Cannabis in Palliative and Hospice Medicine

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Honoring my teachers

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Cannabis (marijuana, hemp) is one of the oldest known psychoactive plants.

First reported use as medicine >3000 years ago.

Introduced into Western Medicine in 1840’s by Dr. W.B. O’Shaughnessy.

Promoted for putative analgesic, sedative, anti-inflammatory, antispasmodic and anticonvulsant properties.
Cannabis as Medicine

- Interest waned in early 1900’s with advent of opiates, barbiturates, chloral hydrate, aspirin and syringes
- First federal restrictions in 1937 with Marihuana Tax Act ($1/oz for medical use, $100/oz for recreational users)
- AMA virtually alone in opposing act
  - Believed objective data re: harmful effects were lacking
  - Act would impede future clinical investigations
    - Removed from US Pharmacopoeia in 1942
Controlled Substance Act 1970

Schedule I Substances

- Marijuana
- Heroin
- LSD
- Mescaline
- Other hallucinogenic amphetamine derivatives
- Methaqualone
- Illicit fentanyl derivatives
- Gamma hydroxybutyrate (GHB)
Cannabis as Medicine

• Contains over 400 chemical compounds
• Highest concentration of bioactive compounds in resin exuded from flowers of female plants
• Main psychoactive component believed to be delta-9-THC
• At least 70 other cannabinoids identified in pyrolysis products
• Delta-8-THC similar in potency but only in small concentration
Non-THC Components of Cannabis

- Δ9-tetrahydrocannabinol (THC) is the primary active ingredient of cannabis
- Secondary compounds may enhance the beneficial effects of THC
- Other cannabinoid and non-cannabinoid compounds may reduce THC-induced anxiety, anticholinergic effects and immunosuppression
- Terpenoids and flavonoids may increase cerebral blood flow, enhance cortical activity, kill respiratory pathogens and provide anti-inflammatory activity
Endogenous Cannabinoid System

Synthesis → Endocannabinoids → Cellular uptake

- CB2 Receptor
- CB1 Receptor
- CBx Receptor
- VR1 Receptor

Signal Transduction

- Immune function
- Cell proliferation
- Inflammation
- Pain

- Appetite
- Immune function
- Muscle control
- Pain
- IOP

- Cognition
- Emesis
- Neuroexcitability
- Reward
- Thermoregulation

- Pain
- Vaso-dilation

- Pain
- Inflammation

Martin 2004
The Endocannabinoids

- Lipid (oil) soluble
- AEA anandamide (AEA). Binds to CB1 receptors. CBD in cannabis inhibits its enzymatic clearance.
- Two-aclglycerol, aka two-arachidonyl glycerol (2 AG). Acts on both CB1 and CB2 receptors. CBD in cannabis stimulates its release.
- We have more (endo)cannabinoid CB1 and CB2 receptors than opiate receptors.

Piomelli 2003
CB₁ receptors for AEA and 2AG endocannabinoids are particularly abundant in the central nervous system, also in adipose tissue, liver, lungs, uterus & placenta.

Activation of CB₁s in central and peripheral nerves can be analgesic.

CB₁s on GABA interneurons which can disinhibit pain projection neurons.

Neuro-transmitters modulated include acetylcholine, norepinephrine, dopamine, 5-hydroxy-tryptamine, GABA and D-aspartate.
Cannabis contains at least 68 cannabinoids such as:

- THC – delta-9tetra-hydro-cannabinol
- CBD – cannabidiol
- CBN, CBG, CBC, THCV

Plus other bioactive components:

- Terpenes – the aromatic oils
- Flavonoids eg anti-inflammatory cannaflavins
**Δ9-THC**

- delta-9-tetra-hydro-cannabinol
- Psychoactive “narcotic” – Sativa *high*, Indica *stone*
  Alters mood, behavior, perception & consciousness.
- CB1 - Receptors primarily in the CNS but also in peripheral nervous system and other organs.
CBD - Cannabidiol

- Stimulates release of endocannabinoid 2-AG which acts on CB1 and CB2 receptors.
- Balances psychotropic effects of THC at CB1s in CNS, reducing disorientation, tachycardia, drowsiness.
- Abundant in Indica leaf & bud.
- Immuno-modulator, anti-inflammatory, analgesic, anxiolytic, lowers BP, anti-nausea, neuroprotective.
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CB2 Receptors

- **CB2** receptors for 2AG / CBD are found in liver, spleen, GI tract, heart, bones, kidneys, and in the peripheral nervous system.

