MDH Minnesota Department of Health

Minnesota Medical Cannabis Program Petition to Add an Approved Delivery Method

Making your petition

- ☐ Any person may petition the Minnesota Department of Health ("the department" or "MDH") to add an approved delivery method to those listed in subdivision 14 of Minnesota Statutes section 152.22.

Petitions are accepted only between June 1 and July 31, each year. Petitions received outside of these dates will not be reviewed.

Petitions must be sent by certified U.S. mail to:

Minnesota Department of Health
Office of Medical Cannabis
P.O. Box 64882
St. Paul, MN 55164-0882

- ☐ You must mail the original copy of the petition with an original signature.
- ☐ Complete each section of this petition and attach all supporting documents. Clearly indicate which section of the petition an attachment is for.
- ☐ Each petition is limited to one proposed approved delivery method.
- ☐ If a petition does not meet the standards for submission, it will be dismissed without being considered.

Petition review process

- ☐ If the petition is accepted for consideration, MDH will post notice of review of the petition on its medical cannabis website and allow public comment and input on the petition for at least 30 days. MDH staff will also provide information about the proposed delivery method and a review of the current literature regarding its effectiveness.
- ☐ The Commissioner will approve or deny the petition by December 1 of the year the petition is accepted for consideration.
- ☐ You may withdraw the petition at any time before it is posted on the website for public comment by submitting a written statement to the Department stating that you wish to withdraw it.

MDH Minnesota Department *of* Health

Section A: Petitioner's Information

Name (First, Middle, Last):
Cassie Annette Traun

Home Address (including Apartment or Suite #):
[redacted]

City:	State:	Zip Code:
Minneapolis	MN	55405

Telephone Number:	E-mail Address:
[redacted]	[redacted]

Section B: Delivery Method You Are Requesting Be Added

Please specify and provide a brief description of the proposed delivery method. Be as precise as possible in describing the delivery method you are requesting be added. *Attach additional pages as needed.*

Please see attached.

MDH Minnesota Department *of* Health

Section C: Anticipated Benefits from the Proposed Delivery Method

Describe the anticipated benefits from the proposed delivery method and why it is better than currently approved delivery methods. Identify patient populations that do not benefit from current delivery methods
Attach additional pages if needed.

Please see attached.

Section D: How Current Delivery Methods Are Inadequate

Provide information regarding the extent to which the currently approved delivery methods are unable to meet the needs of patients enrolled in the medical cannabis program. *Attach additional pages if needed.*

Please see attached.

MDH Minnesota Department *of* Health

Section E (optional): Scientific Evidence of Support for the Delivery Method

It will strengthen your petition to include evidence generally accepted by the medical community and other experts that addresses the effectiveness of the proposed medical cannabis delivery method and discusses its potential risks and benefits. This includes but is not limited to full text, peer-reviewed published journals or other completed medical studies. Please attach complete copies of any article or reference, not abstracts.

☒ ***I have attached relevant articles.*** *(check box if you have attached scientific articles or studies)*

Section F (optional): Letters in Support

Attach letters of support from persons knowledgeable about the use of the delivery method with medical cannabis.

☒ ***I have attached letters of support.*** *(check box if you have attached letters of support)*

Section I: Acknowledgement and Signature

Please Note: Any individually identifiable health information relating to any past, present, or future health condition or health care contained in this petition is classified as a health record under Minnesota Statutes §144.291, and is not subject to public disclosure.

I certify that the information provided in this petition is true and accurate to the best of my knowledge.

SIGNATURE

7/29/2016
DATE (mm/dd/yyyy)

To obtain this information in a different format, call:
(651) 201-5598 in the Metro area and (844) 879-3381 in the Non-metro.

Section A: Petitioner's Information

Co-Petitioners:

Brandan Borgos o/b/o Sensible Minnesota
1021 23rd Ave NE #2
Minneapolis, MN, 55418
612.865.7811
brandan@sensible.mn

Section B: Delivery Method You Are Requesting To Be Added

Vaporization of cannabis flower

Section C: Anticipated Benefits From the Proposed Delivery Method

Allowing the vaporization of cannabis flower for Minnesota's patients would be beneficial in two significant ways.

First, patients would be able to purchase strain specific medications for the first time. The program's currently limited range of products and cannabinoid profiles means that many patients experience a quick increase in tolerance, requiring an increase in medication purchased, which many of those patients cannot afford. Even a slight difference in a strain's cannabinoid profile allows the cannabinoid receptors to "reset" and gives the patient similar effects at lower doses. If patients were allowed to choose from multiple strains that all achieve a specific desired medical effect, patients would be much less likely to experience tolerance issues.

Second, medication costs across the entire range of products would likely decrease, relieving a significant burden on current medical cannabis patients. The Department of Health's report on patient and health care practitioner surveys revealed that the main issue that both patients and their health care providers saw with the medical cannabis program are the costs to patients. Many low and middle-class patients are currently locked out of accessing medical cannabis due to the cost burden, especially those who are disabled and unable to work.

In other states with medical cannabis programs, we don't see this massive cost burden because the majority of other states allow usage of cannabis flower, in addition to oils, pills, liquids, and edibles. What this means is that the processing of oils, pills, liquids, and edibles is done mostly on trim that is left over from processing the cannabis flower for sale. Other states have two sources of revenue: selling cannabis flower to be used and the other processed products. Because the other processed products are created from trim and not the flower, which has a value, both medical and financial, on its own, prices for oils and liquids are lower in other states. For example, one mL of vaporizable cannabis concentrate/oil in Minnesota is about $240 (Minnmed Black). The price for an equivalent product in Oregon is $30-60.

Section D: How Current Delivery Methods Are Inadequate

In addition to the tolerance and price issues noted above, which make oil, pill, and liquid medical cannabis inadequate, some patients are better able to control/titrate the effects from medical cannabis with flower, as it often has lower amounts of THC than some of the vaporizable oils available currently, and flower always includes the full range of cannabinoids and terpenes in a

strain, unlike the current products available. Having access to this full range of cannabinoids and terpenes is essential to the entourage effect.

Also, there are no longitudinal studies of usage of vaporizable cannabis oils and whether or not that is as safe as using cannabis flower. Even longitudinal studies of smoking cannabis flower, which this petition is not asking for, have shown usage of cannabis flower to have limited negative effects on the lungs.[1] Thus, patients should have the option to choose between using cannabis flower or oils, pills, or liquids.

Section F: Letters in Support of Adding the Medical Condition

Letters of support are included from the following individuals:

Maren Schroeder, [redacted] Vice President of Sensible Minnesota
Alexander Troester, Co-Owner of Beehive Extracts
[redacted] Patient
[redacted], Patient
[redacted], Patient
[redacted], Patient
[redacted], Patient
[redacted] Patient

[1] *The effects of marijuana exposure on expiratory airflow. A study of adults who participated in the U.S. National Health and Nutrition Examination Study.* https://www.ncbi.nlm.nih.gov/pubmed/25521349

SECTION E

Clinical Applications of Cannabis: Cancer Care

Center for Spirituality and Healing Conference

Donald I. Abrams, M.D.
Chief, Hematology-Oncology
San Francisco General Hospital
Professor of Clinical Medicine
University of California San Francisco
April 28, 2016

UNIVERSITY OF MINNESOTA

Disclosures

Dr. Abrams has disclosed a relevant financial interest as a consultant with ABCann, Tikun Olam, and Zynerba Pharmaceuticals.

Dr. Abrams will be discussing off-label and/or investigational uses of medical cannabis.

There are no conflicts of interest or relevant financial interests that have been disclosed by the rest of the planners or presenters of this activity that apply to this learning session.

