MEDICAL CANNABIS: WHAT YOU NEED TO KNOW

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What we'll talk about today

- Brief history of medical cannabis use
- Does it work? If so, for what?
- Pros and cons of forms of use
- Reasons not to use it & adverse effects

What *Cannabis* is…

- **A plant From the *Cannabaceae* family:**
  - Hops
  - Hackberry

- ***Cannabis* by any other name*:***

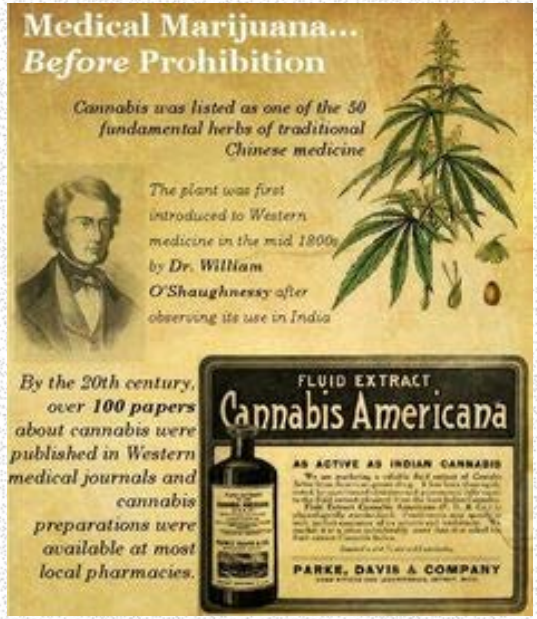
AKA: “grass”, “weed”, “ganja”, “marijuana”, “hash”, “bhang”, etc.

Is still *Cannabis!*

(Russo 2007)

Cannabis History "Tour"

- Medicinal use = before *written* history
- Early written history:
  - >3500 yrs ago in Egypt
  - 1st-2nd century China
  - Intro to modern Western medicine: 1840's



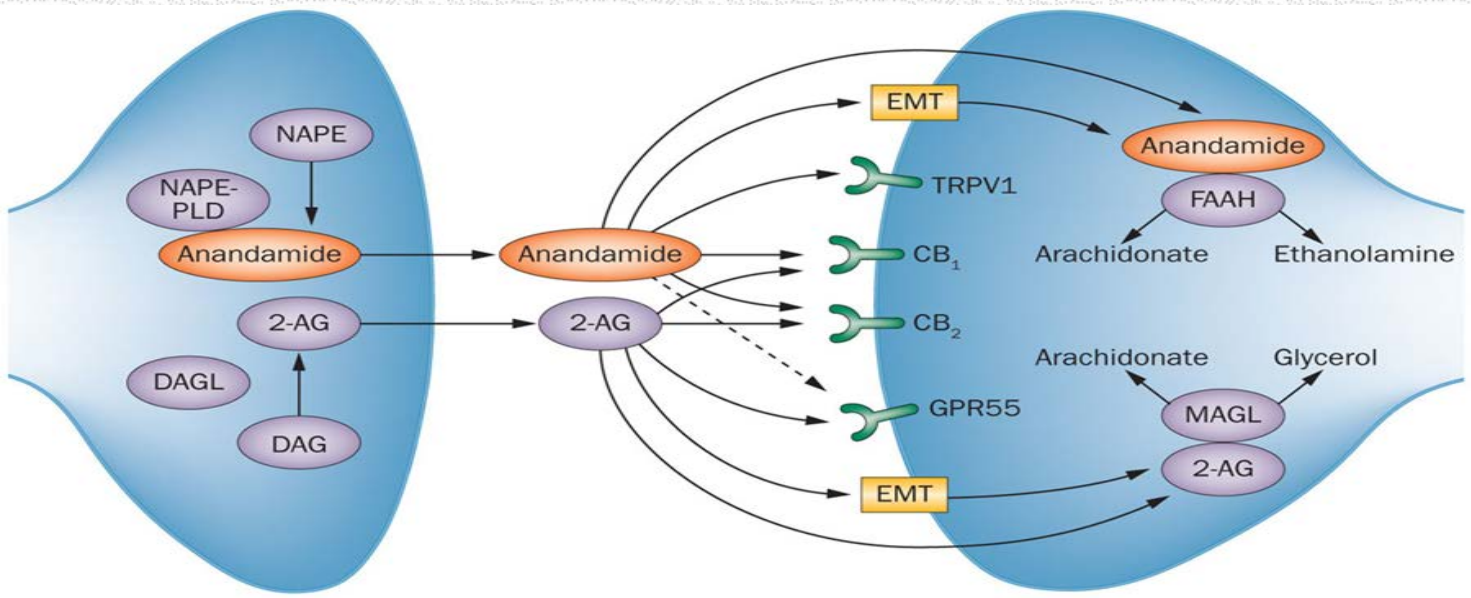
- US ban via taxation: 1937
- Schedule 1 classification (US): 1970