- Many are in **immune** tissues such as spleen, tonsils, lymphatics and leucocytes including in order of concentration: B-cells, NK cells, Monos, PMNs, CD4 and CD8 T cells.
Cannabinoids inhibit the TH1 immune response, with its pro-inflammatory cytokines IL-1, IL-2, IL-12, IL-18, and γIFN.

These may inhibit auto-immune diseases including multiple sclerosis, IDDM1, RA, psoriasis and Crohn’s.

Stimulated by 2-AG and therefore by CBD.
Pharmacological Blockade of the eCB System

Pharmacologically induced deficiency of the eCB system by SR141716 or AM251 may lead to:

- **suppressed feeding and weight loss**  
  Freedland et al. (2000) Pharmacol Biochem Behav; Rowland et al. (2001) Psychopharmacology

- **increased anxiogenic-like behavior**  

- **attenuated responsiveness to rewarding stimuli (e.g., ethanol, sucrose, heroin, nicotine)**  

- **reduced sensitivity to the reinforcing effects of electrical brain stimulation**  
  Deroche-Gamonet et al. (2001) Psychopharmacology

- **increased duration of wakefulness, hyperarousal and vigilance**  
  Santucci et al. (1996) Life Sci

→ **Similarities with melancholic depression**

**Courtesy of Dr. Patrik Roser**
• Give the aroma and flavor to cannabis.
• Pinene, linalool, terpeneols, citronellol, myrcene, caryophyllene, pulegolone, cineole, cymene.
• Sedative and anti-depressant effects.
• Lessen anxiety from other cannabis bio-actives
Cannabis effects

- Topical, ingestible, suppository and vaporized for nausea, appetite, cachexia or pain.
- *Cannabis sativa* can be energizing.
- *Cannabis indica* is more sedating may cause dizziness and impaired memory.
- A balance in the ratio of CBD to THC can reduce intoxication ie indica leaf extract or juice.
Dry mouth, dehydration, reduced saliva and tears, reduced energy, weakness, light-headedness, dizziness, postural hypotension, syncope, immobility ("couch-lock"), mental clouding, confusion, dysphoria, lethargy, anxiety (often re: death or loss of control), impaired memory, amnesia, increased reaction time, reduced motor performance, decreased attention, reduced coordination, nausea, stomachache, colored stool or urine, conjunctival injection (bloodshot eyes), bronchitis, tachycardia.

Intoxication is aggravated by MSG!
Cannabinoid Analgesia

- Somatic pain
- Visceral pain
- Neuropathic pain
- Hyperalgesia
- Allodynia, pain of inflammation
- Muscle spasticity

Severe pain requires both THC and CBD.

Abrams 2011    Martin-Sanchez 2003
Cannabinoids and Pain

- Elevated levels of the CBI receptor – like the opioid – are found in areas of the brain that modulate nociceptive processing
- CB1 and CB2 agonists have peripheral analgesic actions
- CBs may also exert anti-inflammatory effects
- Analgesic effects not blocked by opioid antagonists
In mice and rats, THC greatly enhances analgesic effect of morphine in a synergistic fashion.

Increased potency of other mu opioids (hydromorphone and oxymorphone) seen with oral-Δ-9-THC in mouse models.

