Marijuana: Modern Medical Chimaera

Roland J. Lamarine

Journal of Drug Education

Vol. 42(1) 1-11, 2012

chultes (left), internationally known botanist speci

Chimaera

- **Greek mythology: creature with lion's head, goat's body, & serpent's tail capable of vomiting flames.**
- **Chimerical properties: imaginary, fanciful, or fantastic**

Cannabinoids as Therapeutic Tools

- **Oscar Prospero-Garcia et al.**
- **Marijuana affects series of brain receptors: CB1R, CB2R, etc.**
- **What we know so far:**
- **<u>Endocannabinoids</u> modulate behaviors: food intake, sleep-wake cycle, learning & memory, motivation, pain perception, motor control, & more**

Brief History

- **1964, Mechoulam discovered THC**
- 1988, Howlett receptors in brain (CB1R)
- 1992, Devane isolated anandamide in
- pig's brain; CB2R discovered
- 1994, 2-AG in dogs; oleamide in cats
- So far at least 8 endogenous cannabinoids discovered, 8 synthetic cannabinoids, & 4 therapeutic compounds developed

MARIJUANA EFFECTS

1. Hypothlalamus: increased appetite
2. Brain stem: nausea relief; lowered BP; drowsiness; lowered: pain, spasticity, & tremor
3. Cerebral cortex: altered consciousness; perceptual distortions; memory impairment; delusions; hallucinations
4. Hippocampus: memory impairment
5. Cerebellum: loss of coordination
6. Amygdala: changes in anxiety; panic attacks; lowered traumatic memories; decreased hostility

Theoretical Uses of Cannabinoids

- Facilitation or blockade
- Food Intake: increase calories from sweet snacks
- CB1 antagonism for anorectic effect, Rimonabant (depression/anxiety)
- Sleep: cannabis induces drowsiness;
- Rimonabant for wakefulness?

- Learning + Memory: negative effect on short-term memory
- Extinction of fear memories & maladaptive behaviors: PTSD, OCD?
- Therapeutic Properties:
- Inflammation, pain, muscle spasticity, anxiety, depression, fatigue, insomnia, digestive disorders, etc.

Review of the Literature

- **Review of research literature related to medical applications of various forms of cannabis.**
- **Benefits of medical use examined, as well as, potential risks associated with medical & recreational use.**

Drug Delivery

- **Marinol (dronabinol): synthetic version of delta-9 tetrahydrocannabinol (THC) in sesame oil capsule**
- **Cesamet (nabilone): better absorbed version of dronabinol**
- **Sativex: THC + cannabidiol, natural liquid marijuana extract sprayed into mouth-not approved in U.S.**

Review of literature from past 40 years

- **164 serious adverse events among patients receiving cannabis therapy as compared to 60 such events in controls**
- **Adverse events included primarily respiratory & nervous system disorders**
- **“short term use of existing medical cannabinoids appeared to increase the risk of nonserious adverse events”**

-Wang et al. 2008

Meta-Analysis of Double-blind Randomized Controlled Trials

- Medical marijuana for pain
- Reviewed 93 studies (18 in final analysis)
- Authors concluded that cannabis use in the treatment of pain presented more risks than benefits

-Martin-Sanchez et al., 2009

First Study of Sativex for Intractable Pain

- **Diabetic neuropathy, 38 patients**
- **No more efficacious than placebo**
- **Need for more research**

-Salvarajah et al., 2010

Cannabis for Palliative Care

- Review of all literature from 1996-2010
- Authors noted “systematic reviews on the efficacy of cannabis in pain control for humans suggests that there is as yet inconclusive evidence that cannabis has any major therapeutic role in pain management.”

-Green & DeVries, 2010, p. 2457

Positive Findings from Green & DeVries

- **Literature suggestive of improvements in Quality of Life (QOL) outcomes such as improvements in sleep and abatement of depressive symptoms. Also, reports on opiod-sparing effects-synergistic effects of opiod/cannabinoid preparations**

More Positive Potential

- Cesamet & Sativex potentially efficacious as *adjuvant therapies* for secondary treatment of chronic illness
- Maybe subjective improvement from patient's perception for chronic pain
- Patients may not perceive benefits of oral administration

-Peat, 2010

Sativex for Overactive Bladder with MS

- 135 patients, 10 week double-blind randomized, placebo-controlled trial
- Concluded Sativex did provide some improvements in QOL indicators but *results did not reach statistical significance*.

-Kavia et al., 2010

Sativex for MS related Spasticity

- Meta-analysis of 3 randomized, placebo-controlled, double-blind studies
- 666 patients with MS-related spasticity
- Large numbers of subjects experienced at least one adverse event
- Sativex did reduce spasticity & was well tolerated overall

-Wade et al., 2010

“no solid conclusive data have emerged that would justify the use of cannabis as an alternative to the currently marketed and accepted therapeutic analgesic arsenal.”

-Martin-Sanchez et al. 2009, p. 1354

Risks Associated with Chronic Marijuana Use

Marijuana Abstinence Syndrome (>48 hrs-2 weeks)

1. irritability/anger/agitation
2. anorexia
3. Insomnia/vivid dreams
4. depression
5. anxiety
6. headaches
7. muscle tension

-Lamarine & Sbarbaro. 1996

Lung Damage/Heart Disease

- **Threefold increase of inhaled tar compared to tobacco**
- **Fivefold increase in CO (carboxyhemoglobin) from smoked marijuana → heart disease**
- **Depth of inhalation, volume of smoke inhaled, duration of breath holding**
- **Evidence of obstructive lung disease**
- **Concurrent use with tobacco may produce synergistic effects and increase risk for COPD**

Cancer

- **Inhaled smoke loaded with carcinogens**
- **Increased risk for a wide variety of cancers in smoker and child if smoker is pregnant**

Anxiety

- **Consistent relationship between frequent marijuana use & higher anxiety levels but NOT with anxiety disorders**
- **Anxiety also related to withdrawal syndrome**

-Crippa et al., 2009

PSYCHOSIS

*risk for psychosis in general population <1%

*marijuana users have 40% increase

*heavy users 200% increase

*six major studies in five countries targeting adolescents & young adults

*link only for psychosis, not anxiety, depression, or other mental health problems

*mabe pre-existing problems may lead to BOTH pot use + psychosis??

