Cannabis Science 101

Palliative and Curative Relief Through a Safe and Effective Herbal Medicine

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#1 Rule of Medicine: “First, Do No Harm”

- “Marijuana, in its natural form, is one of the safest therapeutically active substances known to man. By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care.”

  *** (DEA Chief Administrative Law Judge Francis Young, 1988)*

- “[E]xcept for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications.”

  ** U.S. National Academy of Sciences, Institute of Medicine, 1999

- “Research … of cannabinoids and endocannbinoids has reached enormous proportions, with approximately 15,000 articles on cannabis sativa and cannabinoids and over 2,000 articles of endocannabinoids.”

  *** (Medicinal Research Reviews, September 2008)*

#1 Rule of Medicine: “First, Do No Harm”

- **17,000 studies: What do we *know*? We know…**
- Cannabis is not an "intoxicant"
  "toxicum" = poison
- No known LD 50 rating (lethal dose in half)
- Cannabis has an exceptional "safety ratio”
- No “serious adverse effects associated with medical … use” (Degenhardt et al., 2008, *CMAJ*)
- Cannabis interacts with the limbic system, not the brain stem
  --Cannabis is not a CNS depressant

Yet cannabis is not FDA-approved… Why?

Curative vs. Palliative Relief

- Curative -- having the ability to cure
- Palliate -- to ease pain … without curing

- **Cannabis and cannabinoids have the ability act as both a palliative or curative agents!**

Cannabis as a Palliative Agent

- **AIDS/HIV**
  - Appetite stimulant, analgesic, anti-emetic, mood elevator
- **Cancer**
  - anti-emetic, appetite stimulant, anxiolytic action, mood elevator, analgesic
- **Chronic pain/Rheumatoid Arthritis/Neuropathy**
  - Anti-inflammatory activity
- **Crohn's disease (aka inflammatory bowel disease) and other GI disorders**
  - Anti-inflammatory activity, reduced acid reflux, reduced motility

Cannabis as a Palliative Agent

- **Glaucoma**
  - Reduction in intraocular pressure
- **Multiple Sclerosis and other movement disorders**
  - Anti-spasmodic, antidystonic, sedative activity/sleep aid, reduces incontinence
- **Tourette's Syndrome**
  - Reduction in tic severity, reduction in obsessive compulsive disorder (OCD)

Cannabis as a Curative Agent

- **Autoimmune disorders**
  - Multiple Sclerosis, Diabetes, Crohn's disease
- **Neurodegenerative disorders**
  - Alzheimer's, ALS, MS, Parkinson's disease, Huntington's disease
- **Cancer**
  - Cannabinoids stimulate apoptosis and inhibit angiogenesis
- **MRSA**
  - Cannabinoids as anti-bacterial agents
- **Neurotoxicity and Neurotrauma**
  - Stroke, TBI

Autoimmune Disorders

Multiple Sclerosis

- "Cannabinoids may not only offer symptom control but **may also slow the neurodegenerative disease progression** that ultimately leads to the accumulation of disability." (Baker et al., 2008, *Current Pharmaceutical Design*)
- Rog et al., 2007, *Clinical Therapeutics*: patients over a 2-year period reported requiring fewer daily doses of Sativex and reported lower median pain scores the longer they took the drug
- Wade et al., 2006, *Multiple Sclerosis*: 167 patients reported long-term use of Sativex (mean duration: 434 days) relieved MS-associatd pain, spasticity, and incontinence without requiring subjects to increase their dose
- Killestein et al., 2003, *Journal of Neuroimmunology*: administration of oral THC boosted immune function in MS patients; "These results suggest pro-inflammatory disease modifying potential of cannabinoids [for] multiple sclerosis"
- "**Cannabis may also slow the neurodegenerative processes that ultimately lead to chronic disability in multiple sclerosis and probably other diseases**." (Pryce et al., 2003, *Brain*)

Autoimmune Disorders

Diabetes

- Lu et al. 2006, *Autoimmunity*: rats administered CBD protected against diabetes; at a median of 17 weeks all untreated controls had diabetes versus only 40% of rats administered CBD

- El-Remessy et al, 2006, *American Journal of Pathology*: rats treated with CBD were protected against diabetic neuropathy

Autoimmune Disorders

Crohn's/inflammatory bowel disease

- Wright et al. 2005, *Gastroenterology*: "Cannabinoids enhanced epithelial wound closure" in the inflamed lining (membrane) of the GI tract in human tissue

- Sanger. 2007, *British Journal of Pharmacology*: activation of the cannabinoid receptors reduce gastric secretions, GI motility (spontaneous moving), and promotes sphincter relaxation.