Possibility of enhanced and persistent analgesic effect at lower opioid doses.
PTSD, opiates, neurological disorders

- PTSD – Pruning memory, time distortion, altered perceptual state and disinheritance may be useful in moving trauma into long-term memory – “just one of the things that happened in my life”. Rx 8+ mg
- Cannabinoids can reduce opiate use and dependence, and may stand-in for alcohol and other psychoactive drugs.
- May ease anxiety (CBD), Tourette’s, epilepsy, MS, agitated dementia.
- Caution: Sedative drugs interact strongly!
Traditional Antidotes to Intoxication

- Citrus fruit – eg lemons, rind zest.
- Pine nuts
- Black pepper
- Calamus root

Russo 2011
• At age 13 a human child has well-developed pleasure/reward centres so can get high, but has not fully developed pre-frontal cortex until age 24.
• Cannabis primarily acts in the pre-frontal cortex of adults, who are able to use that area to create forethought of consequences of action and to control impulses.
• Early exposure to cannabis may damage brain development and may increase risk of psychoses.
Risk of dependency is about 9%, less than for tobacco, alcohol (15%), cocaine (17%) or heroin (23%).

The hallmarks of dependency are compulsion, craving, loss of control of intake, continuing to use despite negative consequences in physical health or social, recreational or work activities or relationships, tolerance, persistent desire to reduce intake but inability to do so, and withdrawal reactions.

N-acetyl-cysteine helps break dependence  Gray 2012
Drug Withdrawal

- Heavy users who suddenly withdraw may have mild irritability, anger, aggression, restlessness, agitation, sleep disorder, strange dreams, depression, hyperhidrosis, loss of appetite, weight loss, rebound intraocular pressure increase.
- Withdrawal symptoms tend to peak at day 2 to 4, and end by 7 to 14 days.
- THC will clear off in about 35 days, metabolites can be detected in urine for up to 80 days.
Symptom Management Challenges Associated with Cancer and Its Treatments

Anandamide in low concentrations in mice leads to a potent enhancement of appetite.
CBI receptors implicated in food intake control (hypothalamus and limbic system).
CB1 knockout mice eat less than wild type litter mates.
CB1 receptors involved in motivational/reward aspects of eating.
Interest in 70’s prompted by anecdotal reports when available antiemetics were inadequate

In randomized trials, oral THC better than placebo and equivalent or superior to prochlorperanzine

Smoked THC appeared superior to oral

THC < metoclopramide < 5-HT₃ antagonists
Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy (Review)
23 RCTS

N&V decreased in those who received verum vs placebo

Similar to conventional anti-nausea medicines. However, more people experienced side effects such as ‘feeling high’, dizziness, sedation, dysphoria and left the study due to the side effects with cannabis-based medicines, compared with either placebo or other anti-nausea medicines.

In trials where people received cannabis-based medicines and conventional medicines in turn, overall people preferred the cannabis-based medicines

Pain $\rightarrow$ 9 RCTS 1975-2011. 9/9 positive benefit. Dose dependent response

Appetite ad weight $\rightarrow$ 5 RCTS 1986 -2007. 5/5 increased appetite and weight with dose dependence

Drug: herb interactions $\rightarrow$ none with taxanes or irinotecan

No evidence of lung cancer or COPD risk with smoking.
Oncologists’ THC Survey

- 1000 responses from randomly selected members of American Society of Clinical Oncology surveyed in 1990
  - 44% had recommended marijuana to at least one patient
  - Marijuana believed to be more effective than dronabinol by 44%; dronabinol more effective by 13%
  - Doblin et al JCO 1991
THC and Analgesia

• In cancer trials, oral THC 20 mg was comparable to codeine 120 mg but with marked psychological effects

• Cannabinoids also effective in rat model of neuropathic pain
HIV-related painful distal symmetric polyneuropathy is a common problem.

Current therapy for HIV neuropathy pain is inadequate:
- Opioids generally ineffective
- Anticonvulsants in common use currently
- Anecdotal reports of marijuana’s efficacy

Cannabinoids effective in preclinical models of neuropathic pain.

