

Medical Marijuana: Getting In the Weeds

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AGENDA

What is MEDICAL Marijuana (MMJ)?



Is Marijuana Medicine?



Marijuana vs Industrial Hemp



Why Marijuana, Why Now?



Effects and Side Effects of Marijuana



Diseases and Medical Marijuana: What the Studies Show



Smoking and Misuse of Marijuana



Conclusion



What is MMJ?

Dried flowers and leaves of the Cannabis (marijuana) plant taken for a desired medical purpose

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SYNTHETIC "MARIJUANA" FLOODS TAMPA BAY AREA



Associated Press March 28, 2016



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SYNTHETIC "MARIJUANA" IS NOT MEDICAL MARIJUANA

"...What makes spice dangerous is how easy it is to get, its inexpensive price and the difficulty of following through with prosecution. While it is called synthetic marijuana, officials say it **has nothing to do with the leafy drug that is being legalized for medical use and decriminalized in some U.S. states and cities.**

Synthetic marijuana is made by taking dried plant material and soaking it in ever-changing chemical combinations. Packets of the drug used to be available in convenience stores alongside packs of chewing gum and candy bars, and sometimes still are, O'Connor said.

Those packets often are rolled into individual spice cigarettes, which sell on the street for \$1 or \$2 each.

They don't know what they're taking ..."

Associated Press March 28, 2016



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PHARMACEUTICAL CANNABINOIDS ARE NOT MEDICAL MARIJUANA

Synthetic Cannabinoids

Made in laboratories; examples include FDA approved Marinol® (dronabinol) and Cesamet (nabilone)

Marinol®: Synthetic Oral THC

Cesamet®: Synthetic Oral THC Analogue



Phytocannabinoids

Found in the plants, contains hundreds of cannabinoids, most notably THC and CBD

Sativex® (Canada/UK): Herbal Cannabis Extract



HEALTHCARE SOLUTIONS

MARIJUANA REFERS TO DRIED FLOWERS AND LEAVES OF CANNABIS PLANT

- ❑ Various species but *C sativa* and *indica* most common for medical marijuana
 - 2737 BC—Marijuana first used medicinally
 - 1851 AD—Legitimate medical compound in US Pharmacopoeia
 - 1937—Criminalized in the United States
- ❑ Approximately 100M adult Americans have used marijuana and current use rate is reported 17.4 M (SAMHSA)
- ❑ 1.1+ M legal medical marijuana patients registered in the United States (as of Oct 2014, procon.org)
- ❑ Schedule I Federal Controlled Substance
 - Similar to ecstasy, heroin, cocaine, LSD
 - No legitimate medical use, lack of accepted safety under medical supervision, and a high potential for abuse
- ❑ Dried flowers, leaves and stems are usually smoked, but can be vaporized or cooked for ingestion of the extracts
- ❑ Alternative methods of administration avoid combustion and are considered by some less harmful to the lungs than smoking



Number of legal medical marijuana patients. Available at <http://procon.org/medical-marijuana-patients.php?search=0-00000>.

HEALTHCARE SOLUTIONS

MEDICAL MARIJUANA PRODUCTS



EDIBLES



CREAMS/OILS



The New Smoking

- ✓ Smoking is a natural irritant to the lungs
- ✓ Alternative methods avoid combustion and maybe considered less harmful to the lungs
- ✓ BUT battery-operated vape pens produce high temperatures that can transform ingredients into carcinogens and other dangerous toxins

Cookies, Candies, and Bars

- ✓ Effects take longer to start. So can ingest more than needed. Pediatric deaths in Colorado
- ✓ Onset with edibles 30-60 minutes, smoking 30-60 seconds
- ✓ Effects last longer: edibles 4-6 hours, smoking 1-2 hours
- ✓ Dosage not accurate: Analysis only 17% accurate THC levels; 60% lower; 23% higher

Topical Creams

- ✓ Cannabis, CBD, coconut oil, hemp oil, kpanngian butter
- ✓ May not be detectable on urine drug test

Oral Oils

- ✓ CBD Oil, MCT Oil
- ✓ Problems compounding exist for these products

Products available through Google search. Edible ingredients study JAMA. Jan 2015.
How safe is your vape pen? Available at <http://www.cannabiscare.com/your-vape-pen>
3 Tips on how to eat marijuana edibles. Available at <http://www.cannabiscare.com/3-tips-on-how-to-eat-marijuana-edibles>

Main Cannabinoid Chemicals

Anandamide

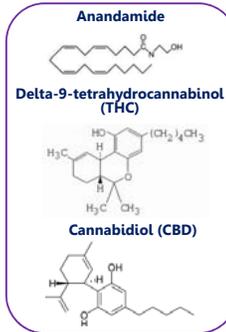
- A natural messenger chemical present in the brain at low levels
- Endocannabinoid; role in pain, depression, appetite, memory and fertility

Delta-9-tetrahydrocannabinol (THC)

