Cannabinoids and Cancer

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Disclosures

Research - Tweed (Canopy)

Consultation - Tilray

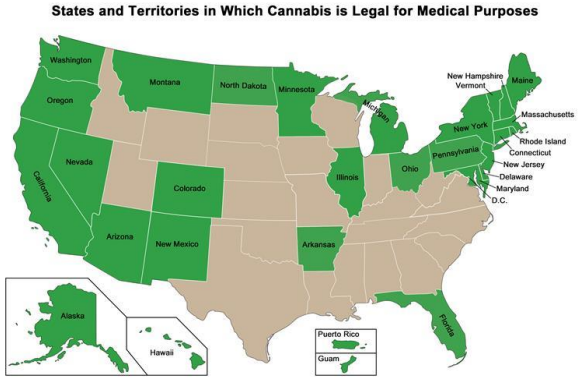
Agenda

- Endocannabinoid System
- Treat Symptoms, not disease
- Synthetic Cannabinoids
- Antiemetic effect
- Appetite Stimulant
- Analgesia
- Anxiety / Sleep
- Cancer Risk of Cannabis
- Cancer Treatment – ‘Say Whaaaat’ [Case study]

https://medsinroute.com/product/525mg-201-cbdthc-organic-olive-oil-tincture/
https://www.innovationtoronto.com/2018/02/medical-cannabis-rather-than-opioids-are-significantly-safer-for-the-elderly-with-chronic-pain/
Both accessed 9/18/18

History of Cannabis - World, US, Canada

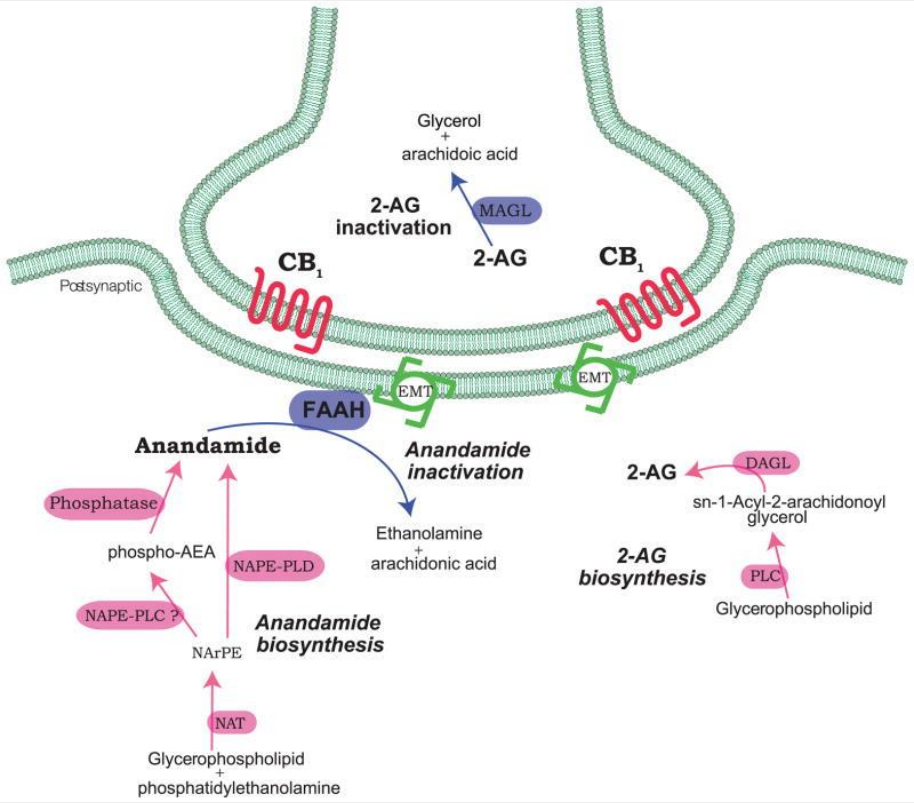
- Used for medical purposes dating back 3,000 years
- 1839 - Dr. W.B.O'Shaughnessy - surgeon
  - Analgeia, sedation, anti-inflammatory, antispasmodic, and anticonvulsant effects
- 1937 - US Treasury Depart. Introduce Marihuana Tax Act - $1 / oz medicinal, $100/oz nonmedical. Physicians paid tax to prescribe
- 1942 - Removal due to concerns to cause harm
- 1996 - Canada - Cannabis becomes only Schedule II Drug
- 2003 - MMAR
- 2013 - MMPR
- 2016 - ACMPR
- 2018 - October 17, 2018 - Legalization