Supported in part by UC CMCR and NIH GCRC Funds.
Cannabis in painful HIV-associated sensory neuropathy
A randomized placebo-controlled trial

D.I. Abrams, MD; C.A. Jay, MD; S.B. Shade, MPH; H. Vizoso, RN; H. Reda, BA; S. Press, BS; M.E. Kelly, MPH; M.C. Rowbotham, MD; and K.L. Petersen, MD

Abstract—Objective: To determine the effect of smoked cannabis on the neuropathic pain of HIV-associated sensory neuropathy and an experimental pain model. Methods: Prospective randomized placebo-controlled trial conducted in the inpatient General Clinical Research Center between May 2003 and May 2005 involving adults with painful HIV-associated sensory neuropathy. Patients were randomly assigned to smoke either cannabis (3.56% tetrahydrocannabinol) or identical placebo cigarettes with the cannabinoids extracted three times daily for 5 days. Primary outcome measures included ratings of chronic pain and the percentage achieving >30% reduction in pain intensity. Acute analgesic and anti-hyperalgesic effects of smoked cannabis were assessed using a cutaneous heat stimulation procedure and the heat/capsaicin sensitization model. Results: Fifty patients completed the entire trial. Smoked cannabis reduced daily pain by 34% (median reduction; IQR = –71, –16) vs 17% (IQR = –29, 8) with placebo (p = 0.03). Greater than 30% reduction in pain was reported by 52% in the cannabis group and by 24% in the placebo group (p = 0.04). The first cannabis cigarette reduced chronic pain by a median of 72% vs 15% with placebo (p = 0.001). Cannabis reduced experimentally induced hyperalgesia to both brush and von Frey hair stimuli (p ≤ 0.05) but appeared to have little effect on the painfulness of noxious heat stimulation. No serious adverse events were reported. Conclusion: Smoked cannabis was well tolerated and effectively relieved chronic neuropathic pain from HIV-associated sensory neuropathy. The findings are comparable to oral drugs used for chronic neuropathic pain.

NEUROLOGY 2007;68:515–521
Cannabis: Opioid Conclusions

- Co-administration of vaporized cannabis with oral sustained release opioids is safe
- Co-administration of vaporized cannabis in subjects on stable doses of morphine or oxycodone appears to enhance analgesia
- Co-administration of vaporized cannabis trends towards lowering concentration of the opioids
  - The PK effects would be expected to reduce the analgesic effects of the opioids
  - The effect of vaporized cannabis to enhance opioid analgesia occurs by a pharmacodynamics, not a pharmacokinetic mechanism
The accumulated data indicate a potential therapeutic value for cannabinoid drugs:

- Pain relief
- Control of nausea and vomiting
- Appetite stimulation

THC therapeutic effects best established.

Effects of cannabinoids generally modest; usually there are more effective medications.
Cannabis-Induced Euphoria

- Often described as a “side-effect” of Rx
- Is it really an “adverse experience” particularly in the terminal patient?
- Is a single treatment that increases appetite, decreases nausea and vomiting, relieves pain and improves mood and sleep a potentially useful tool in palliative medicine?
The Safety of Cannabis

- No deaths have been reported from OD
- Estimate 800 cigarettes required to kill (death secondary to CO not cannabinoid poisoning)
- By comparison, 300 ml of vodka or 60 mg of nicotine would be lethal
- Addictive potential and minor withdrawal syndrome less than or equal to caffeine
Cannabis and MS-related Incontinence

The effect of cannabis on urge incontinence in patients with multiple sclerosis: a multicenter, randomized placebo-controlled trial

Freeman et al 2006
Cannabis as an Anti-Cancer Agent

- Increasing body of preclinical evidence suggests cannabinoids may have activity
- Anti-oxidant and anti-inflammatory effects
- Possibility of anti-tumor activity via cannabinoid receptors inducing apoptosis and impairing tumor vascularization
- Gliomas and skin tumors seem responsive in animal models
Cannabinoids and Cancer

* Cannabinoid administration to nude mice curbs growth of various tumor xenografts
  - Lung carcinoma
  - Thyroid epithelioma
  - Lymphoma
  - Skin carcinoma
  - Glioma
Cannabinoids and Cancer

- Cannabinoids induce apoptosis in gliomas
- Cannabinoids administration in mouse models differentiates tumor vascular hyperplasia
  - Associated with reduced expression of VEGF and VEGF receptors
- Cannabinoids decrease the activity of matrix metalloproteinase-2; hence may also modify glioma invasiveness
  - All of the above in mice with gliomas