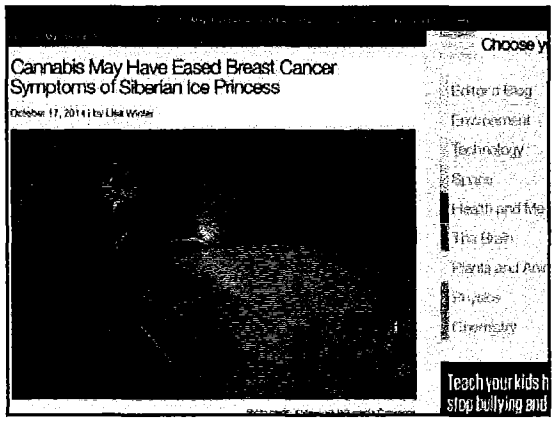
Disclosures: Donald Abrams

- I went to college in the 60's

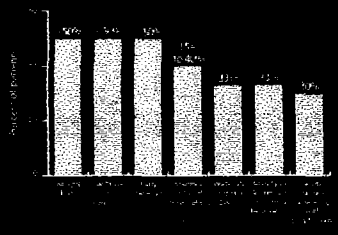
Objectives

- Review results of trials investigating cannabinoids in cancer-related anorexia and nausea
- Describe the potential utility of cannabis in chemotherapy-induced peripheral neuropathy
- Outline the possible ways that cannabinoids may have direct anti-cancer effects

Cannabis sativa



Symptom Management Challenges Associated with Cancer and Its Treatments



Cannabinoids and Appetite

- Anandamide in low concentrations in mice leads to a potent enhancement of appetite
- CB1 receptors implicated in food intake control n.b. lateral hypothalamus and limbic system locations
- CB1 knockout mice eat less than wild type litter mates
- CB1 receptors involved in motivational reward aspects of eating

Cannabinoids and Appetite

- Endocannabinoids enhance reward effects via mesolimbic dopaminergic systems
  - System may be involved in suckling
    Milk has high levels of 2-AG
  - CB1 antagonist given to mice at 24hrs causes them to stop suckling and die
- Phase II clinical trial of CB1 antagonist in obesity encouraging (3-4 kg ↓ in 2wks)

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
- 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
- increased duration of wakefulness, hyperarousal and vigilance

→

Courtesy of Dr. Patrik Roser

Cannabinoids and Appetite

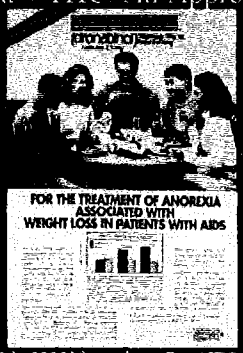
- Randomized double-blind study of 469 adults with advanced cancer and weight loss
  - Dronabinol 2.5 mg bid Appetite ↑ 49%, Wt ↑ 10%: 3%
  - Megestrol 800 mg qd Appetite ↑ 75%, Wt ↑ 10%: 11%*
  - Combination Appetite ↑ 66%, Wt ↑ 10% :8%

» Jatoi, J Clin Oncol 2002

- Smaller RCT of dronabinol in cancer patients demonstrated enhanced chemosensory perception in the treatment group
  - Food tasted better, appetite improved and calories ↑

» Brisbois et al, Annals of Oncology 2011

Oral Delta-9 THC: An Approved Drug



Approved in 1986 for N&V from chemoRx; AIDS anorexia in 1992

Cannabis and Chemotherapy N & V

- 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 prochlorperazine
- Smoked THC appeared superior to oral
- THC<metoclopramide<5-HT_3 antagonists

Cannabinoids in CINV

- Meta-analysis of 30 randomized trials of oral nabilone, oral dronabinol or IM levonantradol; no cannabis trials
  - 1366 patients involved
  - Cannabinoids were more effective than phenothiazines and metoclopramide
  - NNT for nausea control = 6
  - NNT for vomiting = 8
    - » Tramer et al, BMJ 2001
- Similar results from later meta-analysis of 15 studies of nabilone and 14 of dronabinol
  - » Ben Amar et al, *J Ethnopharm* 2006

Cannabis in CINV

- Only 3 controlled cannabis trials in CINV
  - In 2, cannabis only available after dronabinol failed
  - Third was a randomized double-blind, placebo-controlled, cross-over trial in 20 cancer patients
    - 25% reported positive antiemetic response
    - 35% preferred dronabinol, 20% preferred smoked and 45% had no preference
      - » Ben Amar et al, J Ethnopharm 2006
- Phase II trial of nabiximols added to standard antiemetics in 16 pts showed 4.8 sprays/day more effective than placebo
  - » Duran et al, J Clin Pharm 2010

Hi Dr Abrams,
I am contacting you to see about getting an extension of the medicinal marijuana letter you issued me last year which expired on March 21st.
Although I did not use it until my last 5 sessions of chemo (me getting over the stigma of its use), it did what no other drug could do, completely solve the severe nausea I had.
It allowed me to play with my children, attend their sports and school functions, and just function very normally in day to day activities.
I cannot thank you enough for giving me that option!
I am currently on a chemo vacation, after a clean scan and the only time I use medical marijuana now is when I have trouble sleeping. I would like to continue to use it for that purpose instead of relying on pharmaceutical options like zolpidem etc.

Cannabinoids and Pain

- Elevated levels of the CB1 receptor - like the opioid - are found in areas of the brain that modulate nocioceptive processing
- CB1 and CB2 agonists have peripheral analgesic actions
- CBs may also exert anti-inflammatory effects
- Analgesic effects not blocked by opioid antagonists

THC and Analgesia

- Intravenous THC exerts potent antinociceptive effects
- Cannabinoid-induced analgesia appears linked to opioid system
- In cancer trial, oral THC 20 mg was comparable to codeine 120 mg but with marked psychological effects
- Cannabinoids also effective in a rat model of neuropathic pain

Cannabis in HIV Neuropathy

- 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 efficacy of cannabis
- 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 on 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 outcomes 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 in 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 reduced 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

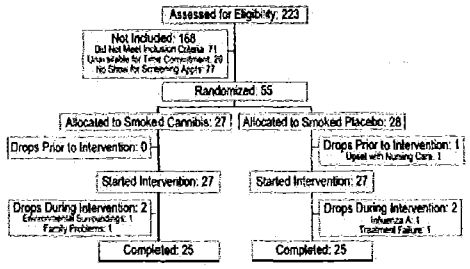
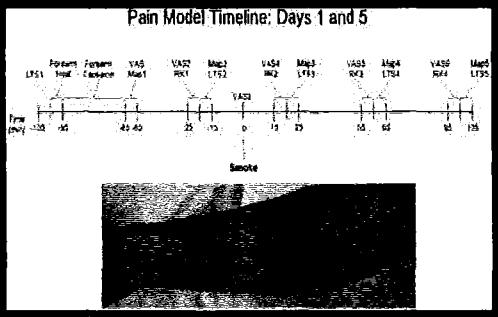


Figure 2. Flow of participants through the trial.

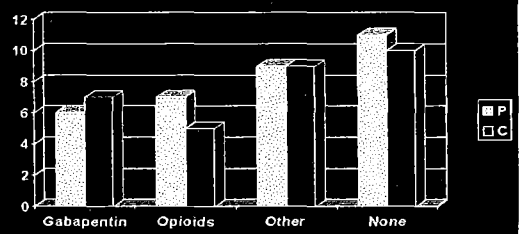
Experimental Pain Model



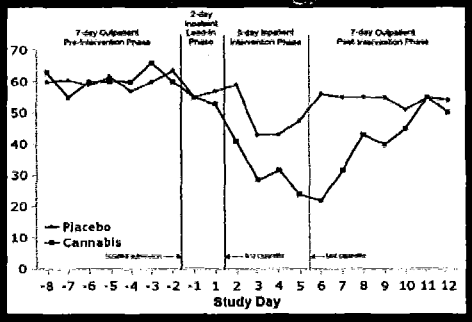
Baseline Characteristics by Study Arm

Placebo N=25		*Cannabis N=25*	
Neuropathy 6 years		*Neuropathy* 6 years	
HIV	7	HIV	10
Meds	14	Meds	12
Both	4	Both	3
Current ART	22	*Current ART*	17
BL Pain	52.0	*BL Pain*	53.8

Baseline Pain Medications

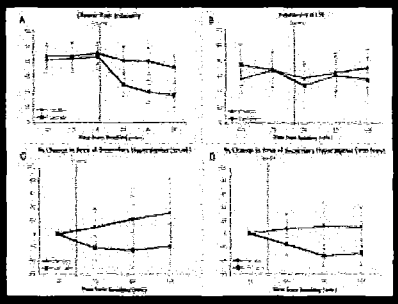


Results: Neurology RCT



Abrams et al Neurology 2007

Results: Neuropathy RCT



Abrams et al Neurology 2007

Neuropathy RCT: Conclusions

- Smoked cannabis is an effective treatment in patients with painful HIV-related peripheral neuropathy
- Smoked cannabis was also effective in attenuating central sensitization produced by a standardized experimental pain model
- The magnitude of pain reduction from smoked cannabis is comparable to that reported in trials of gabapentin for painful HIV-related neuropathy

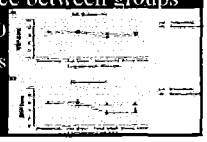
Abrams et al Neurology 2007

Cannabinoids in Chemotherapy-Induced Peripheral Neuropathy

- Activation of CB1 and CB2 receptors suppresses development of vincristine-induced PN in rats
  - » Rahn et al, Br J Pharmacol 2007
- In mice receiving daily cisplatin, anandamide plus a FAAH inhibitor attenuated CIPN
  - » Khasabova et al, J of Neuroscience 2012
- In mice injected with paclitaxel, CBD pre-treatment aborts CIPN
  - » Ward et al, Br J Pharmacol 2014

