CBD OIL: FACTS OR QUACKS

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DISCLOSURES

- I have no relevant financial interests or relationships with manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services in this presentation.
OBJECTIVES

- REVIEW HISTORY OF CANNABIS
- REVIEW CANNABIS CHEMISTRY
- FAMILIARIZE PARTICIPANTS WITH DIFFERENCES IN PRODUCTS AVAILABLE ON THE MARKET
- LEARN THE DIFFERENCE BETWEEN CBD AND HEMP OIL
- FAMILIARIZE PARTICIPANTS WITH EVIDENCE-BASED STUDIES ON CBD AND HEMP OIL

SURVEY

- How many people feel they have a good working knowledge about CBD products?
- How many people have tried or use CBD products?
  - Have you had good success?
- How many people recommend CBD products to patients?
  - Do your patients claim success?
- How many people know that CBD and hemp oil are not the same?
- Do you know if these products show up in a drug screen?
Cannabis use and cultivation dates back 10,000 years.

Cannabis is one of the 50 fundamental herbs in Chinese medicine.

In 1550 BCE Egyptians used cannabis suppositories to treat hemorrhoids. In ancient India it was prescribed for insomnia, headaches, stomach issues, pain and childbirth. The ancient Greeks used cannabis leaves for wounds and nose bleeds. Seeds were ingested to treat tapeworms. Arabic manuscripts from the 8th century documented its use as a diuretic, antiemetic, antiepileptic, anti-inflammatory, analgesic and antipyretic.

Cannabis has been utilized in religious practices for centuries.

Humans have been modifying the plant for 500 years.

In the 1830’s, an Irish physician, William Brooke O’Shaughnessy, “discovered” cannabis in India and brought it back to England.

With the rise of opium in the late 19th century cannabis use, as a form of medical treatment, began to decline.

In 1937 the United States Marihuana Tax Act was enacted and charged doctors a fee for prescribing cannabis.

In 1941 cannabis was removed from the United States Pharmacopeia, a compendium of available drugs published by the United States Pharmacopeial Convention (USP).

Tetrahydrocannabinol (THC) was isolated and synthesized in 1964.

In 1970 cannabis was designated as a controlled substance (Category I) by the Federal Drug Administration.
• There are over 100 cannabnoids found in hemp and marijuana plants.
• For purposes of this discussion the two main cannabinoids are Cannabidiol (CBD) and Tetrahydrocannabinol (THC) which can be found in the seeds, stalks, and flowers of the plants.
• THC (about 12%) is more concentrated in the marijuana plant while CBD is found in higher amounts in hemp (Hemp is defined as having no more than 0.3% THC).
• THC is psychoactive, CBD is not.

• There are two plant species; Indica and Sativa.
• **Indica** is the plant that contains mostly CBD. Its effect is described as a “full body narcotic feel” or a “body high”. It is marketed as the product best for treating pain and sleep.
• **Sativa** is high in THC. It “uplifts the spirits” or gives a “head high”. Sativa might be recommended for depressive symptoms or fatigue.
• Hybrids of Sativa and Indica are also available; typically having a higher ratio of THC to CBD. These hybrids might be suggested to help decrease depression and stimulate the appetite.
• There are over 1000 unique strains of the cannabis plants being grown.
Cannabis interacts with the endocannabinoid system which regulates pain, appetite, mood, memory, immune response, sleep, and cellular life cycle.

- There are two important cannabinoid receptors; cannabinoid 1 (CB1) and cannabinoid 2 (CB2).
- CB1 is found in the brain and central nervous system and confers the psychoactive effects. THC has a high affinity for CB1 receptors.
- CB2 receptors are found in immune system tissues and has no psychoactive properties. CBD has a high affinity for CB2 (and 5HT1A).
- It is believed that CBD indirectly attaches to entice the body to make more CB2 receptors which will then have an effect on the pain and inflammation.

THE LAW

- Seventeen states have approved laws for commercial hemp products. (CBD often falls under these provisions.)
  - Commercial industrial hemp products, utilized to make biodegradable plastic, paper, textiles and fuel, are legal in all 50 states.
- Hemp derived products are legal in 50 states.
- The laws become murky as to the permissibility of CBD oil.
- CBD with a THC concentration less than 0.3% can be sent through the mail. It is legal to buy on-line and ship if less than 0.3% THC.
- Some cruise lines prohibit CBD.
- It is prohibited on international planes because it still illegal in many countries.
Dispensaries and users report that CBD products cannot be detected on a urine test which is not completely accurate.

A positive test can occur with high doses and the percentage of THC in the CBD.

CBD can be detected up to five days after last use.

There is a urine test that specifically targets CBD.

The Agricultural Improvement Act of 2018 also known as the 2018 Farm Bill removed hemp is a controlled substance.

It pressured the FDA to regulate products.

Currently there are no approved CBD marketing application.

There are no FDA approved CBD products.

There are no FDA approved conditions and no proven therapeutic benefits to CBD per the FDA.

There have been warning letters issued in regards to selling unapproved products with unsubstantiated claims.