Velasco Neuropharmacology 04
Cannabidiol and Colon Cancer

- In colorectal cancer cell lines, CBD
  - Protected DNA from oxidative damage
  - Increased endocannabinoid levels
  - Reduced cell proliferation
- In mice treated with azoxymethane, CBD 1 mg/kg decreased aberrant crypt foci polyps and tumor formation
- At non-cytotoxic concentration, CBD anti-proliferative vs colorectal cancer cell lines

Cannabinoids for Cancer

- Cannabinoids inhibit cancer gene expression of Id-1 protein involved in aggressive growth and metastasis of breast & ovarian cancer. McAllister 2007
- Cannabinoids retard angiogenesis Freimuth 2010
- Cannabinoids inhibit inflammation via TNFα Chianchi 2008
Cannabinoids have anti-cancer activities

- directly retard cancer cell growth, e.g., CBD inhibits proliferation by antagonizing GPR55 receptors.  
  Kotsikorou 2013
- selectively kill cancer cells, mutated cells
- THC inhibits angiogenesis  
  Blazquez 2004
- THC inhibits cancer cell respiration even where there are no cannabinoid receptors.  
  Ruiz 1999
- CBD + THC inhibit metastasis  
  Murase 2013
- CBD + THC reduce free radicals of oxygen.
Cannabis for Cancer

- Cannabinoids inhibit the TH1 immune response, with its pro-inflammatory cytokines IL-1, IL-2, IL-12, IL-18, TNFα and γIFN. Borgelt 2013
- Modulate inflammatory growth factors
- THC inhibits EGFR. Blasquez 2004
- THC is anti-cachexic, THC + CBD are anti-nausea.
- Terpenes such as D-limonene also have anti-tumor activity.
Oral THC Pharmacology

- Low (6-20%) and variable bioavailability
- Peak [Plasma] within 1-6 hr; may remain elevated for several hrs
- Initially oxidized in liver to 11-OH-THC, as potent psychoactive metabolite
- Further oxidation of 11-OH-THC leads to elimination products (urine and feces)
- Terminal half life 20-30 hrs
Smoked THC Pharmacology

- Rapidly absorbed into blood stream and redistributed
- Considerable amount of dose lost in smoke and destroyed by pyrolysis
- Peak blood levels achieved at end of smoking decline rapidly over 30 minutes
- Smoking achieves higher peak concentration but shorter duration of effect
- Smaller amounts 11-OH-THC formed
GW Pharmaceuticals, England

~ 50 : 50 mix of THC & CBD

**Whole plant extract** – terpenes, flavonoids

Oral spray – corrosive to gingiva

Approved in Canada. Expensive

Rx for neuropathic pain and muscle spasticity

Gets many patients too high

Johnson 2013
Marinol® (dronabinol)

- THC pill – 2.5, 5 or 10 mg
- High blood levels of psychoactive 11-hydroxy-THC
- Expensive, less effective than cannabis  
  
  Cooper 2013

Nabilone®

- Synthetic THC from Cesamet, circa 2006
- For pain, chemo nausea, vomiting, loss of appetite
- 50% drop out: dizziness, sedation, dysphoria
- Most users prefer cannabis
Multiple variables dictate that dosing be highly individualized
A patient-determined self-dosing model is recommended
Self titration model acceptable in view of the plant and host variables and the low toxicity of cannabis
Gabapentin and example of another drug with relatively low toxicity and high dosing limits titrated to effect

Carter et al IDrugs 2004
A joint = 0.5 to 0.8 grams of cannabis with about 4 to 8% THC
About 20 to 70% of that ~ 5 mg of THC reaches the lungs.
5 to 50% of the THC is bioavailable - into systemic circulation,
31% of CBD - cannabidiol reach systemic circulation,
38% of CBN - cannabinoids reach systemic circulation.
Plasma peaks of THC occur in 3 to 10 minutes, often before finishing a joint.
The most psychoactive metabolite 11-hydroxy-THC reaches a peak in 13 minutes.
It rapidly moves into highly vascular tissues, then slowly distributes into fatty tissue.
Plasma clears in about 3 hours, and the high usually lasts about 1 to 2 hours, sometimes up to 4 hours.  
*The Pot Book 2010*
Vaporization