https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq#section/_5

Endocannabinoid System

- CB1 (1990), CB2 (1993)
- G-Couple Proteins
- Presynaptic Inhibition



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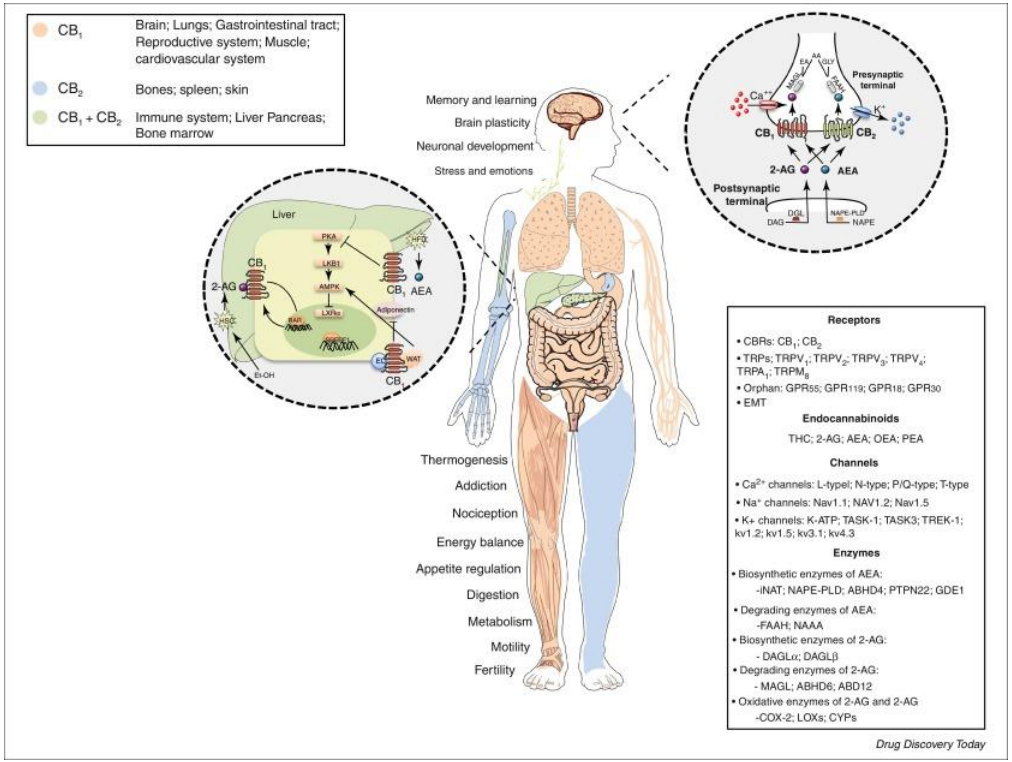
Endocannabinoid System



Drug Discovery Today, Vol 22, Issue 1, January 2017

Synthetic Cannabinoids

1. Cesamet (Nabilone) - THC only product, Capsule
    a. Nausea associated with chemotherapy
    b. 0.25mg, 0.5mg (ODB), 1mg (ODB)
    c. Max 2mg per dose, Max 6mg per day
    d. Off label - pain, sleep
    e. ODB and 3rd party coverage
2. Sativex (Nabiximol) - THC / CBD, buccal spray
    a. Spasticity associated with MS
    b. 2.5mg THC / 2.7mg CBD per spray
    c. Max 12 sprays per day
    d. Off Label - Pain
    e. EAP Required, 3rd Party coverage
3. Marinol (Dronabinol) - THC only product
    a. USA Only - Nausea - Chemotherapy, HIV