"high risk for abuse,
… no accepted medical use"

(Russo 2007; NIH-NCI; Backes 2014)

Our Endocannabinoid System

- Receptors: CB1 (nervous system) & CB2 (immune cells)
- Endocannabinoids
- Enzymes



Schicho, R. & Storr, M. (2013) Patients with IBD find symptom relief in the *Cannabis* field *Nat. Rev. Gastroenterol. Hepatol.* doi:10.1038/nrgastro.2013.245

(Battista 2012, Vemuri & Makriyannis 2015)

What's so special about Cannabis?

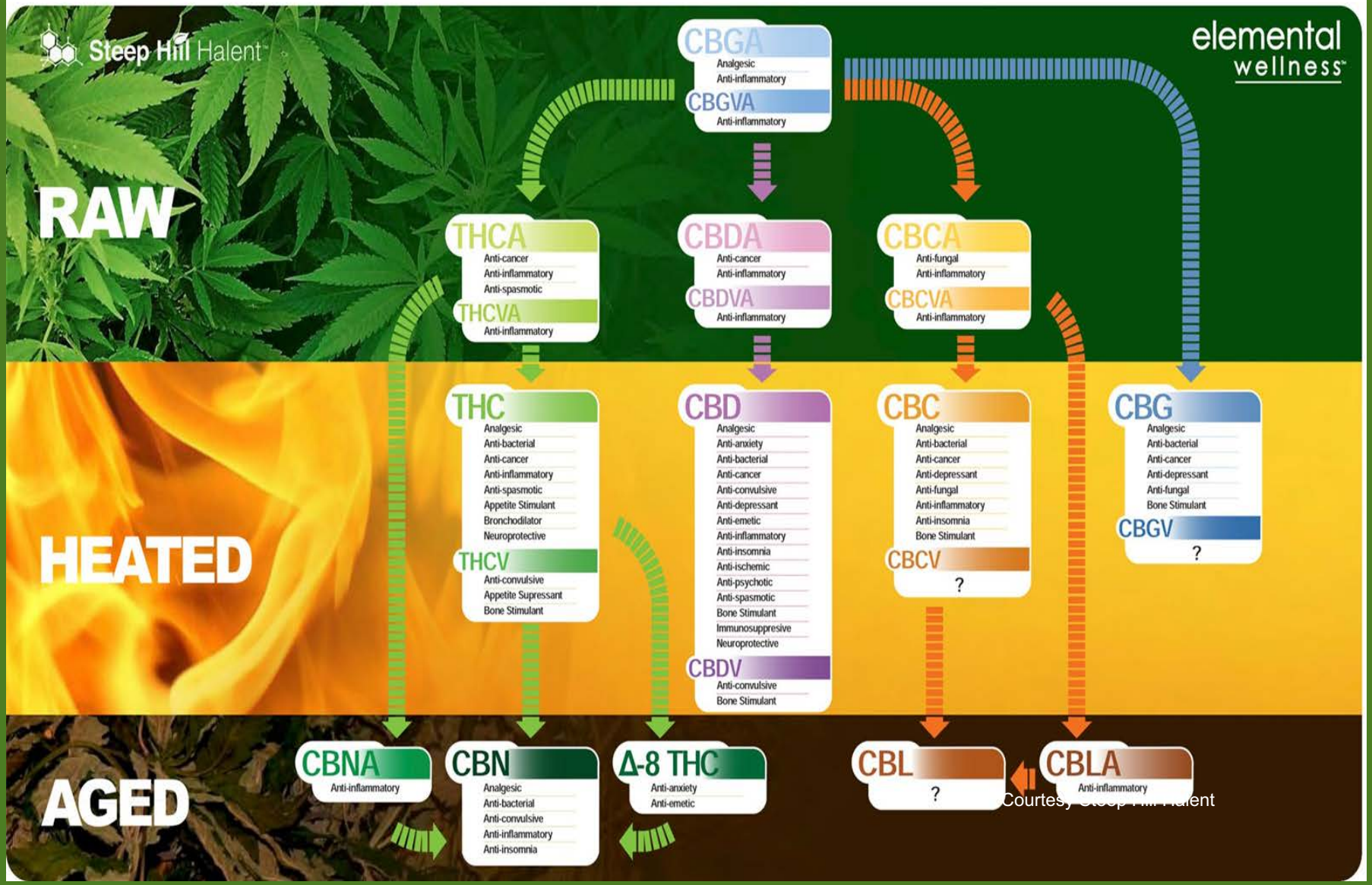
- **Phytocannabinoids:**
  - "…any plant-derived natural product capable of either directly interacting with cannabinoid receptors or sharing chemical similarity with cannabinoids, or both."
  - 110+ in cannabis