- Lower temperature, low particulates and markedly less of toxic carbon monoxide make this much safer and cleaner than smoking.
- There is markedly better THC delivery to blood compared to smoking - 30% of THC content is lost to pyrolysis (combustion) in smoking.
“Hash Oil”

- Ambrosia hybrid iso/ethyl extract contains 48 mg/mL THC + 8 mg CBD. Thinned in MCT to 12-24 mg THC/mL.
- Regular strength morning dose for pain, spasm, anxiety, depression, PTSD, etc. 0.15 mL which delivers 0.3 mg CBD, 1.8 mg THC.
- A larger dose later in the day may be 0.25 mL, yielding 0.5 mg CBD and 3 mg THC. Like smoking hash.
- “High Test” dose: 0.40 mL = 0.8 mg CBD & 4.8 mg THC
- At 24% an Extra Strength HT 0.4 mL cap = 9.6 mg THC
Edibles

- [www.hempology.ca](http://www.hempology.ca)  Ted Smith
- Cannoil: 43 gm bud, 1 litre olive oil, strain, add 11 Tbsp. lecithin
- Green butter: 2 oz. leaf, 1 lb butter, strain, add 5 Tbsp. lecithin
- Buddha oil: 4 2/3 oz leaf, 1 litre olive or grapeseed oil, strain, add 11 Tbsp. lecithin
Cannabutter

- Kettle of water – bring to a boil and add
- 1 pound butter.
- 1 ounce good bud
- Boil 2 hours, making sure temp doesn’t exceed 212° F - don’t let the pot boil dry.
- Strain out plant material, add water, re-boil.
- Mix both batches, let cool. The butter will congeal on top.
- Store butter covered, in fridge.
Olive Oil Infusion

* Decarboxylate herb 15 minutes in oven at 250° (or 1 hour at 150°).
* One ounce of bud, leaf or ”shake” per cup of oil
* Put in crock pot on LOW setting for 20+ minutes
* Strain through cheesecloth

* Coconut or grapeseed oil as also used.
Buddha Balls for Cachexia

Buddha Balls are carefully designed to be easy on compromised digestive systems such as those with Crohn’s disease and diabetics, and are a complete meal replacement. They contain oats, hemp protein, hemp hearts, soy protein, whey protein, coconut, sunflower seeds, almond powder, honey, and cannabis infused olive oil.
Buddha Balls Recipe

Combine:
- 4 cups oats
- 3 cups coconut
- 1 cup raw unsalted sunflower seeds
- 1 1/2 cups whey protein
- 1 1/2 cups soy protein
- 1/2 cup hemp protein
- 1/2 cup hemp hearts

Mix......

1 cup Buddha Ball Oil (Cannabis infused olive oil)
Mix......

400g honey (2 1/2 ladles)
Mix thoroughly.....

Put 1 cup almond powder in a small bowl
Form the balls and use almonds to coat the outside
Add 1/2 cup chocolate chips for 1/2 the batch

........Makes 24
Topical Cannabis Oil

Olive or coconut oil extracts are effective for many skin disorders, and can be rubbed into sore joints. 4 2/3 oz leaf, 1 liter oil, ½ bottle vitamin E oil

Rick Simpson dilutes the *phoenix tears* type oil in 5 parts 99% iso-propyl alcohol for topical use, and claims this “most medicinal plant in the world” cured his skin cancer.
Cannabis Suppositories

- Grind decarboxylated bud 15’@ 250° to flour consistency
- Melt cocoa butter and/or beeswax in a double-boiler. Coconut oil can also be used.
- Mix equal parts cannabis flour, or 1 – 2 gm RSO hemp oil, per 100 gm cocoa butter.
- Add up to 4% beeswax for shape and healing.
- Pour into moulds or shape into cylinders on wax paper.
- Refrigerate/freeze until needed.
Cannabis as a Cancer Treatment?

Active against cholangiocarcinoma, glioblastoma, carcinoid, breast, lung, prostate, pancreatic, leukemia – *in vitro* and in pre-clinical animal studies via ceramide, akt/mTOR, MMP, PPARγ, autophagy, EGFR, apoptosis, etc……..