Treat Symptoms, Not Disease

Treat Symptoms, Not Disease

- Antiemetic Effect
- Appetite Stimulation
- Analgesia
- Anxiety
- Sleep

Anti-emetic Effects

Animal Studies

- CB1 and 5-HT3 receptors colocalize on GABAnergic neurons, opposing effects
- CB1 Antagonist elicit emesis in shrew that was reversed with CB1 agonists
- CB1 antagonist reverse effects of THC and other synthetic cannabinoid CB1 receptors caused by cisplatin in shrew and lithium in shrew.
- CBD itself shown to be effective

Anti-emetic Effects

Human Studies

- Both Dronabinol and Nabilone, Synthetic Δ-9 THC products shown to be effective for nausea in chemotherapy
- Systematic Review found cannabinoids superior than many standard
  - Prochlorperazine, metoclopramide, chlorpromazine, thiethylperazine, haloperidol, domperidone, and alizapride.
- Meta-analyses found cannabinoids to cause absence from nausea
- Varying response among cannabis and nausea
  - No response (Cyclophosphamide, doxorubicin), statistically sign high-dose methotrexate
- New antiemetics (ie 5-HT3 Antagonists) have not been directly studied

Appetite Stimulation

Animal Models

- CB1 Receptors in hypothalamus involved in motivation and reward of eating
- Anandamide potently enhances appetite in mice

Human Models

- Dronabinol inferior to megace in cancer patients BUT superior to placebo in HIV / AIDs patient
- No difference among patients given varying doses of cannabis extract
- Inhaled cannabis has not been evaluated

Analgesia - Endocannabinoid System

- Analgesia achieved through supraspinal, spinal, and peripheral mode of action - ascending and descending pain pathways

CB1 Receptor

- CB1 found in CNS and Peripheral nerve terminals
- Increased levels found in areas of nociceptive processing

CB2 Receptor

- May modulate pain through anti-inflammatory effects
- Acts on mast cells, reducing histamine and serotonin release

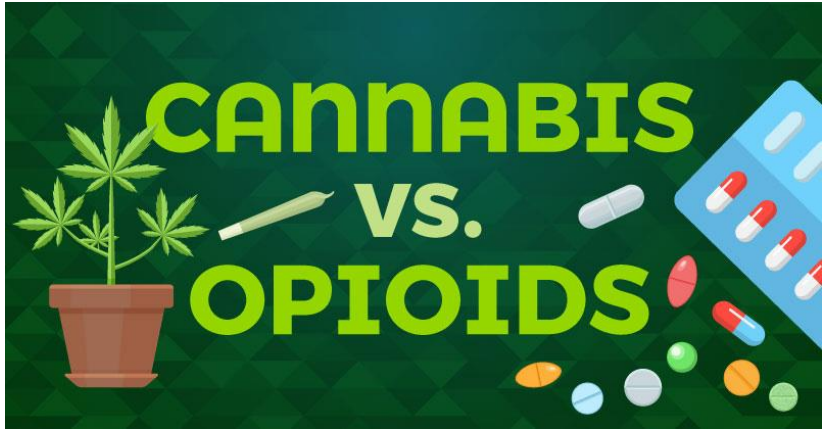
Analgesia - Efficacy

Animal Model

- Prevent chemotherapy-induced neuropathy with exposure to paclitaxel, vincristine, and cisplatin

Analgesia - Efficacy

- 15mg & 20mg Delta-9THC associated with substantial analgesia
- 10mg & 20mg equivalent 60mg & 120mg codeine respectively
- Cannabinoids achieve relief of 30% or greater in general
- Both THC and CBD found to be effective
- Reports 45% reduction in pain in 20 minutes