- **Properties:**
  - Pain-relieving
  - Anti-anxiety
  - Anti-seizure
  - Anti-nausea
  - Anti-inflammatory
  - Anti-oxidant
  - Anti-tumor
  - Neuroprotective

And the list goes on!

(Pacher et al. 2006; Gertsch et al. 2010; Russo 2011; Ahmed et al. 2015)

Cannabinoids and Their Therapeutic Effects



(NIH-NCI; Backes 2014)

The "Most Studied" Cannabinoids

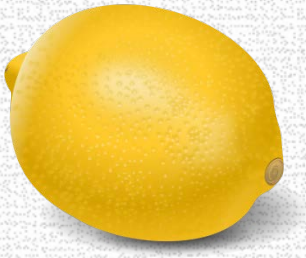
Cannabinoid:	Receptor Activity:	Major Effects:	Associated Rx drug:
THC:	CB1: nervous system (strong) CB2: immune cells (weak)	Psychoactive Anti-nausea Pain relief Anti-spasmodic Anti-inflammatory	Marinol (dronabinol) Cesamet (nabilone) Sativex (nabiximols) Levonantradol
CBD:	CB1: nervous system (weak) CB2: immune cells (weak)	Pain relief Neuroprotective Anti-seizure Anti-anxiety Anti-nausea	Sativex (nabiximols) Epidiolex (cannabidiol)

(Russo 2011)

Terpenoids in Cannabis

- Essential oil components
- Characteristic aroma
- Pharma effects

- Limonene
- Myrcene
- Pinene
- Linalool
- Caryophyllene(s)
- Nerolidol
- Phytol



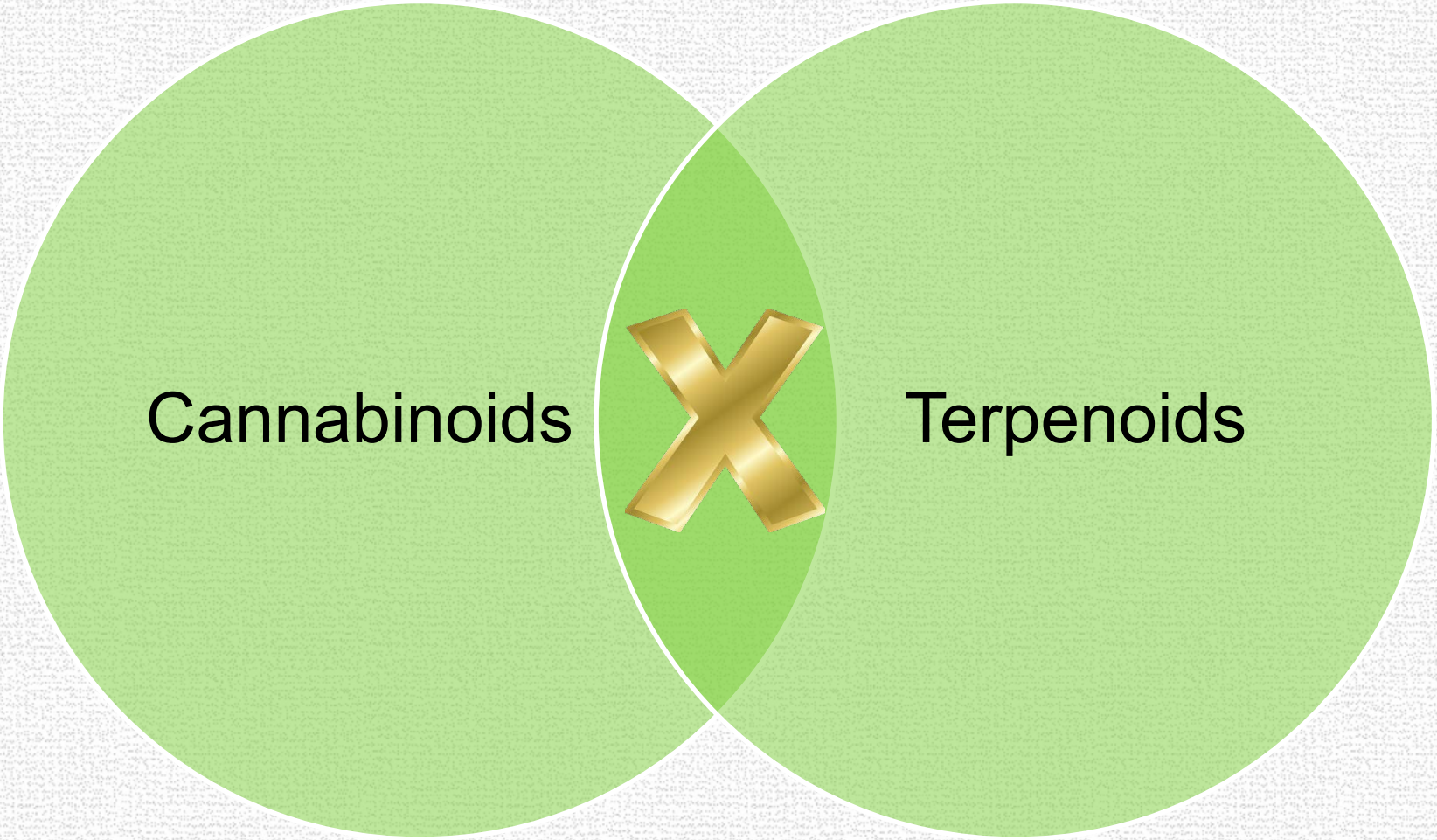
(Russo 2011)

