica*)
- **hemp = <0.5% THC, marijuana = 0.5 -15% THC**
- many years of selection and breeding have led to super high THC strains (but poorly studied..)
- no alkaloids, but terpenophenolics, accumulate mostly in **female flower buds**.
- complex **biological effects**: analgesic for chronic pain, apetite stimulant, anti-emetic.

3. Chemistry

- 450 different phytochemicals of different families, >100 different cannabinoids. These **terpenophenolics** are what make this plant unique.
- two major types of TPs: i) **tetrahydrocannabinol** (THC)
  ii) **cannabidiols** (CBD)

Tetrahydrocannabinol is the major psychoactive compound.
- synthesized as tetrahydrocannabinolic acid (THCA), decarboxylated by heating (smoking)

Biosynthetic precursors: **hexanoyl-CoA** and malonyl-CoA
Specific **Polyketide Synthase** (PKS) makes **olivetolic acid**

Depending on flux into CBD or THC pathway, plants have different chemotypes and properties.

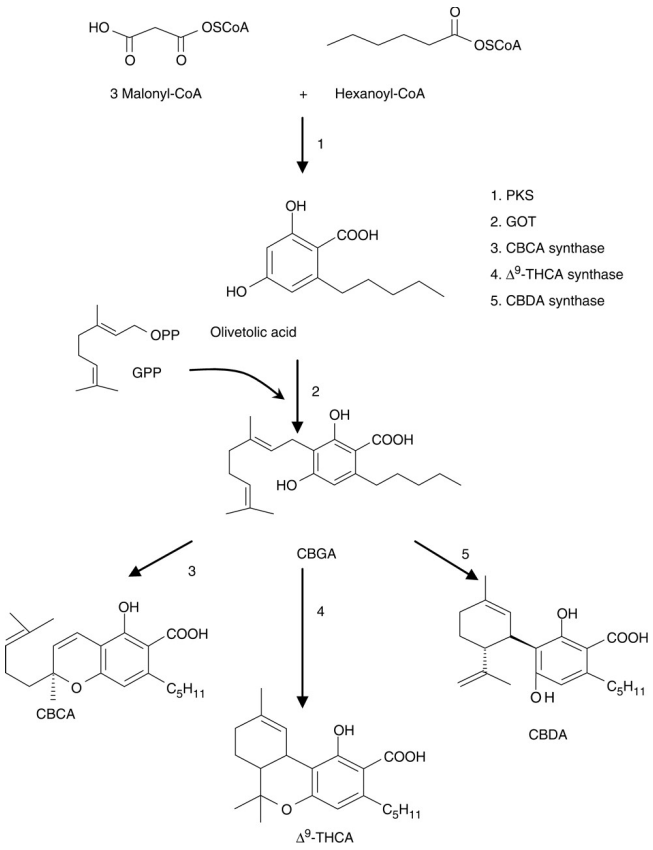
Marijuana - high THC:CBD
Hemp: low THC: CBD

Insight by *Cannabis* genomics: Hemp and marijuana varieties differ by expression levels (transcription factors??), but not by gene copy number.

4. (Biological) challenges surrounding medical marijuana in Canada

- pest and pathogen control in 'greenhouses'
- environmental control of cannabinoid levels
- positive identification of Cannabis strains
- analysis and quality control of the final product

-> possibilities for metabolic engineering?



Review of Secondary Metabolic connections