Nabiximols in Chemotherapy-Induced Peripheral Neuropathy

- Nabiximols has been shown to be effective in relief of pain associated with multiple sclerosis, cancer and rheumatoid arthritis
- 16 patients with CIPN randomized to nabiximols or placebo in crossover pilot study
- Overall, no significant difference between groups
  - 5 pts reported 2 point ↓ on 0-10
  - Average ↓ 2.6 in the 5 responders
  - NNT=5



Lynch et al, J Pain Symptom Management, 2013

Cannabinoid:Opioid Interactions

- Share several pharmacologic properties
  - Antinociception
  - Hypothermia
  - Sedation
  - Hypotension
  - Inhibition of intestinal motility and locomotion
- Initially thought to act on same pathways to produce their pharmacologic actions

Cannabinoid:Opioid Interactions

- 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

Welch and Cichewicz, multiple refs

Cannabinoid:Opioid Interaction Trial: Objectives

- Evaluate effect of vaporized cannabis on blood levels of prescribed opioids
  - Sustained release morphine
  - Sustained release oxycodone
- Determine the short-term side-effects of co-administration of cannabis and opioids
- Assess effect of vaporized cannabis on level of chronic pain

Funded in part by NIDA and NIH CRC grants

Cannabinoid:Opioid Interaction Trial: Design

- 5-day inpatient study in Clinical Research Center at SFGH
- 12-hour blood sampling on day 1 on stable daily dose of opioid analgesic
- Vaporization of 3.2% THC cannabis commences at 8 pm day 1; then three times daily at 8am, 2pm, 8pm
- After 8am vaporization on day 5, plasma sampled for 12 hours for opioid and THC levels
- Subjects complete drug effects questionnaire re: pain and other symptoms during PK draws

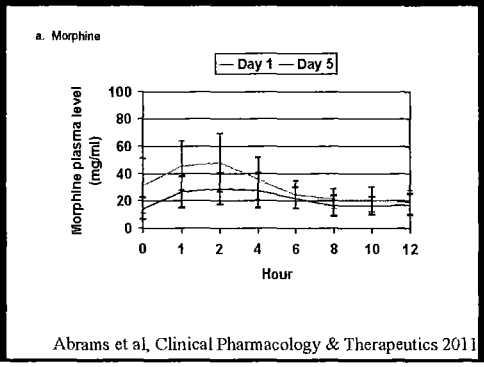
Participant Characteristics

Morphine		Oxycodone
10	Number Enrolled	11
4	Women	6
8	Caucasian	9
42.9 (33-55)	Age	47.1 (28-61)
62 mg bid (10-200)	Opioid Dose	53 mg bid (10-120)
34.8 (29.4, 40.1)	Pain Score day 1	43.8 (38.6, 49.1)

Pain Characteristics

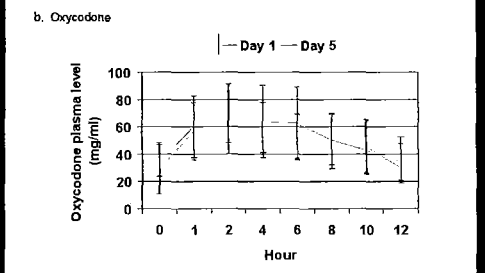
• Musculoskeletal NOS	7
• Post-traumatic	4
• Arthritis	2
• Peripheral neuropathy	2
• Cancer	1
• Fibromyalgia	1
• Migraine	1
• Multiple sclerosis	1
• Sickle cell disease	1
• Thoracic outlet syndrome	1

Mean Morphine Level By Study Day



Abrams et al, Clinical Pharmacology & Therapeutics 2011

Mean Oxycodone Level By Study Day



Abrams et al. Clinical Pharmacology & Therapeutics 2011

Pain by Study Day

	n	Day 1 Mean (95% CI)	Day 5 Mean (95% CI)	Difference Mean (95% CI)*
Overall	21	39.6 (35.8, 43.3)	29.1 (25.4, 32.8)	**-10.7 (-14.4, -7.3)**
Morphine	10	34.8 (29.4, 40.1)	24.1 (18.8, 29.4)	**-11.2 (16.5, -6.0)**
Oxycodone	11	43.8 (38.6, 49.1)	33.6 (28.5, 38.6)	**-10.3 (14.8, -5.8)**

*p<0.001

Abrams et al. Clinical Pharmacology & Therapeutics 2011

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 pharmacodynamic, not a pharmacokinetic mechanism

Cannabis as an Anti-Cancer Agent

- In 1975 NIH investigators reported that delta-9-THC, delta-8-THC and CBD inhibited Lewis lung adenocarcinoma cell growth in vitro and in mice
- Increasing body of preclinical evidence suggests cannabinoids may have anti-cancer activity
- Anti-oxidant and anti-inflammatory effects may contribute as well
- Possibility of anti-tumor activity via cannabinoid receptors inducing apoptosis and impairing tumor vascularization

Cannabinoids and Cancer

- Multiple tumor cell lines inhibited *in vitro*
- Cannabinoid administration to nude mice curbs growth of various tumor xenografts
  - Lung, breast, colorectal and pancreas carcinoma
  - Skin carcinoma
  - Melanoma
  - Thyroid epithelioma
  - Lymphoma
  - Glioma

» Velasco et al, Neuropharmacology 2004

Cannabinoids and Cancer

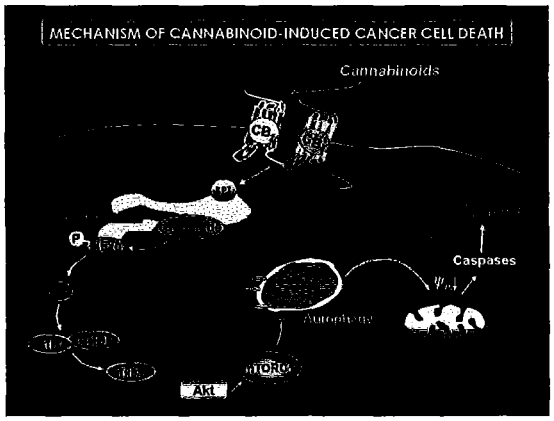
- Cannabinoids induce apoptosis in mouse gliomas
- Cannabinoids *administration in mouse models* differentiates tumor vascular hyperplasia
  - Associated with reduced expression of VEGF and VEGF receptors (inhibition of tumor angiogenesis)
- Cannabinoids decrease the activity of matrix metalloproteinase-2; hence may also modify glioma invasiveness (inhibition of metastasis)
- Despite above, normal glial cells unaffected

Velasco et al, Neuropharmacology 2004

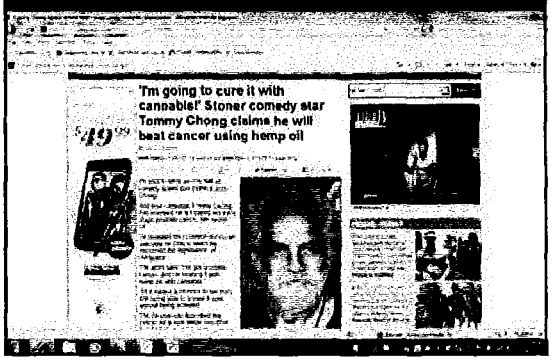
Cannabidiol and Cancer

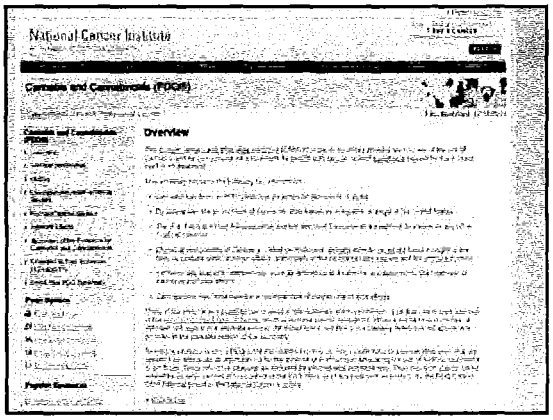
- Id helix-loop-helix proteins control processes related to tumor progression
- CBD down-regulates Id-1 expression in aggressive human breast cancer cells *in vitro*

  McAllister et al, Breast CA 2011
- Addition of CBD to colorectal cancer cell lines led to reduced cell proliferation
- In mice, treatment with CBD decreased azoxymethane induced aberrent crypt foci, polyps and tumor formation Aviello et al, J Molec Med 2012



What About Cannabis Oil?