Some Terpenoid Activities

Terpenoid:	Noted Effects:
• Limonene	anti-anxiety, anti-depressant
• Myrcene	anti-inflammatory, sedative
• Pinene	anti-inflammatory, bronchodilator
• Linalool	anti-anxiety, anti-convulsant
• Caryophyllenes	anti-inflammatory, anti-fungal
• Nerodilol	sedative, anti-protozoal

(Russo 2011)

The “Entourage Effect”



Noted “entourage” effects

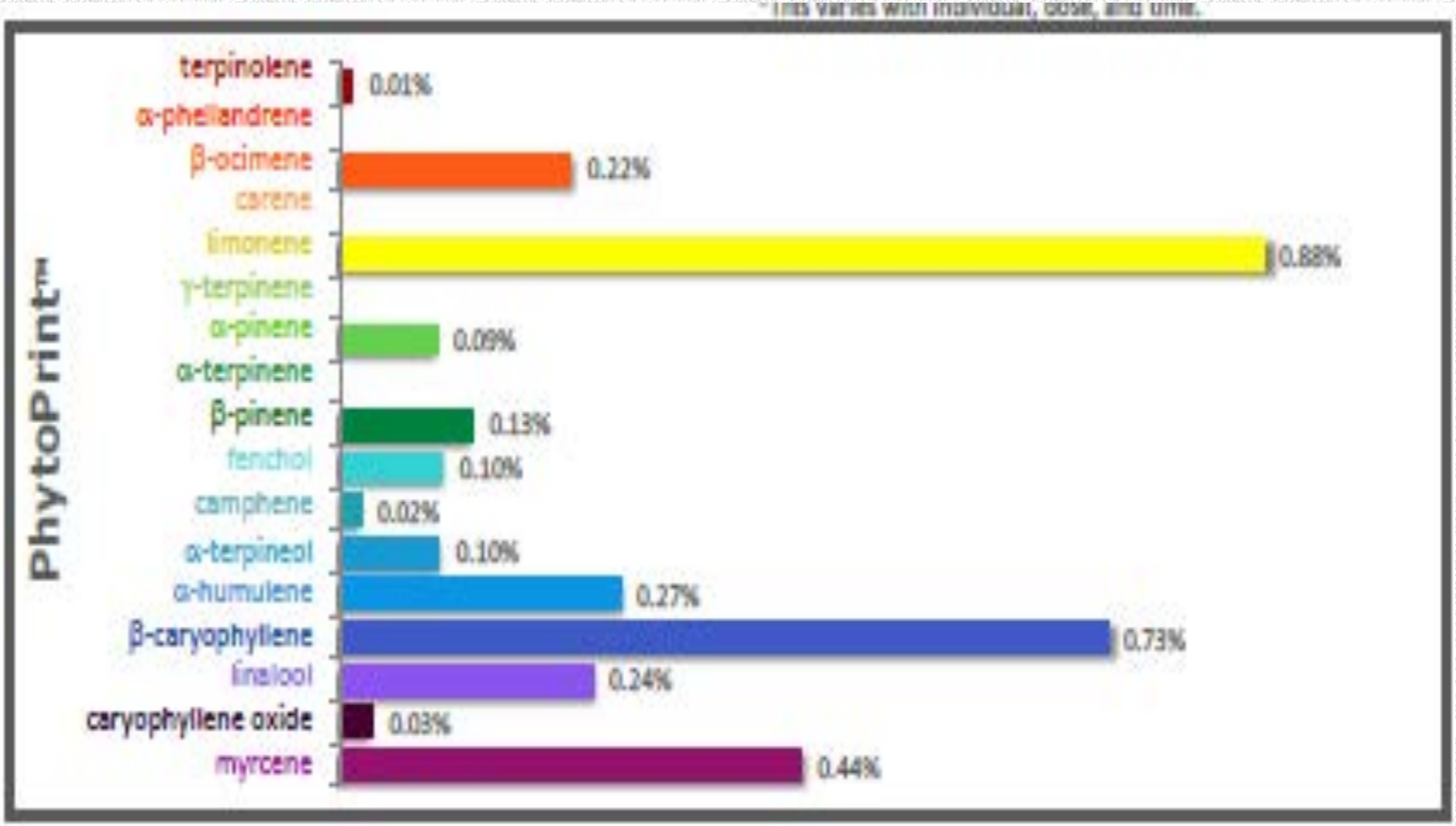
- When THC:CBD @ ~ 1:1
  - ↓ anxiety, memory issues
  - May ↑ pain control
- Terpenoids
  - Caryophyllene: ↓ pain, inflammation
  - Linalool, limonene: ↓ anxiety
  - Myrcene: sedating, ↓ pain
  - Pinene: ↓ memory issues

(Russo & Guy 2006; Morgan et al. 2010; Russo 2011, Nielsen et al. 2017)

- Indica? Sativa? Strains?
- "New speak" = Chemovars
  - Type I: THC predominant
  - Type II: THC & CBD
  - Type III: CBD predominant
- Additional distinctions: terpenoid profile

(Lewis et al. 2018)

Terpenoid Analysis