Neurodegenerative Disorders

Alzheimer's disease

- Marchalant et al., 2007, *Neuroscience*: rats administered a cannabis agonist possessed a **50%** improvement in memory compared to controls in a water maze memory test.

- "[C]annabinoids offer a multi-faceted approach for the treatment of Alzheimer's disease by providing **neuroprotection and reducing neuroinflammation**, whilst simultaneously supporting the brain's intrinsic repair mechanisms by … **enhancing neurogenesis**. ... [This] offers a pharmacological approach for the treatment of AD that **may be more efficacious than current treatment regimens**." (Campbell et al., 2007, *British Journal of Pharmacology*)

- Eubanks et al., 2006, *Molecular Pharmaceutics*: THC inhibits the enzyme responsible for the aggregation of amyloidal plaque -- the primary marker for Alzheimer's disease -- in a manner "**considerably superior**" to approved Alzheimer's drugs such as donepezil and tacrine. "Our results provide a mechanism whereby the THC molecule can **directly impact Alzheimer's disease pathology**. … THC and its analogues may provide an improved therapeutic [option] for Alzheimer's disease [by]... **simultaneously treating both the symptoms and the progression of [the] disease**."

Neurodegenerative Disorders

Amyotrophic Lateral Sclerosis (aka Lou Gehrig's Disease)

- Raman et al, 2004, *Amyotrophic Lateral Sclerosis & Other Motor Neuron Disorders*: administration of THC in mice both before and after the onset of ALS symptoms **staved disease progression and increased survival** compared to controls.

- "Marijuana is a substance with many properties that may be applicable to the management of amyotrophic lateral sclerosis (ALS). These include analgesia, muscle relaxation, bronchodilation, saliva reduction, appetite stimulation, and sleep induction. In addition, marijuana has **now been shown to have strong antioxidative and neuroprotective effects, which may prolong neuronal cell survival**. … [M]arijuana should be considered in the pharmacological management of ALS." (Carter et al, 2001, *The American Journal of Hospice and Palliative Care*)

Cancer

- Sarfaraz et al, 2008, *Cancer Research*: cannabinoids show anti-cancer activity in the treatment of **gliomas** (brain cancer), **prostate cancer**, **breast cancer**, **lung cancer**, **skin cancer**, **pancreatic cancer**, and **lymphoma**

- Guzman et al, 2006, *British Journal of Cancer*: intracranial administration of THC prolonged survival and decreased tumor cell proliferation in two of nine patients with advanced stage GBM

- Ligresti et al, 2006, *JPET Fast Forward*: CBD halts the spread of breast cancer cells by triggering apoptosis (programmed cell death)

- Allister et al., 2005, Journal of *Neurooncology*: THC selectively targets malignant glioma cells, inducing cell death and decreasing their proliferation more rapidly than a synthetic agonist.

Cancer

- Massi et al., 2004, *JPET Fast Forward*: CBD inhibited glioma tumor growth in animal and human cell samples by altering blood flow (angiogenesis)

- Guzman et al., 2003, *Nature*: cannabinoids show anti-cancer activity in the treatment of **lung cancer**, **brain cancer**, **thyroid cancer**, **lymphoma**, **skin cancer**, cancer of the **uterus**, **breast cancer**, and **prostate cancer**.

- "Cannabinoids **inhibit tumor growth** in laboratory animals. They do so by modulating key cell-signaling pathways, **thereby inducing direct growth arrest and death of tumor cells**, as well as by inhibiting tumor angiogenesis and metastasis. Cannabinoids are selective antitumor compounds, **as they can kill tumor cells without affecting their non-transformed counterparts**."

MRSA (Multidrug Resistant Infections)

- Appendino et al, 2008, *Journal of Natural Products*: administration of five select cannabinoids -- THC, CBD, CBG, CBC, and CBN -- reduced skin colonization by MRSA and other drug resistant bacteria.
  - "Although the use of cannabinoids as systemic antibacterial agents awaits rigorous clinical trials, … their topical application to reduce skin colonization by MRSA seems promising. … **Cannabis sativa … represents an interesting source of antibacterial agents to address the problem of multidrug resistance in MRSA and other pathogenic bacteria**."
- Elsohly et al., 2008, *Phytochemistry*: non-cannabinoid constituents (e.g., flavonoids) in marijuana possess anti-bacterial properties against malaria, methicillim-resistant Staphyloccus aureus (aka MRSA), and other potentially drug-resistant pathogens.