Abrams, Weil, Guzman 2009
Singh & Bali 2013 – a case report
“Rick Simpson Hemp Oil”

- Rick Simpson used one pound of high THC Indicas.
- 8 litres of toxic and dangerous naptha or butane solvents.
- Short contact of herb with solvent www.phoenixtears.ca
- Yield – about 60 grams of thick, greasy oil.
- Consume 60 + grams RSO in 90 days
Phoenix Tears Oil Today

- Ideal is 1:1 mix of ethyl and isopropyl alcohols.
- Iso yields ~ 25 gm oil / lb > than pure ethanol.
- 15 minute ice-cold maceration maximizes bio-actives and GI tolerability of the oil.
- Using high CBD:THC hybrids: Cannatonic - 6%/6%

Romano 2013
Taking “RSO” hemp oil

- Warm the syringe in hot water.
- Dose 4 to 72 insulin units, up to 1 gm/day.
- Start at bedtime, as needed add doses at breakfast, lunch and 5 pm.
- Use citicoline to prevent excess intoxication, or lemonade, pine nuts.
- Ψ A/Es – avoid alcohol & sedatives!
1 gram oil = 0.71 mL = “00” capsule = ¼ tsp
Anecdotes and Legends

Brain scan of 8 month old Cannabis patient. Oil on pacifier twice daily = cured inoperable cancerous tumor, returned brain to normal.

Cannabis Club Australia

Third Annual Palliative Care Institute Conference
Brain tumour cured by cannabis?
No chemotherapy, no diet change – just RSO
Documentation of healthcare professional’s authorization to engage in the Medical Use of Cannabis in the State of Washington

Authorization for: Patient name here  DOB: __________

Designation of insert another close person who is authorized to pick up medicine at dispensary as PRIMARY CAREGIVER under Wash. Rev. Code §§69.51A.010, 69.51A.040 (2007).

I, your name, am a licensed naturopathic physician in the State of Washington under Washington statute 18.36A, and I have diagnosed the above individual as having a debilitating condition as defined in RCW 69.51A.010(6).

I have advised the above named individual about the potential risks and benefits of the medical use of cannabis. I have a long medical relationship with this person and am familiar with the extent and nature of their disease state; in my medical opinion they will likely benefit from medical cannabis.

Your name and credentials. WA License __________

Signed on __________

This recommendation expires on __________

Documentation of risk/benefit is in the medical record.

CBD rich concentrated extract: A 30-day supply as stipulated in WA RCW 69.51A.010(6) for this person is 60 mL Tincture, two ounces dry marijuana or 60 mL Oil Infusion / extract, 1 Gram Co2-Raw Oil-CBD Rich or 60 mL. Refill PRN.
Bibliography

- Integrative Oncology by Donald Abrams and Andrew Weil, 2nd ed.
Websites of interest

* [www.hempology.ca](http://www.hempology.ca)
* [www.rxmarijuana.com](http://www.rxmarijuana.com)
* [www.marijuanauses.com](http://www.marijuanauses.com)
* [www.medicalmarijuanastrains.com](http://www.medicalmarijuanastrains.com)
* [http://safeaccess.ca](http://www.safeaccess.ca)
* [www.phoenixtears.ca](http://www.phoenixtears.ca)
* [www.leafly.com](http://www.leafly.com)
* [www.cbdproject.org](http://www.cbdproject.org)
1. Cannabis is useful therapy for some patients. Don’t be afraid to recommend to your patients. Ask about prior use.
2. Visit your local cannabis dispensary and ask for a tour.
3. Start small dose orally. 5 mg CBD and 1 mg THC. Take before bed. Increase dose until JND in mood, pain, appetite.
4. Wide therapeutic dose range.
5. Refer your pt to a trusted medical dispensary near you.
6. Tell the dispensary to provide a low dose capsule or high dose oil in a 1 ml syringe. Call the dispensary and consult with them.
7. Certified organic cannabis may be hard to obtain. So teach pts how to grow make their own at home.
End of presentation
Will western palliative and hospice medicine be using psychedelic drugs to improve QOL and the death and dying experience?
Is there a role for psychedelic medicines in modern western end-of-life care?