- Most psychoactive cannabinoid of >200 identified
- Interacts with cannabinoid receptors in the body giving the effects of feeling high
- High concentrations in *sativa* species, moderate in *indica* species

Cannabidiol (CBD)

- Nonpsychoactive; interacts differently with receptors along with a serotonin receptor giving the effects of feeling relaxed and heavy aka stoned
- Higher concentrations in *indica* species vs *sativa* species



INDUSTRIAL HEMP VS MEDICAL MARIJUANA

INDUSTRIAL HEMP

- ❑ Low THC <0.3% *C. sativa* plant bred for fiber for clothing, construction, oils and topical ointments (not psychoactive)
- ❑ 2014 Fed Farm Bill allows university and state departments to grow industrial hemp
- ❑ Sale, production and distribution of CBD products from imported raw material industrial hemp is legal ... cannabinoids in industrial hemp, including oil, were never scheduled under the Controlled Substances Act ...
- ❑ Raw materials shipped to the US obtained from Europe
- ❑ Several CBD products used for medical conditions (no medical claims allowed FDA)
 - Charlotte's Web Products
 - Hemp Meds
 - Others

MEDICAL MARIJUANA

- ❑ CBD/THC (THC higher than 0.3%)
- ❑ Current THC is 18% to 30%
- ❑ Reports of pesticides greater (6X) than that seen in food
- ❑ House members ... restrict DEA from using funds to go after medical marijuana operations legal under state laws
- ❑ Almost half of states legalized medical use; more expected to legalize recreational use
- ❑ Unclear if any federal bills will follow suit

Hemp as an agricultural commodity. Available at <https://www.fda.org/oc/industrial-hemp-01-17-2018.pdf>
 State industrial hemp statute. Available at <https://www.fda.gov/oc/industrial-hemp-01-17-2018.pdf#st=state>
 Industrial hemp. Available at <https://www.fda.gov/oc/industrial-hemp-01-17-2018.pdf#st=industrial-hemp>
 Budget bill passed by congress prevents the DEA from spending money on CBD enforcement. Available at <https://www.eurotimes.com/news/budget-bill-passed-by-congress-prevents-the-dea-from-spending-money-on-cbd-enforcement/>
 Hemp oil in food. Available at <https://www.fda.gov/oc/industrial-hemp-01-17-2018.pdf#st=hemp-oil-in-food>
 The Cannabis Difference. Available at <https://www.cannabis.com/the-cannabis-difference/>
 100% MEDICAL MARIJUANA. Available at <https://www.100percentmedicalmarijuana.com/>

Why the Interest?

SIDE EFFECTS OF SMOKING MARIJUANA

Wadsworth et al, 2006	Ammerman et al, 2015
<ul style="list-style-type: none"> <input type="checkbox"/> Short-term memory problems <input type="checkbox"/> Impaired thinking and ability to perform tasks requiring mental alertness <input type="checkbox"/> Loss of balance and motor function (eg, coordination) <input type="checkbox"/> Decreased ability to concentrate <input type="checkbox"/> Changes in sensory perception <input type="checkbox"/> Decreased reaction time 	<ul style="list-style-type: none"> <input type="checkbox"/> Increased heart rate <input type="checkbox"/> Increased blood pressure <input type="checkbox"/> Dry mouth <input type="checkbox"/> Increased appetite, thirst <input type="checkbox"/> Drowsiness <input type="checkbox"/> Anxiety, insomnia, panic attacks <input type="checkbox"/> Hallucinations <input type="checkbox"/> Conjunctival injection

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LONG-TERM EFFECTS OF SMOKING MARIJUANA

- Increased risk of lung cancer
 - 3 to 4 joints = 20 tobacco cigarettes
- Increased risk of psychosis
 - 3 year study (535 patients)
 - 54% schizophrenia-spectrum disorder
- Increased risk of periodontal disease
- Younger users: decline in IQ (permanent cognitive impairment)
- Males
 - Suppression of testosterone secretion decreasing libido and/or gynecomastia
 - Decreased sperm count and motility leading to an increased chance of infertility
- Withdrawal syndrome
 - Restlessness, insomnia, anxiety, aggression, tremors
 - Daily dose of 180 mg THC (1-2 joints) for 11-21 days

Four times the amount of tar is deposited in the lungs compared to tobacco smokers

Dependence occurs in 1 out of 10 people

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EFFECTS OF SYSTEMIC CBD: NOT ALL IS GOOD

Side Effects of CBD	Drug Interactions- CBD
<ul style="list-style-type: none"> <input type="checkbox"/> Effects on the immune system may be possible, worsening of disease progression - HIV infection, tumor genesis, and metastases <input type="checkbox"/> Sedation <input type="checkbox"/> Question effects on blood sugar <input type="checkbox"/> Feeling heavy <input type="checkbox"/> Overdoses in monkeys: tremors, convulsions, vomiting, sedation to prostration in 30 minutes, cardiac failure 	<ul style="list-style-type: none"> <input type="checkbox"/> May cause drug interactions and increase or decrease their effects or make them toxic <input type="checkbox"/> Significant number of drug interactions to make it a concern <input type="checkbox"/> CBD could interact with anticancer drugs <input type="checkbox"/> CBD possible interaction with other pain meds like NSAIDs (eg, Motrin, Aleve)