Reviewing the Evidence

- **Available studies will include:**
  - Synthetic THC (dronabinol, nabilone)
  - Extracted THC +/- CBD
  - Less often: “whole cannabis”

Nausea/Vomiting

Cannabinoid	Control	Results	Reference
Dronabinol Levonantradol Nabilone	Anti-nausea meds & Placebo	➢ More effective ➢ Preferred	Tramer et al. 2001
Dronabinol Nabilone Levonantradol	Anti-nausea meds	Dronabinol: decreased nausea, was preferred NS NS	Rocha et al. 2008
Nabilone	Anti-nausea meds	80%: ↓ nausea 78%: people: preferred	Ware et al. 2008
Dronabinol	Ondansetron & Placebo	Dronabinol: 71% Ondansetron: 64% Placebo: 15%	Parker et al. 2011

Appetite

- **Dronabinol vs. Megestrol acetate** (Jatoi et al. 2002)
  - Improved appetite:

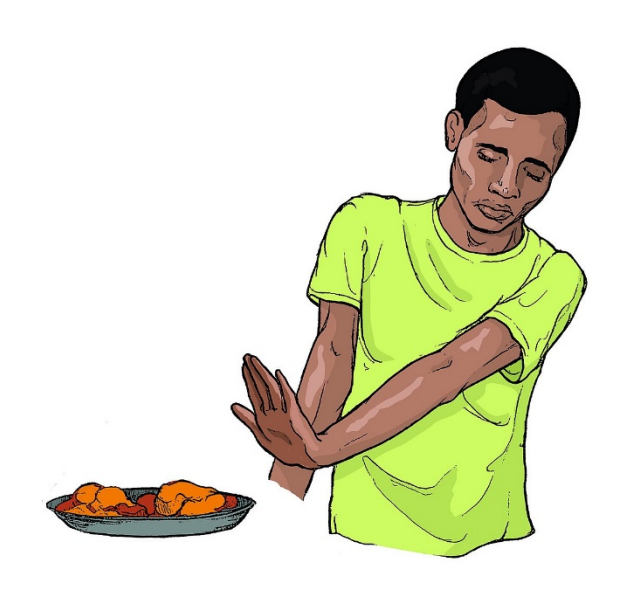
    Megace 75% vs. Dronabinol 49%

  - Advanced cancer patients

Appetite

- **THC+CBD vs. THC vs. Placebo** (Strasser et al. 2006)
  - No Difference

*Very low dose studied (2.5 mg THC)