Zammit, et al. *The Lancet*, July 27, 2007

Also poor outcomes in schizophrenic users

ADDICTION RATES FOR USERS OF SELECTED DRUGS

MARIJUANA	9%
ALCOHOL	15%
HEROIN	23%
TOBACCO	32%

Conclusions

1. **Risk/benefit outcomes inconclusive**
2. **Smoking as a delivery mechanism has significant health risks & concerns regarding dosage administration**
3. **Clinical trials have not presented clear evidence of significant efficacy**
4. **Synergistic opiod-sparing effect appears promising**

4. Risks with “medical” use appear to be minor but not insignificant

5. Does long-term marijuana use increase risk for psychosis?

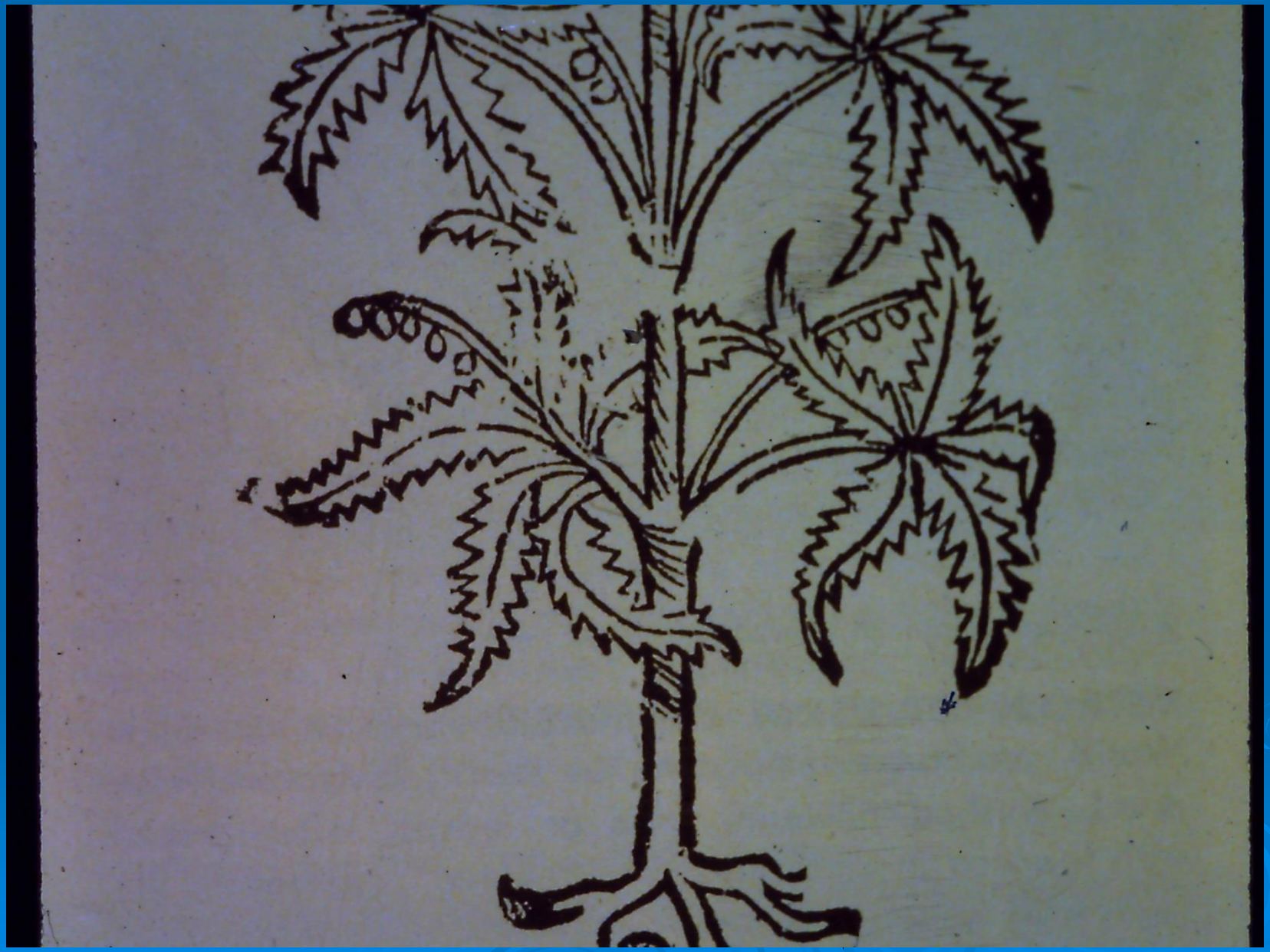
6. Anxiety risks appear to be dose-related & of short-term duration

7. Moving cannabis to Schedule II would facilitate more research

Chinese characters T
oldest known name f

大 = TA (pronounce
Literally this means a
man, and by extensio
signify great or tall.

麻 = MA. It repres
fiber plant, literally a
plants (林), growing
dwelling (广). Hence
two symbols together
"the tall fiber plant,"
which everywhere in
China signifies canna



- To request a PDF of my article or Power Point on medical marijuana, send an email to:

- rlamarine@csuchico.edu