IOM: Efficacy of Cannabinoid Drugs

- 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 palliative care setting?
- Is a single treatment that increases appetite, decreases nausea and vomiting, relieves pain and improves mood and sleep a potentially useful tool in symptom management?

Cannabis in Supportive Care

- 211 Israeli cancer patients seeking cannabis licenses were interviewed at baseline
- 131 had a second interview 6-8 weeks later
  - 25 had stopped treatment after one week
    - More CNS involvement more likely to stop
    - Less CINV, anorexia or weight loss in those who stopped
  - 106 who continued clearly a biased sample
    - All cancer or treatment related side effects significantly improved
      - Nausea, vomiting, mood disorders, fatigue, wt loss, anorexia, sexual function, sleep, itching and pain (P< 0.001)
      - 43% *reduced pain meds*, 33% reduced antidepressants
        - » Bar-Sela et al, Evidence-Based Comp + Alt Med, 2013

May 30, 2013

CLINICAL DECISIONS

Medicinal Use of Marijuana — Polling Results

- Readers responded to the case of Marilyn, a 68 yo with metastatic breast cancer, seeking cannabis to alleviate symptoms
- 1446 votes cast from 72 countries and 56 states and provinces in North America (1063 total)
- "We were surprised by the outcome of polling and comments with 76% of all votes in favor of the use of marijuana for medicinal purposes- even though marijuana use is illegal in most countries"

WebMD Physician Survey 2014

- WebMD/Medscape survey of 1544 MDs from more than 12 specialties in 48 states
  - 68% say it can help with certain Rx and conditions
  - 67% say it should be a medical option for patients
  - 56% support making it legal nationwide
    - 50% in states where it is not legal say it should be legal
    - 52% in states considering new law say it should be legal
- Oncologists and hematologists show highest level of support among specialists (82%)

April 2, 2014

Cannabis and Chemotherapy

- No adverse effect of cannabis tea with irinotecan or docetaxel
  - » Engels et al, Oncologist 2007
- Cannabinoids with chemotherapy acts synergistically to reduce tumor growth in mice
  - THC plus temozolamide effective in glioma xenografts even in temozolamide-resistant tumors
  - Adding CBD enhanced effect even with lower THC
    - » Torres et al, Mol CA Therapy 2011
- Gemcitabine combined with different cannabinoids reduces viability of pancreatic cancer cells
  - » Donadelli et al, Cell Death Disease 2011

History Of Medicine

- 2000 B.C. - Here, eat this root.
- 1000 A.D. - That root is heathen. Here, say this prayer.
- 1850 A.D. - That prayer is superstition. Here, drink this potion.
- 1940 A.D. - That potion is snake oil. Here, swallow this pill.
- 1985 A.D. - That pill is ineffective. Here, take this antibiotic.
- 2000 A.D. - That antibiotic is artificial. Here, eat this root.

Selected Bibliographic Sources

- Abrams DI. Integrating cannabis into clinical cancer care. Current Oncology 2016; 23:S8-S14.
- Abrams DI and Guzman M. Cannabis in Cancer Care. Clin Pharm and Ther 2015; 97:575-586.
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Medical Cannabis and The Endocannabinoid System

Center for Spirituality and Healing Conference

Donald I. Abrams, MD
Chief, Hematology-Oncology
Zuckerberg San Francisco General
Professor of Clinical Medicine
University of California San Francisco

April 28, 2016

UNIVERSITY OF MINNESOTA

Disclosures

Dr. Abrams has disclosed a relevant financial interest as a consultant with ABCann, Tikun Olam, and Zynerba Pharmaceuticals.

Dr. Abrams will be discussing off-label and or investigational uses of medical cannabis.

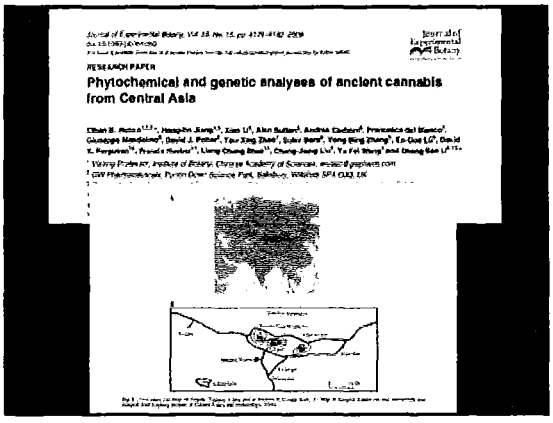
There are no conflicts of interest or relevant financial interests that have been disclosed by the rest of the planners or presenters of this activity that apply to this learning session.

Disclosures: Donald Abrams

- I went to college in the 60's

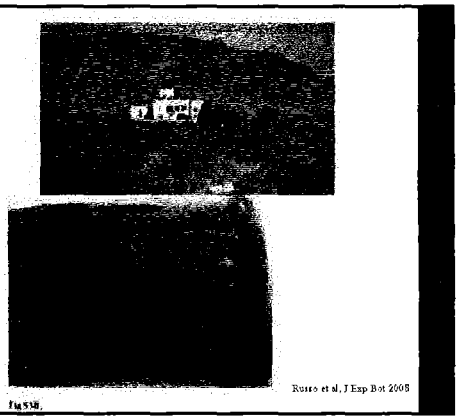
Objectives

- Describe the nature and structure of cannabinoid receptors and endocannabinoids
- Review plant phyocannabinoids and discuss their potential therapeutic benefits
- Discuss ways in which the endocannabinoid:cannabis receptor interaction can be modulated pharmacologically for therapeutic effects

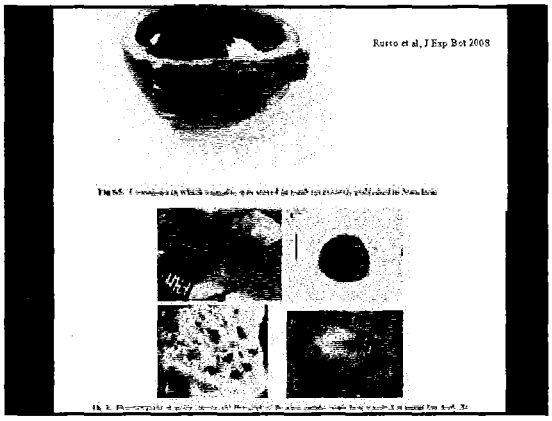


RESEARCH PAPER

Phytochemical and genetic analyses of ancient cannabis from Central Asia

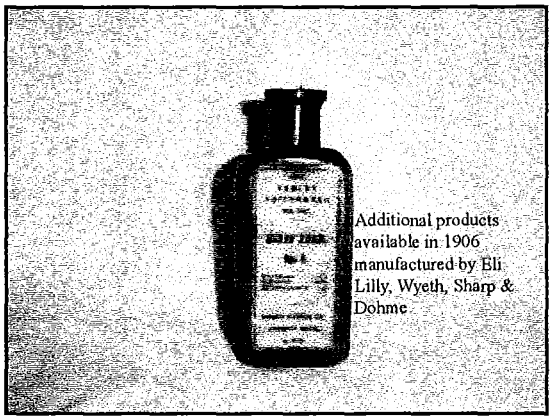


Russo et al, J Exp Bot 2008



Cannabis as Medicine

- 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



Additional products available in 1906 manufactured by Eli Lilly, Wyeth, Sharp & Dohme

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 Substances Act 1970

	Schedule I	Schedule II
Potential for abuse	High	High
Accepted medical use	No	Yes
Safety	Lack of accepted safety for use under medical supervision	Abuse of drug may lead to future psychological or physical dependence

Schedule I Substances

- Marijuana
- Heroin
- LSD
- Mescaline
- Other hallucinogenic amphetamine derivatives
- Methaqualone
- Illicit fentanyl derivatives
- Gammahydroxybutyrate (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-tetrahydrocannabinol (THC)
- At least 100 other cannabinoids identified in the plant
- delta-8-THC similar in potency but only in small concentration

Non-THC Cannabinoids

- Cannabidiol CBD
- Cannabinol CBN
- Cannabichromene CBC
- Cannabigerol CBG
- Delta-8-THC Δ^8-THC
- Tetrahydrocannabivirin THCV

Cannabidiol (CBD)

- Modulates the pharmacokinetics of THC
  - Very low affinity for CB1 and CB2 receptors
    - Slight affinity for CB receptors as an antagonist
  - May modulate downstream signal transduction
  - Potent cytochrome P450 3A11 inhibitor thus blocking formation of 11-OH metabolite
- CBD possesses sedative properties, reduces anxiety and other unpleasant psychological side effects of pure THC