BIGGEST CAUTION

Safety and side effects of cannabidiol, a cannabis sativa constituent. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3111311/Burgmansch_2011.pdf. Identification of cytochrome P450 enzymes responsible for metabolism of cannabidiol by human liver microsomes. Available at <http://neuropharmacology.elsevier.com/locate/S0165381314000144>. The role of cannabis and cannabinoids in diabetes. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3718683/>. The Endocannabinoidome. Copyright 2015.

HEALTHCARE SOLUTIONS 21

ADVERSE EFFECTS OF MARIJUANA ON HEALTH AND WELL-BEING

ADVERSE EFFECT	LEVEL OF EVIDENCE
Addiction to drugs	HIGH
Low lifetime achievement	HIGH
Increased motor vehicle accidents	HIGH
Chronic bronchitis	HIGH
Abnormal development of brain	MEDIUM
Progression to other drug use	MEDIUM
Comorbid anxiety or depression	MEDIUM
Schizophrenia	MEDIUM
Lung cancer	LOW

NON-MEDICAL MARIJUANA AND PRESCRIPTION DRUG MISUSE CONTINUES IN THE UNITED STATES

- Lab data (22,000+ UDTs) correlation between marijuana and prescription drug use in national population
- Marijuana most frequently detected non-prescribed drug in >26% of patients who do not use medications as prescribed
- Marijuana most frequently detected drug in the nation's workforce. Quest *March 2013 drug test index report*
- Approximately 45% of patients who use recreational marijuana also used other non-prescribed drugs (ie, sedatives and narcotics)
- 37% of medical marijuana users misused other drugs



Diseases

Use in Epilepsy



Therapeutic potential but no controlled trials for safety and efficacy of cannabinoids in epilepsy—WLDI 2016

- Interest in use for resistant epilepsy the result of a mix of science, politics, and social phenomena
- Anecdotal evidence (no controlled trials) of seizure control, but results with CBD encouraging; might be considered under close physician supervision after failure of all conventional therapies
- Evidence for medical marijuana being harmful to developing brain (eg, schizophrenia)



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Future Research Funded



- Colorado Board of Health awards \$8 M to study medical marijuana's therapy potential
- First government money for efficacy research rather than just looking for negative effects
- Funded by state medical marijuana patient user fees—medical use legalized in 2000, recreational use in 2012
- Other studies: anxiety, ADHD, substance abuse, epilepsy, pain, nausea, arthritis, PTSD, schizophrenia, sickle cell disease, sleep apnea, spasticity/MS (<https://ClinicalTrials.gov>)



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LACK OF EVIDENCE FOR SMOKED MEDICAL MARIJUANA

Much of the evidence is anecdotal; few double-blind, randomized, controlled trials; most of poor quality as a result of Federal Class I designation

American Medical Association (AMA)

- Despite the public controversy, less than 20 small randomized controlled trials of short duration involving ~300 patients have been conducted over the last 35 years on smoked cannabis.
- Large variability in specific cannabinoids in various medical marijuana products
- Reduce the schedule and conduct more research

Institute of Medicine (IOM)

- Smoking marijuana is not recommended. The long-term harm caused by smoking marijuana makes it a poor drug delivery system, particularly for patients with chronic illnesses.
- Development of non-smoked, reliable delivery systems and testing needed



Report 3 of the council on science and public health. 2009. Available at <https://www.nationalacademies.org/2009/04/03/03-report-3-of-the-council-on-science-and-public-health-2009>
Marijuana and Medicine. Mar 1999 Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1450064/>



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Bottom Clinical Lines

"Physicians should not recommend that patients use marijuana for medical purposes because it is a dangerous, addictive drug and is not approved by the FDA --American Society Addiction Medicine

Despite legalization by several states, marijuana use is still illegal in the United States at the federal level (which considers marijuana a schedule I controlled substance), and individuals prescribing or using marijuana for medical use are at risk for prosecution. -- UpToDate. Online database. Apr 2016

"Cannabinoids—Not recommended for pain ... there are no quality studies supporting cannabinoid use, and there are serious risks ... it is very difficult to do controlled studies with a drug that is psychoactive because it is hard to blind to these effects ... high doses increase pain ... [and] declines in cognitive performance ... integral to a patient's work and lifestyle ... adding a cannabinoid to opioid therapy ... more study needed.

Smoking anything is unacceptable ... Cannabis is unstable and unpredictable and the drug should be subject to the same standards that apply to other medications. For every disease and disorder for which marijuana has been recommended, there is a better, FDA-approved medication." --Work Loss Data Institute Apr 2016,

QUESTIONS



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