Neurotoxicity and Neurotrauma

CBD and THC are neuroprotective antioxidents

- Hamelink et al., 2005, *JPET Fast Forward*: CBD is significantly more neuroprotective against ethanol-induced brain injury (alcohol poisoning) than standard treatment therapies.
- Mishima et al, 2005, *Stroke*: CBD prevented brain injury caused by ischemia (a reduction of blood flow to the brain that causes cell death)
- Knoller et al., 2002, *Critical Care Medicine*: HU-211 relieved intracranial pressure (TBI) and trended toward better neurological outcomes in 67 TBI patients
- Hampson et al., 1998, *Proceedings of the National Academy of Sciences*: THC and CBD were more protective against glutamate neurotoxicity and oxidative brain damage than standard treatment therapies
- **US Patent #6630507 -- Cannabinoids as antioxidants and neuroprotectants**
  - US Patent issued: October 7, 2003
  - Grantee: **The United States of America** as represented by the Department of Health and Human Services
  - What does this patent mean? Were cannabinoids to become a federally recognized medicine, **no private or public company could market them for these medical purposes**.

Routes of Cannabis Administration

- **Smoking (joints, pipes, water-pipes)**
  - Fast acting, easy titration
- **Oral ingestion**
  - Delayed onset, longer-lasting, more difficult to titrate, greater psychoactivity
- **Transdermal delivery**
  - Poor permeation, delayed onset, high concentrations required
  - Potential use as a topical anti-bacterial agent or localized analgesic
- **Vaporization**
  - Fast acting, easy titration
  - Vaporization of marijuana does not result in exposure to combustion gases and [was] preferred by most subjects compared to marijuana cigarettes. … **[It] is an effective and apparently safe vehicle for THC delivery**, and warrants further investigation in clinical trials of cannabis for medical purposes." (Abrams et al., 2007, *Clinical Pharmacology & Therapeutics*)

When Is Medical Cannabis Not Recommended?

- The patient has a personal or family history of mental illness or schizophrenia
- The patient will be driving shortly after administration
- The patient is pregnant
- The patients is an adolescent
- The patients suffers from lung problems
- The patient has a history of heart disease or heart attack
- The patient has high blood pressure
- The patient has diagnosed liver disorders
- **BOTTOM LINE: Always consult with your physician before beginning cannabis therapy!**

What About Marinol?

- Single, isolated synthetic cannabinoid
- Lacks the synergistic effect of multiple cannabinoids, flavonoids, and terpines
- Highly psychoactive/dysphoric
- Difficult to titrate
- Delayed onset/first pass syndrome
- Typically more expensive than natural cannabis
- Patients prefer natural cannabis when given the choice (Musty et al., 2001, *Journal of Cannabis Therapeutics*)
- **Marinol/dronabinol is legal**

Other Cannabis-Derived Pharmaceuticals

- Cessamet/Nabilone
- Rimonabant/Acomplia
- Sativex
- “The growing interest in the underlying science has been matched by a growth in the number of cannabinoid drugs in pharmaceutical development from two in 1995 to 27 in 2004.” (NIH, 2006)

More About Me

Paul Armentano is the Deputy Director of NORML and the NORML Foundation, where he has worked for over twelve years. Mr. Armentano is an expert in the field of marijuana policy, health, and pharmacology. He has served as a consultant for Health Canada, The Beth Israel Deaconess Medical Center, Safety First: A Reality-Based Approach to Teens and Drugs, and the Canadian Public Health Association, and he is a former consultant to GW Pharmaceuticals. He frequently serves as a legal consultant and expert witness for the defense in cannabis-associated criminal cases. Mr. Armentano is the author of over 500 published papers and magazine articles, and was a 2008 recipient of the 'Project Censored Real News Award for Outstanding Investigative Journalism.' He is the co-author of the book Marijuana is Safer: So Why Are We Driving People to Drink? (2009, Chelsea Green). He is on the faculty of Oaksterdam University in Oakland. He lives in northern California with his wife and son.

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For More Information

- Emerging Clinical Applications for Cannabis and Cannabinoids
  - http://www.norml.org
- International Association of Cannabis as Medicine
  - http://www.cannabis-med.org
- Medical Marijuana Pro Con
  - http://medicalmarijuana.procon.org
- ASA's booklets on medical marijuana conditions
  - http://www.safeaccessnow.org/section.php?id=135
- *Marijuana Medical Handbook* (Gieringer et al, 2008, Quick American)
- National Center of Biotechnology Information
  - http://www.ncbi.nlm.nih.gov