Non-THC Components of Cannabis

- Δ9-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, cholinergic effects and immunosuppression
- Terpenoids and flavonoids may increase cerebral blood flow, enhance cortical activity, kill respiratory pathogens and provide anti-inflammatory activity

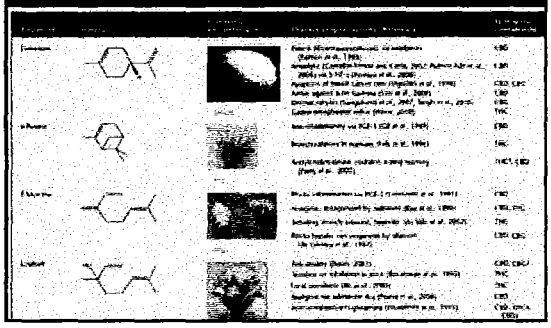
Cannabis Terpenoids

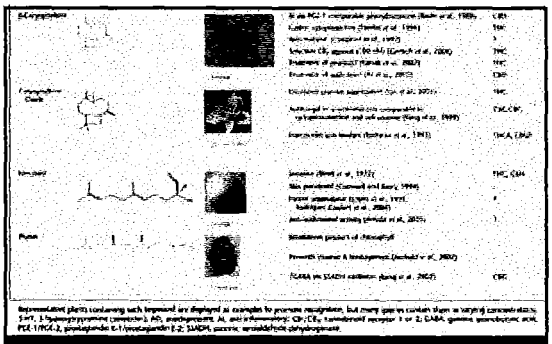
- Unique smell of cannabis derived from ~100 terpenoid compounds present
- Terpenoids derive from repeating C_5H_8 (isoprene)
- Final structures range from linear chains to complex polycyclic molecules including alcohol, ether, aldehyde, ketone or ester functional groups
- Easily extracted from plant by steam distillation or vaporization as essential or volatile oil

Cannabis Terpenoids

- Terpenoids vaporize near same temperature as THC, are lipophilic and permeate BBB
- May bind to cannabinoid receptors
- May also increase BBB permeability
- Act as serotonin uptake inhibitors, enhance norepinephrine, increase dopamine and augment GABA- provide synergy for cannabis-mediated pain and mood effects

Main Cannabis Terpenoids





Russo E. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. BJPharmacol, 2011

Cannabis Flavones

- Flavonoids are aromatic, polycyclic phenols
- Cannabis contains ~20 as free flavonoids and conjugated glycosides
- Some are volatile, lipophilic, permeate membranes and retain pharmacologic activity in cannabis smoke
- May modulate THC PK via inhibition of P450 3A4 and 3A11enzymes

Cannabis Flavones

- **Apigenin** has anxiolytic activity, inhibits TNF-α production and interacts with estrogen receptors, low estrogenic potential
- ***Quercetin*** *is a potent anti-oxidant*
- **Cannflavin A**, unique to cannabis, potent PGE, COX and lipoxygenase inhibitor
- **β-Sitosterol** reduces inflammation and edema; 5-α-reductase inhibitor of saw palmetto and nettle

Cannabinoids 101

- A group of C_{21} terpenophenolic compounds uniquely produced by cannabis
- Phytocannabinoids suggested to designate C_{21} compounds produced by cannabis
- Synthetic cannabinoids e.g. HU-210 have been developed
- Endogenous cannabinoids e.g. anandamide are termed endocannabinoids

Cannabinoids 101

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Cannabinoid Receptors

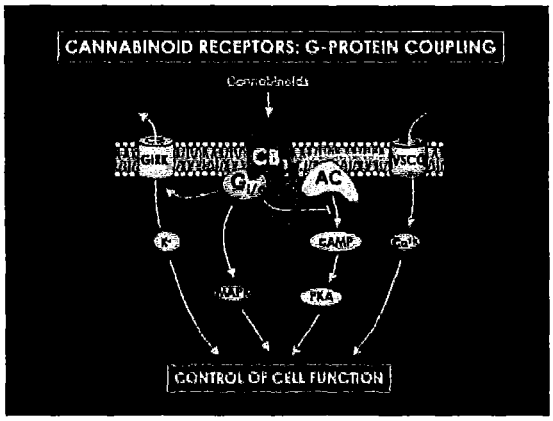
- CB_1 and CB_2 receptors identified
- Receptors encoded by separate genes on separate chromosomes; shared 48% amino acid identity
- G-protein coupled receptors that inhibit adenylyl cyclase on activation
  - Decreases cyclic AMP and protein kinase A activity
  - Inhibition of Ca^{++} influx through various Ca^{++} channels
  - Stimulation of inwardly rectifying K^+ channels and mitogen-activated protein kinase cascades

Cannabinoid$_1$ Receptor

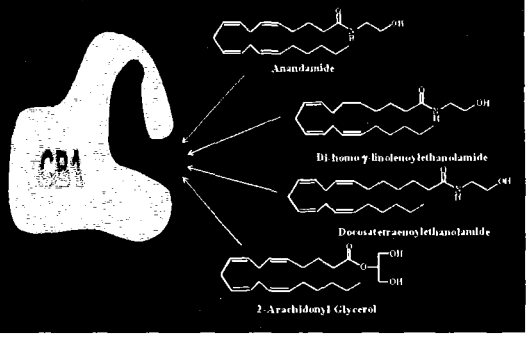
- CB_1 receptors identified throughout central and peripheral nervous system
  - Density highest in cingulate gyrus, frontal cortex, hippocampus, cerebellum and basal ganglia
  - CB1 receptors present in virtually all organs and tissues

Cannabinoid$_2$ Receptor

- CB_2 receptor originally detected in macrophages and marginal zone of the spleen
- Largest concentration in peripheral blood present in B-cells and NK cells
- Also found in bone and to a lesser degree liver and nerve cells



Endocannabinoids



Endocannabinoids

- Anandamide is a partial agonist at CBRs, binding with slightly higher affinity at CB_1
- 2-AG binds equally well with slightly higher affinity for CB_1
- 2-AG has greater potency and efficacy than anandamide at the receptors

CB_1 Receptor Activation

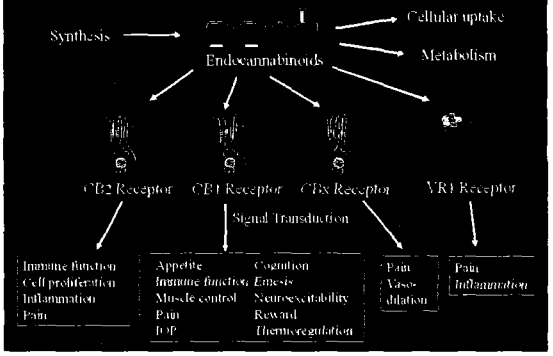
- Overall effect is suppression of neurotransmitter release at both excitatory and inhibitory synapses
- Inhibition occurs through a retrograde signaling mecahnism
  - ECs are synthesized and released *from* post-synaptic neurons
  - Diffuse backward across the synaptic cleft and bind to CB_1 receptors on the pre-synaptic terminals

Figure 1 HC Monograph

The Fate of the Endocannabinoids

- Anandamide and 2-AG re-enter the post- or pre-synaptic nerve terminals
- Likely requires a specialized transporter
  - Anandamide metabolized by fatty acid amide hydrolase (FAAH) to arachidonic acid and glycerol
  - 2-AG metabolized by monoacylglycerol lipase (MAGL) to arachidonic acid and ethanolamine

Endogenous Cannabinoid System



Manipulation of Endogenous Cannabinoid System

Activation	Inhibition
CB_1 Receptor agonist	CB_1 Receptor antagonist
CB_2 Receptor agonist	CB_2 Receptor antagonist
Enhanced EC synthesis	Decreased EC synthesis
Decreased EC metabolism	Increased EC metabolism
Transporter blocker	Transporter activator
Altered signaling pathway	Altered signaling pathway

FAAH Inhibitor Tragedy

Cannabinoids and Appetite

- Anandamide in low concentrations in mice leads to a potent enhancement of appetite
- CB1 receptors implicated in food intake control n.b. lateral hypothalamus and limbic system locations
- CB1 knockout mice eat less than wild type litter mates
- CB1 receptors involved in motivational reward aspects of eating

Cannabinoids and Appetite

- Endocannabinoids enhance reward effects via mesolimbic dopaminergic systems
  - System may be involved in suckling
  - Milk has high levels of 2-AG
  - CB1 antagonist given to mice at 24hrs causes them to stop suckling and die
- Phase II clinical trial of CB1 antagonist in obesity encouraging (3-4 kg ↓ in 2wks)