Taste and Smell

- **THC vs. placebo** (Brisbois et al. 2011)
  - Chemosensory response:
    - Significant improvement: 36% THC vs. 15% placebo
  - "Food tastes better":
    - 55% THC, 10% placebo (p = 0.04)
  - Pre-meal Appetite score:
    THC > placebo
  - Pilot study: n= 11 (THC), 10 placebo

Pain/neuropathy

Cannabinoid	Pain	Results	Notes	Ref
Mixed	CA, other	Canna > Effective than placebo	Significant Adverse effects	1
Mixed	Neuro, other	15/18 trials: sig, modest effect	No severe AEs, no dropouts; placebo or active control	2
Mixed	CA, other	27/38 RCTs: sig relief	Placebo or active control	3
Cannabis	Neuro	6 RCTs: All = sig relief	3 studies: clinically meaningful relief 45, 53, 61% C vs. 18, 24, 26% p	4

(1: Martin-Sanchez 2009; 2: Lynch & Campbell 2011; 3: Aggarwal 2013; 4: Deshpande 2015)

Cannabis (smoked)

Prospective, observational study: n = 131

Symptom	Grade	Change
Nausea	None Mod Severe	+37% -38% +1%
Vomiting	None Mod	+23% -23%
Anorexia	None Mod Severe	+36% -38% +2%
Weight loss	None Mod Severe	+35% -32% -5%

- P>0.001 for trend (after 6-8 wks)

(Bar-Sela et al. 2013)

Cannabis (smoked)

Prospective, observational study: n = 131

Symptom	Grade	Change
Pain	None Mod Sev	+23% +3% -26%

- P>0.001 for trend (after 6-8 wks)

(Bar-Sela et al. 2013)

Cannabis a “Cancer Cure”?

- Limited Preclinical Evidence:
  - *In vitro, In vivo*
  - 1 small human study: GBM

- Potential? *maybe*
- Certainty? No

- Needs more research!!

Cannabis Administration Routes

Inhalation (Smoking & Vaping)

- Onset: 5 – 10 minutes
- Duration: 2-4 hours
- Bioavailability: 10-35%

- Vaping: less toxic byproduct (than smoking)

(Grotenhermen 2003; Huestis 2007; MacCallum & Russo 2018)

Caution…

- What is a “dab”?
  - Volatile “concentrate”
  - Extracted via solvents, liquid gas, CO2
- Safety concerns:
  - Residual solvents: >80% samples
  - Pesticides: 33% samples
    - Paclobutrazol: not listed with EPA for use on food crops
  - Increased in adverse effects*
- Best avoided as medicine

(Raber et al. 2015, MacCallum & Russo 2018)

Caution…

- Risk to the severely immunocompromised patient…
  - Bacteria, molds on green bud
  - Few case reports: aspergillus via inhaled cannabis

    *can be fatal

- Testing?
- Sterilization?

(Ruchlemer 2015)

Oral Ingestion: Edibles, Capsules

- Onset: 1 - 3 hours
- Duration: 6 - 8 hours
- Bioavailability: variable, 4-20%

- *First-pass metabolism: 11-OH-THC
  - *Potent psychoactive*
  - *Reduces bioavailability THC*

- **More difficult to determine dose**

(Grotenhermen 2003; Huestis 2007; MacCallum & Russo 2018)

Caution…

- Labeling inaccuracies…
- Content analysis:
  - 17% accurately labeled
  - 23% under-labeled (had >THC content!)
  - 60% over-labeled
- Contributes to:
  - Overdosing
  - Difficulty dosing

Cannabaceutical™ Facts

Tested On: **January 1, 2011**

YOUR LOGO HERE

Blue Dream

Sativa Hyb.