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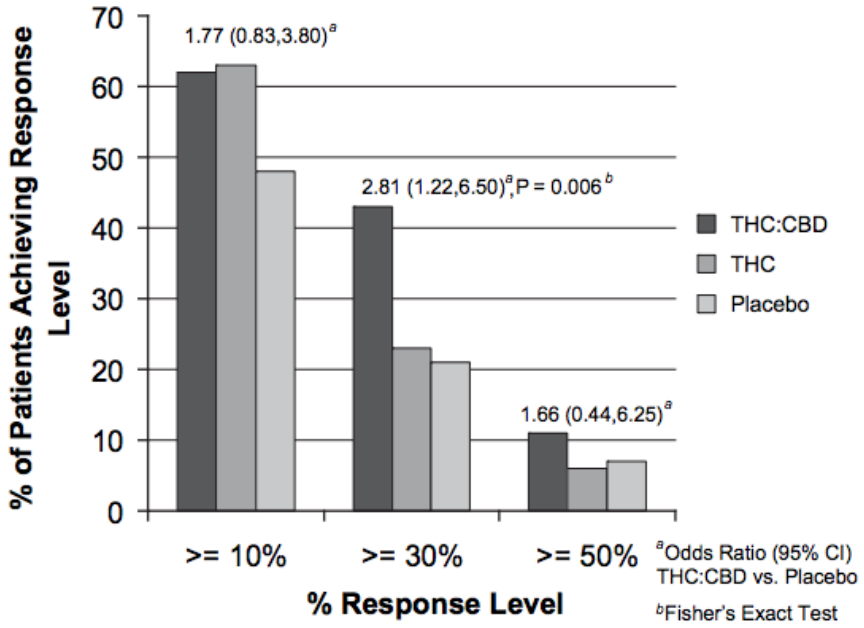
Analgesia - Efficacy



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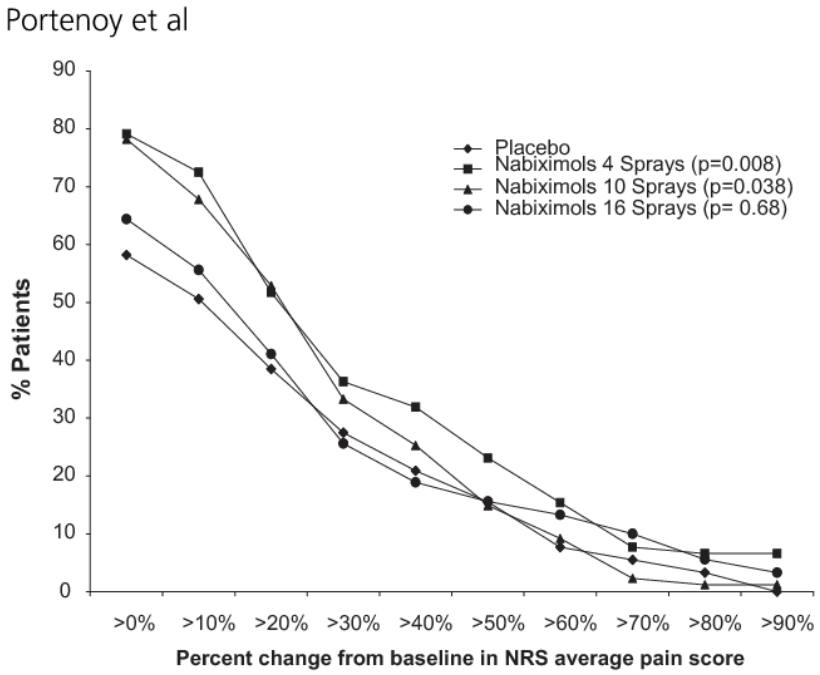
Analgesia - Efficacy



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Anxiety / Sleep

- Euphoria, Mood elevation much depends on set and setting with prior exposure with cannabinoids
- Cannabis has both anxiogenic and anxiolytic properties
- CBD has been shown to inhibit THC-induced anxieties
- THC may decrease sleep latency
- CBD reduce nightmares, improve sleep with chronic pain through REM sleep