Pharmacological Blockade of the eCB System

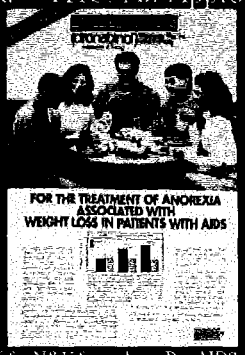
Pharmacologically induced deficiency of the eCB system by SR141716 or AM251 may lead to:

- suppressed feeding and weight loss
- 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
- increased duration of wakefulness, hyperarousal and vigilance

→

Courtesy of Dr. Patrik Roser

Oral Delta-9 THC: An Approved Drug



Approved in 1986 for N&V from chemoRx; AIDS anorexia in 1992

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, a potent psychoactive metabolite
- Further oxidation of 11-OH-THC leads to elimination products (urine and feces)
- Terminal half life 20-30 hrs

Inhaled THC Pharmacology

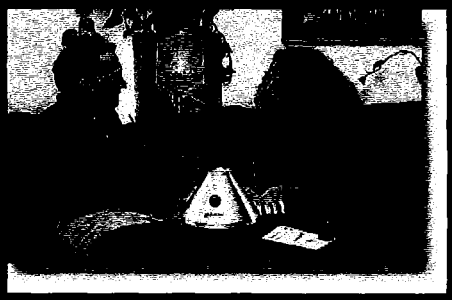
- Rapidly absorbed into blood stream and redistributed
- Considerable amount of dose lost in smoke and destroyed by combustion
- Peak blood levels achieved at end of smoking, decline rapidly over 30 minutes
- Smoking achieves higher peak concentration but shorter duration of effect
- Smaller amts 11-OH-THC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

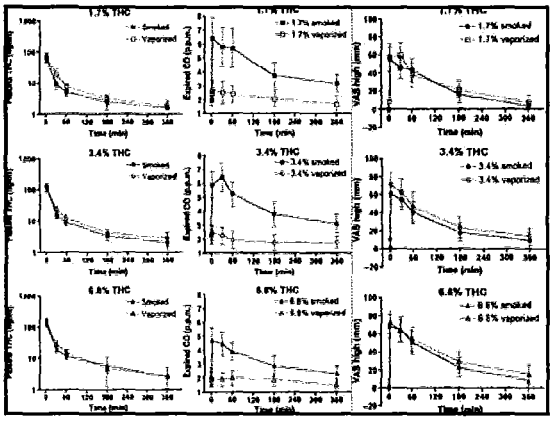
Vaporization

- THC vaporizes at a lower temperature than it burns
- Vaporizer heats cannabis to 155° C, below the burning point of combustible plant
- Vapors are cooler, purer and probably less toxic than smoke
- May be more psychoactive as less of THC content has been burned off

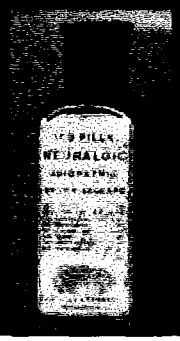
* Gieringer 1996

Vaporization of Cannabis





Dosing of Medicinal Cannabis



- Dosing of botanicals always complex
  - Plant products vary in potency
  - Contain varying amounts of components
- Difficult to standardize dose of inhaled medicine
- Individual variation in response to cannabis
  - Prior experience
  - ? Pharmacogenomics

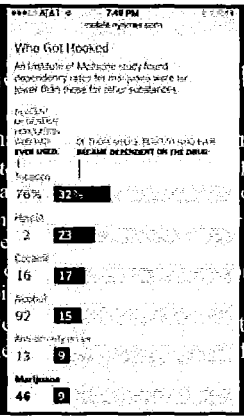
Cannabis Dose Guidelines

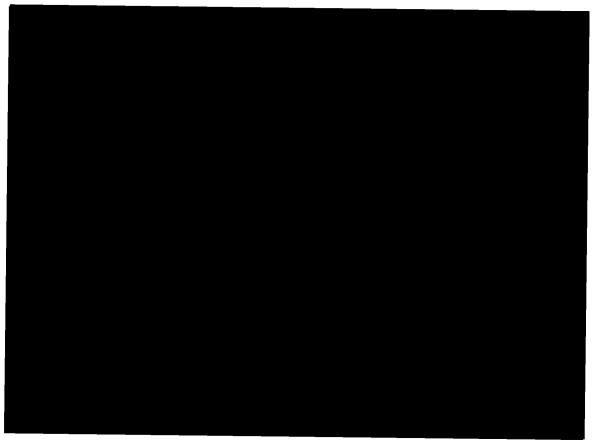
- Multiple variables dictate that dosing be highly individualized
- A patient-determined self-dosing model is recommended
- Self titration model acceptable in view of the plant and host variables and the low toxicity of cannabis
- Gabapentin an example of another drug with relatively low toxicity and high dosing limits titrated to effect

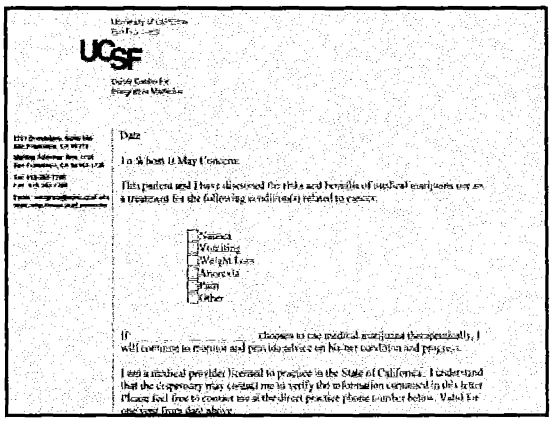
Carter et al JDrugs 2004

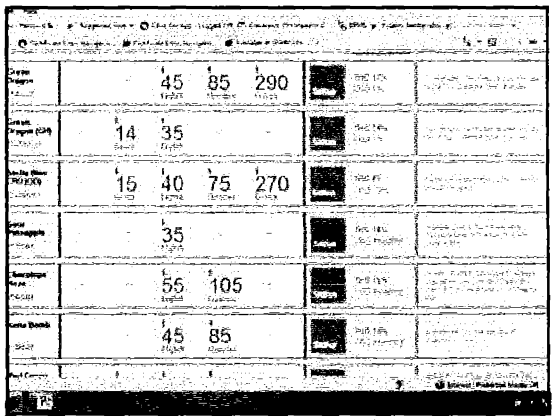
Th bis

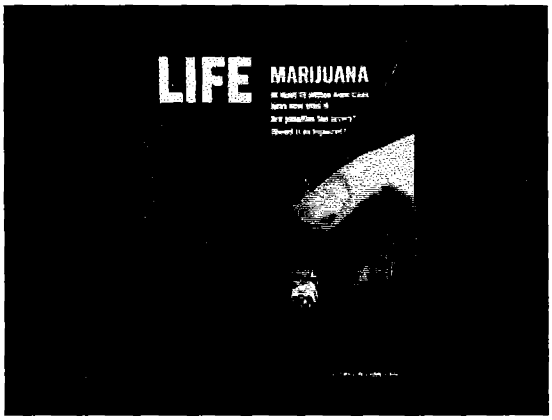
- No death m OD
  - Estimat kill (death
    seconda oisoning)
  - By com 60 mg of
    nicotine
  - Unlike rainstem
    cannabi
- Addictiv thdrawal
  syndrome ffeine











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SECTION F

603 Reichel Circle NE
Stewartville, MN 55976

Sensible policies, safer communities.

Sensible Minnesota

July 29, 2016

Commissioner Dr. Edward Ehlinger
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re: Petition to add whole plant cannabis as an allowable ingestion method

Dear Dr. Ehlinger,

I write today, as the Vice President of Sensible Minnesota and as the director responsible for our Patient Program, in favor of adding vaporizing whole plant cannabis as an allowable ingestion method. The benefits of vaporized or smoked whole plant cannabis are well documented and researched, as this is the primary method of consumption for patients throughout the world.

We understand the law does not allow for smoking – and we are not asking for you to approve of smoking whole flower cannabis. The law does allow, however, patients to vaporize product, and as such, we encourage you to add this as an allowable ingestion method.

Over the past year, Sensible Minnesota has developed a patient advocacy program that provides advocates to work with patients on a one-to-one basis to determine if they qualify for the program, help find a certifying provider, and provide assistance in the registration process. One of the most difficult parts of this advocacy is having to explain to patients that the cost of the product itself may prevent them receiving benefit from as a medical cannabis patient.