* Some Central America indigenous groups use psilocybe mushrooms as a sacrament.
* Some Southwest American indigenous groups use peyote as a sacrament.
* 78% of Amazonian basic tribal indigenous groups use ayahuasca as a sacramental tea.
* Used in tribal groups as a community and family medicine.
* Most psychedelic natural and synthetic products are powerful 5-HT1a receptor agonists.
* Santo Daime Church and Uñiao do Vegetal Church use ayahuasca as a sacramental tea.
Psychedelic medicine clinical trials and practice

- LSD used by psychiatrists in 1960’s and 70’s dose 1 mcg/kg = 0.001 mg/kg for treating anxiety, depression, drug and alcohol dependence and OCD.
- Became FDA schedule I in 1970 and LSD research stopped and use went underground
- Psilocybin reduced fear of death in psilocybin trial at UCLA (Grob et al 2010) 0.2 mg/kg dose
- Psilocybin human studies at Johns Hopkins and NYU in normal adults
- MDMA trial starting soon for PTSD.
Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance.

Griffiths RR, Richards WA, McCann U, Jesse R. Psychopharmacology (Berl). 2006 Aug;187(3)
B. caapi vine/stem
Psychotria viridis leaves and flowers
P. Viridis in cultivation in Peru
Towards an FDA, IRB and DEA approval clinical trial of ayahuasca for the treatment of moderate recurrent depression in adults
Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin

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Psilocybin is the prodrug of psilocin (4-hydroxy-dimethyltryptamine, 4-OH-DMT), the psychoactive constituent of magic mushrooms, and a classic psychedelic (“mind-manifesting”) drug. Recent research has shown that psilocybin can induce profound, long-lasting changes in consciousness and cognition, and that it can elicit a transient state of altered reality that closely resembles the classic psychedelic experience. The authors report the results of a double-blind, placebo-controlled, randomized study comparing psilocybin to placebo in a group of healthy volunteers.

Results

Forty-five healthy volunteers were scanned using ASL to determine the effects of acute psilocybin administration on brain activity. The study was divided into two phases: a placebo phase and a psilocybin phase. The placebo phase was followed by the psilocybin phase, with a washout period in between.

The authors found that psilocybin administration induced a significant increase in cerebral blood flow (CBF) in several brain regions, including the prefrontal cortex and the posterior cingulate cortex. These changes were not observed in the placebo group. The authors also noted that the changes in CBF were associated with changes in subjective experience, as measured by a questionnaire.

Discussion

The results of this study suggest that psilocybin induces a transient state of altered reality that closely resembles the classic psychedelic experience. This finding is consistent with previous studies that have shown that psilocybin can elicit a state of consciousness that is qualitatively different from the normal waking state.

In conclusion, these findings suggest that psilocybin may have potential applications in the treatment of psychiatric disorders, such as depression and anxiety. Further studies are needed to investigate the potential therapeutic uses of psilocybin.


The authors declare no conflict of interest.

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Fig. 2. Decreased CBF after psilocybin (ASL perfusion fMRI). Regions where there was significantly decreased CBF after psilocybin versus after placebo are shown in blue (z: 2.3–3.7). Mixed effects analysis, z > 2.3, P < 0.05 whole-brain cluster-corrected, n = 15. LH, left hemisphere; RH, right hemisphere. Note, we observed no increases in CBF in any region.
Fig. 4. Brain deactivations after psilocybin. (Upper) Regions where there was a significant decrease in the BOLD signal after psilocybin versus after placebo (z: 1.8–3). Mixed-effects analysis, z > 1.8, P < 0.05 whole brain cluster corrected, n = 15. (Lower) Regions where there was a consistent decrease in CBF and BOLD after psilocybin. For display purposes, significant BOLD decreases were calculated within a mask based on the ASL result (Fig. 2) at an uncorrected voxel level threshold of P = 0.05. Note, we observed no increases in CBF or BOLD signal in any region.
Fig 1

Statistical maps showing regions where BOLD signal of the DMN (rest > task) decreases after Ayahuasca ingestion.

P < 0.05 uncorrected.
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