14.20% Wt. Loss on Drying

Δ^9-THC Max:	**13.6 %**
Δ^9-THCA	14.9 %
Δ^9-THC	0.53 %
CBD Max:	**7.60 %**
CBDA	8.12 %
CBD	0.48 %
CBN:	**0.25 %**

Safety Screen

Total Aerobic	GOLD
Enterobacteria	SILVER
Yeast & Mold	BRONZE
Pesticides	PASS

Patients can visit www.TheWercShop.com to learn more about this label and the test types reported.

Do not use while operating a car or heavy machinery. Keep out of reach of children. For medical use only. % = W/%

(Vandrey et al. 2015)

Oromucosal: Sprays, Tinctures

- Onset: ~15 – 45 minutes (average)
- Duration: 6 - 8 hours
- Bioavailability:
  - Highly variable
  - Inhaled > OM >/= oral
  - Increases with food
  - *Less first-pass metabolism

(Guy & Robson 2003, MacCallum & Russo 2018)

Rectal

- **Suppositories**
  - Favored for absorption, no first-pass metabolism
  - Peak concentration: 1-8 hours
  - Bioavailability : ~2 X that of oral
  - Availability?
  - *Best to avoid during chemo

(Huestis 2007; Grotenhermen 2003)

Skin

- **Creams, Ointments**
  - Few Studies
  - Local effect only

- **Transdermal Patch**

  Preclinical research
  - Animal model → plasma for 48 hrs

  - ***More research needed***

(www.hc-sc.gc.ca/dhp-mps/marihuana)

Contraindications

- Allergy
- Pregnancy & breastfeeding
- Heart, Respiratory
- Hepatic, Renal
- Mental health hx
  - schizophrenia, bipolar d/o, depression

(Kahan 2014, Sachs 2015, Health Canada)

Use with Caution

- History of: Heart, Angina
- High Blood Pressure
- Asthma, COPD
  (inhaled)

(Kahan 2014, Sachs 2015, Health Canada)

Adverse Effects

Most Common:

- Drowsiness/fatigue
- Dizziness
- Anxiety
- Nausea
- Cognitive effects (confusion, disorientation, hallucination, impaired memory)
- Cough/phlegm/bronchitis (with smoking)

Common:

- Euphoria (adverse?)
- Blurred vision
- Headache

Rare:

- Hypotension
- Psychosis/paranoia
- Rapid heart rate
- Hyperemesis
- Diarrhea
- Loss of coordination

(MacCallum & Russo 2018)

Cannabis-Drug Interactions

Drug effects increased by cannabis:

- THC:
  - Alcohol
  - Benzodiazepines (Ativan, Valium, Xanax, Restoril, etc.)
  - Opiates: codeine, fentanyl, morphine

- CBD (high dose):
  - Clobazapam – will need dose reduction

(MacCallum & Russo 2018)

About Dosing…

- **“Start low, go slow, stay low”**
  - Helps limit fatigue, high heart rate, dizziness
  - Aids tolerance to psychoactive effects
- Consider Type II (THC + CBD) or Type III (CBD)
  - CBD tempers unwanted THC effects
- Chronic issues: oral product* = “mainstay”

  *If tolerated
- Acute/breakthrough symptoms: vaporization useful

(MacCallum & Russo 2018, Ware et al. 2015)