…. There has not been studies looking specifically at patients with cancer

Risk of Cannabis

- Most studies are cross-sectional or rely on self-reported health
- Longitudinal study found only association with poorer gum disease
- In regards to burden of disease
  - Risk of dependence 8-9%
  - Cannabis dependence carries ~2 million years of life lived with disability (compared to >100 million for tobacco and alcohol each)
- Increased risk of Accidents / Injuries - warn on driving
- Increased risk bronchitis with combustion
- Increased risk of MI with combustion (4.8 fold in first hour)
- Similar inflammatory effects seen as smoking with combuation
- Increased CO exposure with combustion
- Possible Brain developmental issues in heavy users in adolescents

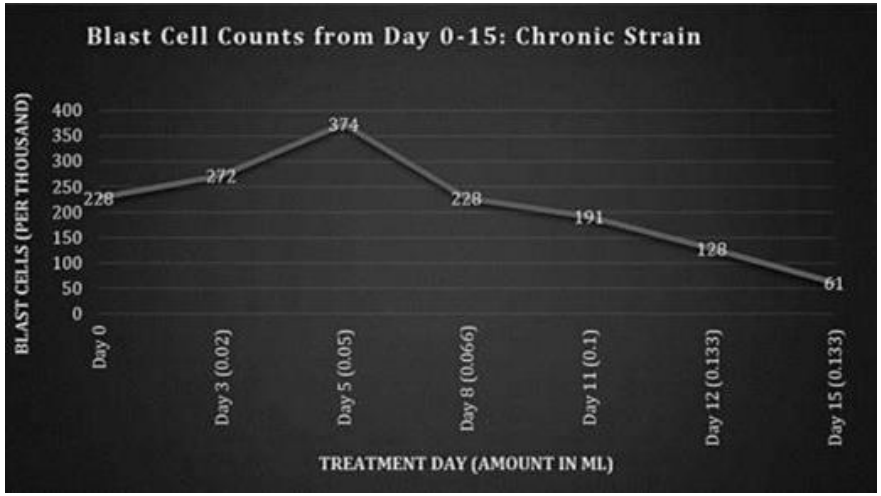
Risk of Cannabis

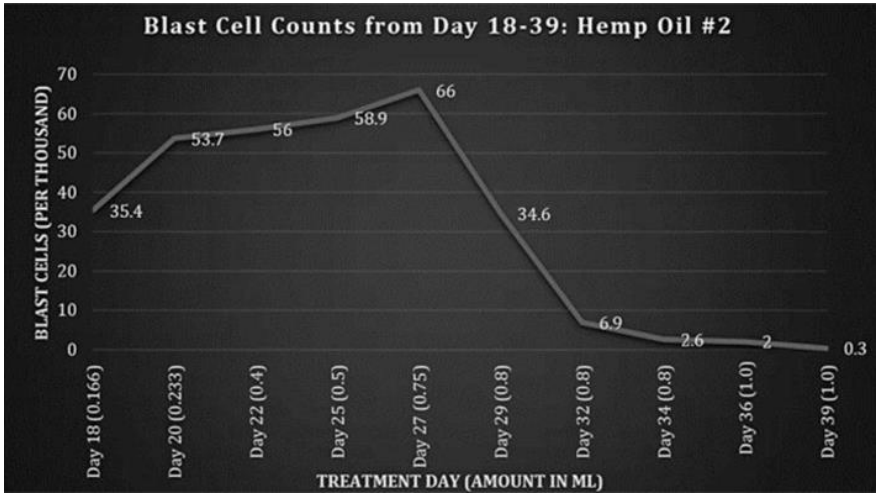
- Does not increase risk of cancer - lung, head, neck
- May increase risk of one subtype of testicular cancer