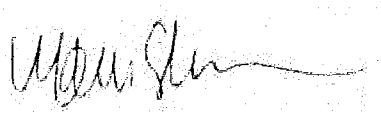
Many of the patients we have worked with enter the program only to find they cannot afford the medical cannabis available in Minnesota. These patients are forced back to the black market, either partially or completely, and continue to risk arrest and prosecution for using cannabis as a therapeutic tool. Many patients prefer to use the plant as it preserves all of the cannabinoids, terpenes, and flavonoids that may be lost during processing. These limitations of the current available ingestion methods are dangerous for patients and go against the spirit of the law that was written to protect medical cannabis patients from arrest and prosecution.

603 Reichel Circle NE
Stewartville, MN 55976

As advocates, we see two main ways to bring affordability for patients (1) insurance coverage, and (2) allowing for whole plant cannabis. Until the federal government reschedules cannabis and the FDA begins approving its use as a medicine, the first option is unavailable, and this is out of our hands on a local basis. However, we believe that by allowing whole plant cannabis, patients will have a more affordable product available that will also subsidize the cost of refined oils – which some patients prefer to whole plant. We have spoken with medical cannabis providers in other states, researched prices, and evaluated the market place to reach this conclusion. The easiest, most efficient way to bring down the cost is to allow patients to purchase raw plant for vaporizing.

We advocate for safer polices that allow for accessible and affordable medical cannabis in Minnesota. Therefore, we strongly urge you to make the right decision and allow for vaporized, whole plant cannabis, as an allowable ingestion method in Minnesota.

Sincerely,



Maren Schroeder, MBA, RP®, MnCP
Vice President, Sensible Minnesota

SECTION F

Alexander D. Troester
13311 S. Glenn Dr.
Mulino, OR 97042

July 22, 2016

To whom it may concern:

As a partial owner of Beehive Extracts, a cannabis extract company located in Portland, Oregon, I believe that the current medical cannabis laws in Minnesota are creating a system in which prices are inflated, options for patients are limited, and the products that are readily available are ones which lack many beneficial compounds found in cannabis. Registered patients should have access to the cannabis flower in its natural form. Making this seemingly basic product available would help to lower costs at a production level, and would give patients a wider arsenal of medications from which to seek relief. My father currently lives with Multiple Sclerosis and Degenerative Disk Disease in Brownsville, Minnesota, and currently cannot afford the medicines available through dispensaries in the state. He currently vaporizes flowers found on the black market. For Minnesota's cannabis program to work, it is essential to keep prices competitive with the black market.

The options currently available to patients in Minnesota consist of products made with THC and CBD concentrates of the whole cannabis flower. While these products may be effective for some patients, they are more expensive due to the high-tech refinement techniques used in processing whole cannabis flowers. The majority of the cannabis industry does not make concentrates out of flowers, however, as doing so either creates an ineffective way to recoup the costs of growing, or creates a product with a cost that is far too expensive for the end user. Instead, growers will typically harvest a cannabis plant by drying it and removing excess foliage around the inner flowers. These dried flowers are then sold to patients without any further processing required.

Current wholesale market prices for trimmed cannabis flowers in Oregon are around $1800/lb. This price is still high enough to allow growers to come out ahead against costs associated with growing. Even with traditional mark-ups at dispensaries, patients are able to purchase trimmed cannabis flowers at costs as low as $5/gram in Oregon. With every pound of cannabis flowers produced, there is also a small amount of trim created - the product typically used for processing concentrates. A grower is able to recoup his production costs simply by selling the dried, trimmed flowers, and the excess foliage removed from the buds is often considered a "bonus". My company currently purchases this trim from growers at $500/lb.

We currently use two state-of-the-art closed loop hydrocarbon extraction machines made by a company called Precision. Each batch can be tested for THC and CBD potency, terpene potency, presence of mold, mildew, or pesticides, and for residual amounts of solvents remaining in the product. Using butane and propane blends, we are able to create products which can test at over 80% THC. Using vacuum ovens, we

are able to remove any remaining solvents, and are left with a product not only high in THC, but high in terpenes as well. Terpenes are molecules that attribute to the flavors and smells in cannabis, and they have been shown to have medicinal values of their own. Many of the terpenes found in cannabis can be found in other plants as well. Take myrcene, for example. Found in mangoes, this molecule has been shown to help THC pass a person's blood-brain barrier more effectively, giving a patient more relief than if there were no myrcene present.

Typical yields in hydrocarbon-based concentrate production average around 13%, depending on the strain. If we use Oregon's current wholesale value of $1800/lb for cannabis flowers, then the grower, if using whole flowers, needs to generate $1800 worth of concentrates to cover costs. A 13% yield from one pound of flowers is 58.5 grams. To generate $1800, the grower then needs to be able to wholesale this product for $30.77/gram, creating a cost typically over $60/gram to the end user. If only the excess trimmed foliage is used, however, then the grower only needs to make $500 back from his pound of trim. The same 58.5 grams is now only worth $8.50/gram. My company is able to cover the costs of processing by wholesaling our concentrates to dispensaries for $12-20/gram. The cost to patients then becomes an affordable $20-40/gram.

Hydrocarbon based extractions can also be used in the production of vaporizer cartridges. Even after accounting for the costs of producing these cartridges, a 500mg container can be purchased in Oregon for around $35, around half of the current prices found in Minnesota.

Minnesota must stop wasting money on production methods that remove essential compounds found in cannabis. I implore the state to consider including whole cannabis flowers in their list of allowable products, which would help lower costs to both production facilities and patients. This would help Minnesota's program to compete with black market prices, which currently force patients to buy untested, unregulated products whose origins cannot be verified.

Sincerely,

Alexander D. Troester
Owner, Lab Operations
Beehive Extracts
(507)272-3787

SECTION F

[redacted]
North Saint Paul, MN 55109

To whom it may concern:
I was a registered patient in the MN Medical Marijuana program from July 15, 2015 until July 15, 2016. I have only bought medicine on a few occasions because this program is far too expensive. I tried to remain positive and give it a chance, but it has been a great let down and a terrible tease. The dispensaries have medicine that I know helps my quality of life, but have it priced at such astronomical prices I cannot afford to medicate legally. I have been forced to return to the black market because I cannot afford the $2000.00 a month on medicine. Disability does not discriminate, and unfortunately a lot of people who need this medication are living on fixed incomes like myself and are frustrated with the illusion of a working medical cannabis program. I paid for my certification and then spent far too much money trying the costly designer oils (from both dispensaries) and liquid suspension from Leafline with only minor results because I couldn't afford to continue medicating at the therapeutic levels my body needs. This scenario should not be one that plays out. Especially when we have the medicine to help people. So what can we do about it?

We currently do not have whole plant medicine in our program, but allowing it would help drive prices down and give more patients the opportunity to choose cannabis over opiates. It saddens me that we have this program in Minnesota, but because the prices are so extreme people are being left out. I cannot tell you how many people I have talked to personally who said they qualify for the program, but cannot afford the medicine so they are not enrolling. Minnesota is missing out on a great opportunity, and people should be able to choose to medicate their own body with a plant over synthetic heroin. Flower cannabis will never kill anyone, but opiates do every day at alarming rates. Let me remind you of the current opiate epidemic with some facts from the American Society of Addiction and Medicine:

National Opioid Overdose Epidemic

- Drug overdose is the leading cause of accidental death in the US, with 47,055 lethal drug overdoses in 2014. Opioid addiction is driving this epidemic, with 18,893 overdose deaths related to prescription pain relievers, and 10,574 overdose deaths related to heroin in 2014.5
- From 1999 to 2008, overdose death rates, sales and substance use disorder treatment admissions related to prescription pain relievers increased in parallel. The overdose death rate in 2008 was nearly four times the 1999 rate; sales of prescription pain relievers in 2010 were four times those in 1999; and the substance use disorder treatment admission rate in 2009 was six times the 1999 rate.6
- In 2012, 259 million prescriptions were written for opioids, which is more than enough to give every American adult their own bottle of pills.7
- Four in five new heroin users started out misusing prescription painkillers. As a consequence, the rate of heroin overdose deaths nearly quadrupled from 2000 to 2013. During this 14-year period, the rate of heroin overdose showed an average increase of 6% per year from 2000 to 2010, followed by a larger average increase of 37% per year from 2010 to 2013.8
- 94% of respondents in a 2014 survey of people in treatment for opioid addiction said they chose to use heroin because prescription opioids were "far more expensive and harder to obtain."9
- In 2014, 467,000 adolescents were current nonmedical users of pain reliever, with 168,000 having an addiction to prescription pain relievers.