About dosing… THC

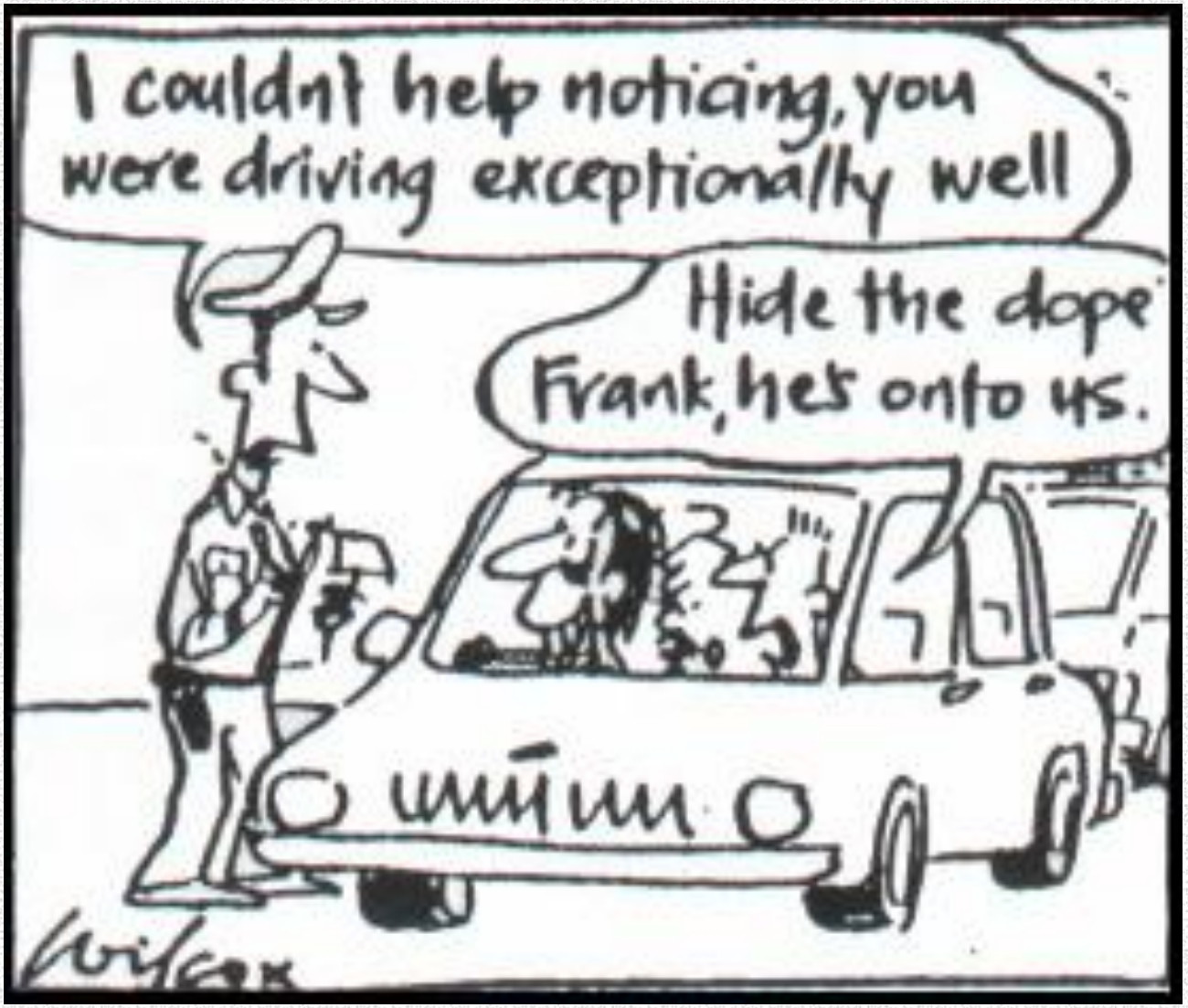
- Starting and increasing (*per* MacCallum & Russo 2018):
- At bed time:
  - Day 1-2: 1.25 – 2.5 mg THC (lower if >65 yrs old)
  - If tolerating: may ↑ by 1.25 – 2.5 mg every 2 days til desired effect
- If day time use:
  - Day 1-2: 2.5 mg THC
  - Day 3-4: 2.5 mg THC 3x/day
  - May increase (slowly!) as tolerated towards 5 mg 3x/day
  - Include CBD @ equal amount to ↓THC side effects
- Amounts > 20-30 mg THC/day = ↑ side effects, don't improve effects

About dosing… CBD

- CBD = fewer side effects (not psychoactive)
- No well-established dose guidelines
- Possible benefit:
  - 5-20 mg /day
  - Divide into 2x/day or 3x/day
  - Example: if taking 10 mg total,
    take 3 mg 3x/day or 5 mg 2x/day
- Possible interaction:
  - May increase sedation of benzodiazepines at high dose (>400 mg)

(MacCallum & Russo 2018)

Don’t Drive!!!


I couldn't help noticing, you were driving exceptionally well
Hide the dope Frank, he's onto us.

In Summary

- Cannabis
  - has a long history of medical use
  - may be effective for some conditions
- Pros/cons include:
  - Mode of use: difference in effects, contaminants, variability
  - Individual medical history
- Best dose: lowest for relief, good tolerance

Resources

- International Association for Cannabis as Medicine
  - cannabis-med.org – database of studies
- Americans for Safe Access
  - Safeaccessnow.org
- “Cannabis Pharmacy” *by* Michael Backes
- “Chronic Relief” *by* Nishi Whitely
- MacCallum & Russo, “Practical considerations in medical cannabis administration and dosing”, European Journal of Internal Medicine, 2018, 49:12-19.