Case Study

- 14 year old presenting to Sick Kids with SOB, Weakness, Bruising.
- Dx ALL with Blasts > 300K.
- Acute chemo with standard for 6mo - March 2006
    - Needed bone marrow transplant - Aug 2006 (45 day isolation)
        - Gleevac 500mg BID - Feb 2007
            - Nov 2007 - Presence premature blast cells - no further transplants
                - Sprycel BID without chemo - Feb 2008
                    - 10 brain radiation treatments, suspected infiltration the CNS - Oct 2008
                        - Hematochezia, Blast Cells return - Feb 2009 - Palliative Care
                        - Informed she will suffer a stroke

Singh, Y. & Bali C. Cannabis Extract Treatment for Terminal Acute Lymphoblastic Leukemia with a Philadelphia Chromosome Mutation. Case Rep Oncol. 2013 Sep-Dec; 6(3): 585-592.





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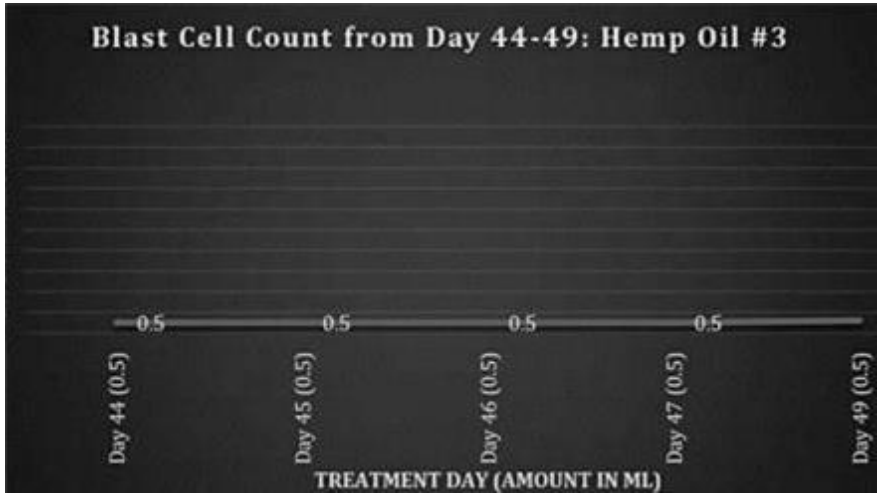