- In 2014, an estimated 28,000 adolescents had used heroin in the past year, and an estimated 16,000 were current heroin users. Additionally, an estimated 18,000 adolescents had heroin a heroin use disorder in 2014.3
- People often share their unused pain relievers, unaware of the dangers of nonmedical opioid use. Most adolescents who misuse prescription pain relievers are given them for free by a friend or relative.
- The prescribing rates for prescription opioids among adolescents and young adults nearly doubled from 1994 to 2007.11
- Women are more likely to have chronic pain, be prescribed prescription pain relievers, be given higher doses, and use them for longer time periods than men. Women may become dependent on prescription pain relievers more quickly than men.
- 48,000 women died of prescription pain reliever overdoses between 1999 and 2010.12
- Prescription pain reliever overdose deaths among women increased more than 400% from 1999 to 2010, compared to 237% among men.
- Heroin overdose deaths among women have tripled in the last few years. From 2010 through 2013, female heroin overdoses increased from 0.4 to 1.2 per 100,000.8

***http://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf

Adding flower cannabis to the medical program would bring down prices enough and get more Minnesotans away from the opiate epidemic. The people want and need another option. Cannabis is the answer. Please allow whole plant medicine into the program. Many lives and quality of lives are depending on it.

Cannabis also works better as whole plant medicine due to the entourage effect."First described in 1998 by Israeli scientists Shimon Ben-Shabat and Raphael Mechoulam, the basic idea of the entourage effect is that cannabinoids within the cannabis plant work together, or possess synergy, and affect the body in a mechanism similar to the body's own endocannabinoid system." This is very true, and when the dispensaries extract and separate different cannabinoids to make the designer oils they are missing out on this synergy. Knowing that whole plant medicine also works better in terms of science with your body is just another reason to add this option to the program.

Sincerely,

[redacted]
Cannabis patient and Activist

Sources

Burnett, Dr. Malik. "Medical Marijuana: Much More Than Just THC and CBD." *The Entourage Effect: Whole-Plant Cannabis Medicine*. The Cannabis Classroom, 14 May 2014. Web. 26 July 2016.

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I am a MN registered Medical Cannabis patient, but as of now I cannot afford to get any more Cannabis medications. There are many medicinal benefits to vaporizing the whole plant as an herb and can be combined with many natural herbs as well for nutritional and medicinal benefits. For patients to be able to buy the plant itself would be cheaper than converted Medical Cannabis offered now. Cannabis has many different strains and they treat different symptoms as well. With access to the whole plant and being able to grow the certain strain that treats each individual's symptoms would be cost effective for the patients and the manufacturers.

I am back on pharmaceuticals and feeling all the side effects. The combination of the pills and the side effects of them in combination makes me so ill for days at a time. I am unable to drive or leave my house. I am lethargic and no appetite. When on Medical Cannabis treatment I was doing very well. My body was healing and my muscles were building back up. Now I have a hard time walking around my house.

Thank you.

[redacted]

SECTION F

[redacted]

07/26/2016

Dear Minnesota Department of Health,

I'm petitioning to expand Minnesota's Medical Cannabis Program to add legal whole plant access to raw Cannabis Indica, Sativa and Hybrid strains.

On July 2nd 2015, I was certified into Minnesota's Medical Cannabis Program under two qualifying medical conditions, "Persistent & Severe Muscle Spasms" and "Crohn's Disease". I also suffer from the medical conditions Pancreatitis, Cervical Spondyliitis, Sacroiliitis and Osteo Arthritis.

The Medical Cannabis products available from MinnMed & Leafline are not medically effective in treating my life threatening medical conditions because they lack potency and access to a full spectrum of cannabinoids that are purposely removed by both companies. I have also suffered painful side effects, been personally injured and I cannot keep myself alive with the Medical Cannabis products available from MinnMed or Leafline. As a patient I'm left with no other choice but to continue to illegally treat myself to stay alive by using raw whole plant Cannabis Indica and continue to petition Minnesota's Department of Health.

Thank you for your time,

[redacted]

Nancy Bentley BS Dietetics
6419 Shetand Dr NW
Rochester, Minnesota

SECTION F

July 11, 2016

I am writing this letter in support of whole plant raw Cannabis.

The emphasis on whole fresh plants in the diet is stronger and stronger in health and the prevention of disease. The same is true for the whole raw cannabis plant. The body is riddled with cannabinoid receptors that use cannabis to modulate and strengthen body systems. Using the whole fresh plant has these advantages:

1. The high is avoided because cannabis must be heated to activate THC
2. Patients are able to ingest higher amount of non psychoactive substances for health purposes
3. Versatility: Raw cannabis can be mixed with foods and juicing. It is easier to make medicine for oneself and especially to make medicine for children.
4. Raw Cannabis avoids smoking
5. Raw Cannabis is a potent disease fighter.
6. Whole plant cannabis has an entourage effect where the different cannabinoids work together in synchronicity.

To quote Hippocrates; "Let food be thy medicine and medicine thy food."

Please add raw whole plant cannabis to the medical marijuana options.

Sincerely,
Nancy Bentley

SECTION F

To Whom It May Concern:

I'm writing in support of the petition to include whole-plant as a qualifying form of cannabis for Minnesota's medical cannabis program.

I am currently enrolled as a medical cannabis patient and have been for nearly a year, now. My qualifying condition is HIV. I believe that I have greatly benefited from utilizing cannabis as a tool for combating symptoms. When I am able to afford the cannabis medicine, my survey scores have consistently been marked as "0" for depression and "0-1" for anxiety symptom relief; "0" meaning symptom not present. I believe it is important for more forms and delivery methods of cannabis to be made available, so that all patients can have access and find what works best for them. It is to my knowledge that there are many therapeutic compounds within the whole plant/flower that are currently not being utilized in MN's medical cannabis program. More potent forms of cannabis, such as wax & oils (compared to whole-plant), are currently available for MN's patients.

I am a current student and use cannabis daily. I am prescribed Marinol (synthetic THC; missing other therapeutic cannabis compounds) for when I can't afford the medicine from MN's medical cannabis program. I work with a team of doctors at Hennepin County Medical Center. I have maintained a 4.0 GPA since returning to school after becoming ill, and I truly believe cannabis has helped me do so. I am able to function normally when using cannabis. I have not experienced any negative side effects from cannabis. I'm prescribed Klonopin and Nortriptyline for anxiety and depression/peripheral neuropathy, and have found both drugs to be addictive and limited in their efficacy compared with cannabis. Cannabis has also helped me find relief from pain, insomnia, nausea, and has also been an appetite stimulant.

Whole-plant availability is less expensive and less potent than waxes and oils; allowing patients affected by economic and racial disparities an affordable/safe option in finding symptom relief. Also, when patients are forced to turn to the streets for their medicine, there is potential to be exposed to other harmful substances, as well as the fact that the street-cannabis isn't tested for potentially harmful contaminants. Testing for molds, heavy metals, and other harmful pollutants would greatly benefit patients with weakened immune systems. It is to my understanding that patients are already using street-cannabis. Undermining the illegal market is important in providing safe and legal access to an important tool which provides a multitude of symptom relief, as experienced with cannabis. I implore you to find compassion/empathy for patients and understanding of cannabis as a safe medicine, and include whole-plant as an appropriate addition in Minnesota's medical cannabis program. Thank you.

Sincerely,

[redacted]

[redacted]

SECTION F

Sensible policies, safer communities.

July 26, 2016

Commissioner Dr. Edward Ehlinger
Minnesota Department of Health
Office of Medical Cannabis
PO Box 64882
St. Paul, MN 55164-0882

Re:Petition to add whole plant cannabis as an allowable ingestion method

Dear Dr. Ehlinger,

I write today in support of the petition to add whole plant cannabis as an allowable ingestion method. The benefits of vaporized or smoked whole plant cannabis are well documented and researched, as this is the primary method of consumption for patients throughout the world.

I understand the law does not allow for smoking – and I'm not asking for you to approve of smoking whole flower cannabis. The law does allow, however, patients to vaporize product, and encourage you to add this as an allowable ingestion method.

Over the past year, I have been a patient on the program and I cannot tell you what a difference the medication makes in my muscle spasms, pain and general exhaustion. But I cannot afford it. The price must come down and allowing whole leaf vaporizing can help that.

I fear arrest and prosecution if I try and procur medicine I can afford on the street or I must go back on the multiple prescriptions I was on before but are covered by my private insurance which costs thousands and have side effects.

Therefore, I strongly urge you to make the right decision and allow for vaporized, whole plant cannabis, as an allowable ingestion method in Minnesota.

Please feel free to contact me for more information. I am also on the task force and am very disappointed in how that is being run.
Sincerely,

[redacted]