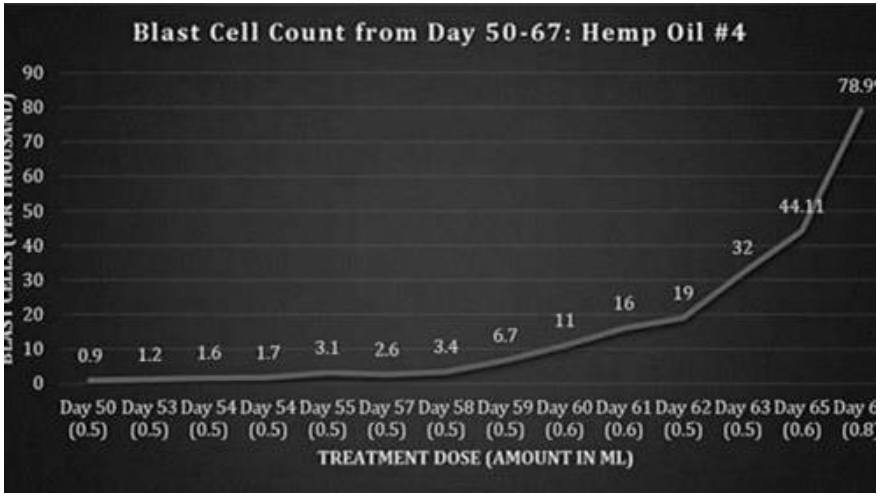

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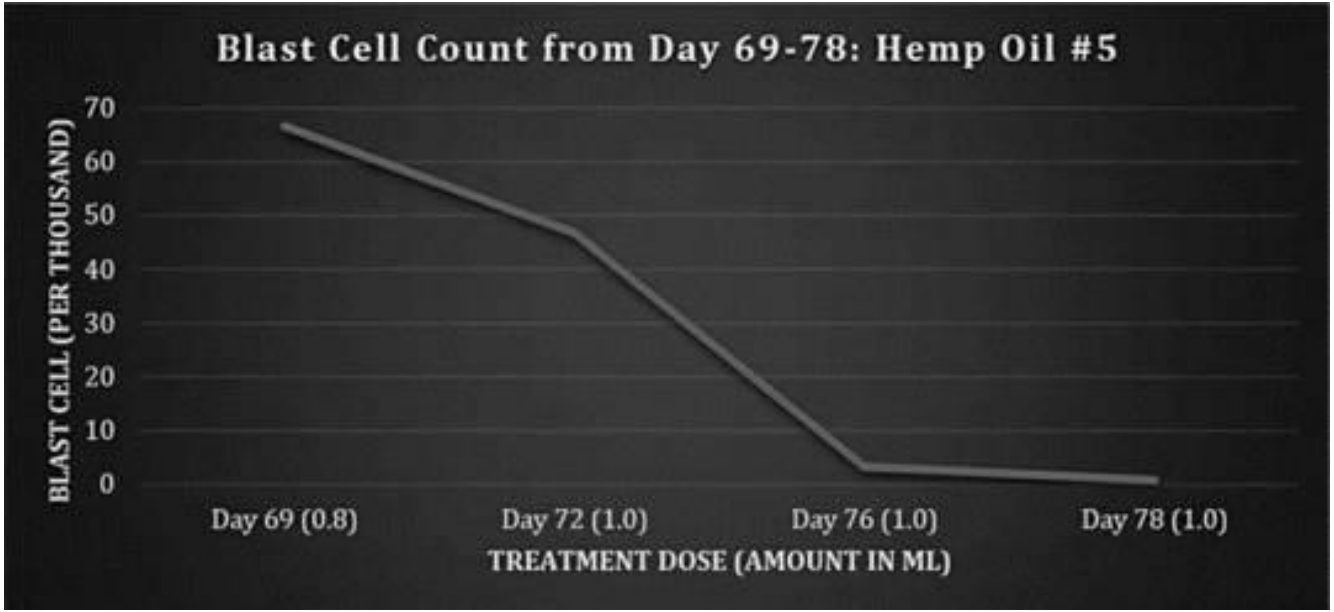

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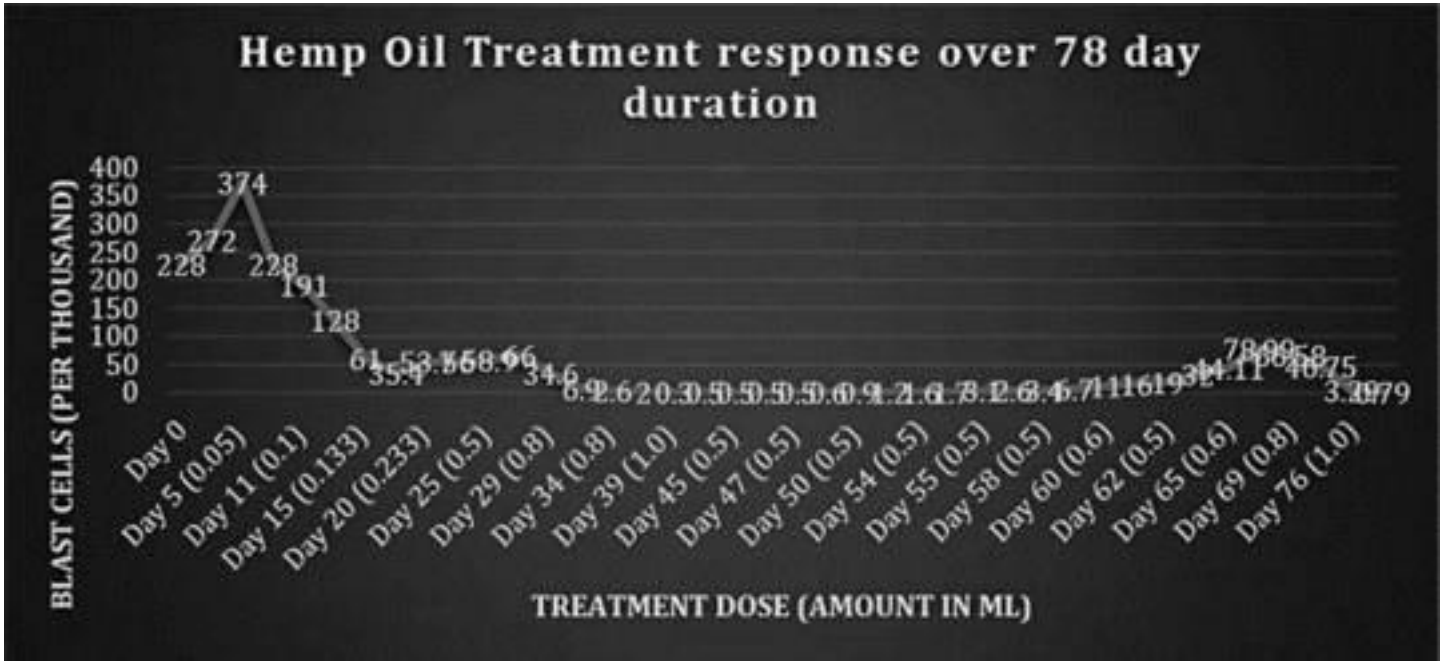

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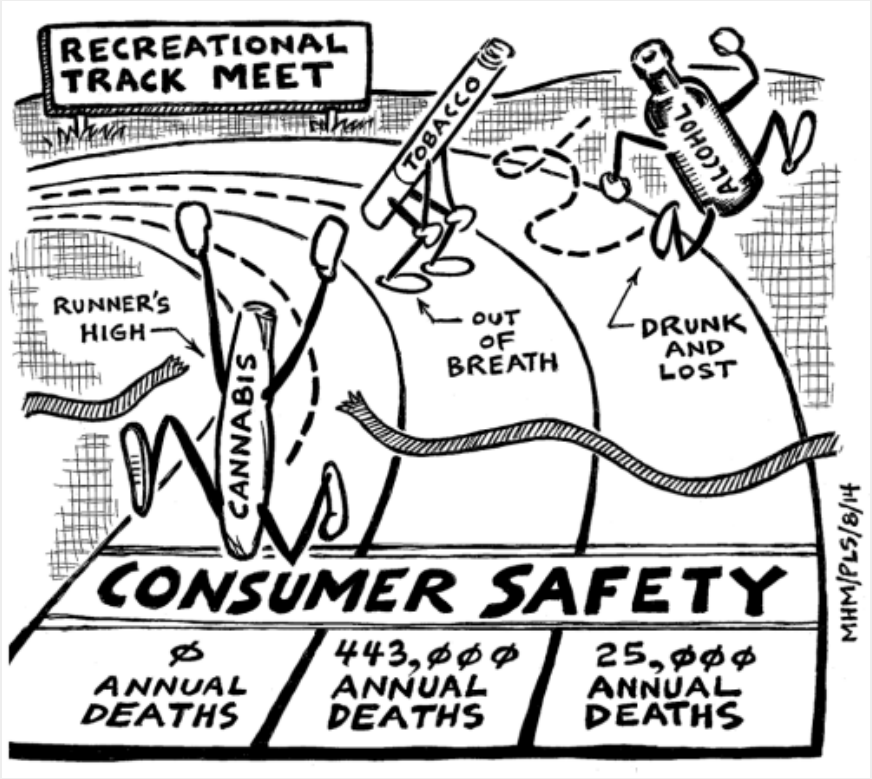
Overdose Potential

No documented deaths directly attributed to cannabis or cannabinoids.

We have not found LD50 nor LD100



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? Questions ?

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