The FDA concludes that THC and CBD are excluded from dietary supplement definitions.

The FDA has stated it has no real understanding of the risk or benefits of CBD.
FDA (cont.)

• FDA Commissioner Scott Gottlieb, MD produced a memorandum on April 2, 2019 that stated that CBD should be treated like any other product and that the FDA should form an internal agency to explore pathways to marketing this product.

• FDA does not regulate safety or purity as it is considered a supplement and not a medication.

• It is not known yet what might be a therapeutic dose of CBD.

FDA (cont.)

• There are only three cannabis related products that have been approved by prescription only:
  • Epidiolex (Cannabidiol)- for seizures related to Lennox-Gastaut and Dravet Syndrome in children under the age of two years.
  • Marinol (Tetrahydrocannabinol) for anorexia and weight loss secondary to HIV and cancer treatments.
  • Cesamet (Nabilone) a synthetically derived product for nausea related to cancer treatments.
LET'S GO SHOPPING!

- OILS
- CREAMS
- SALVES
- PILLS
- TINCTURES
- POWDERS
- EDIBLES
- YOU CAN EVEN BUY SOMETHING FOR YOUR FURRY FRIENDS!

SUGGESTIONS ON PURCHASING

- Quality of the product.
- People will respond differently, so it is recommended to try different products
- Cost-Do you get what you pay for?
- Use a certified dispensary
- Look for pure organically manufactured products
- Look for other ingredients such as essential oils, odors, and flavors.
- CBD is not necessarily state-sanctioned and may be unregulated.
- Why do you want to use it and in what form does it comes in?
  - The impact of topicalcs can vary from person to person; some people feel the effect right away and in some it takes hours
  - If ingesting the product, the effect may take more than 30 minutes
• Product testing can be inconsistent.
• Products have been found:
  • Not to have the amount of product as listed on the label
  • Containing harmful content such as heavy metals, and contaminants like mold and bacteria
• Look for other ingredients on label.
• Know the terms on the label.
• Avoid any product that has sweeping health claims.

• A Certificate of Analysis (COA) refers to an authenticated document that is issued by Illumina’s Quality Assurance Department that ascertains that a product has met its predetermined product release specification(s) and quality. COA's can be used to satisfy qualification and/or acceptance activities by customers that are subject to regulatory agencies such as: Food and Drug Administration (FDA) and Clinical Laboratory Improvement Amendments (CLIA).
• Product should be tested by a third party lab to obtain a COA. The lab also should have an accreditation by the International Organization for Standardization or ISO (Standard ISO 17025).
• Avoid using a product without COA or from a company that refuses to provide COA. (Barcode or QR code on the label allows downloading of the COA.)
• There are no regulations on how often a product is tested; if the COA is greater than three years old it is probably not a good product.
• Look at where your hemp is sourced as Colorado sets the gold standard for growing so it is recommended using products from Colorado.
• International products are not recommended.
• Reputable growers avoid using harmful chemicals as cannabis plants readily pick up heavy metals and pesticides.

• CBD industry is expected to expand sevenfold by 2021.
• Sales were $292 million in 2016 and are projected to be $2.1 billion by 2021.
• CBD costs 5-10 cents/ mg to 16 cents/mg
• Hemp $9-18 an ounce (about 28,000 mg)
HEMP OIL? NOW I’M TOTALLY CONFUSED!

- Remember there are two varieties of the Cannabis plant: hemp and marijuana.
- Hemp oil is not the same as CBD oil.
- CBD is made from flowers, buds, stands, and leaves but still must be under 0.3% THC.
- Hemp oil has no detectable THC and is made from the seeds.
- Hemp oil is much less expensive than CBD oil and consumers are often taken in; believing a product is CBD when it is actually hemp.

- Hemp seed oil is considered a better skincare product than CBD oil because it does not clog pores.
- Hemp oil is high in alpha linolenic and oleic fatty acids. These are purported to balance out the skin by reducing sebum production which is why it is often used as a cosmetic to treat eczema, dermatitis, psoriasis, and rosacea.
- It is reported to resist infection.
- It is reported that it protects the brain from inflammation due to polyphenols.
- It is reported to be heart healthy to treat hypertension, atherosclerosis, and high cholesterol due to the linoleic acid which is what is found in fish oil.
- Hemp oil is often used for food preparation.
- Hemp seeds are also sold for ingesting.
- In one test of three popular hemp oil products it was found that the amount of THC in the product was 1250% higher than the legal limit.
  - This equates to 3.8 mg per gram of hemp seed.
  - Typically people are recommended to ingest 30 g of hemp seed daily.
• Both CBD and hemp oils are often mixed with coconut, sunflower, olive, macadamia nut oils.
• They are commonly flavored with citrus, vanilla, or mint.
• The oils may be mixed with various herbs like turmeric.
• They can also be mixed with medium chain triglycerides (MCT) which is an extract of coconut oil and 50% fatty acids.

BIOAVAILABILITY OF CBD

• Intranasal: 34 to 46%
• Vapor: 40% (shortest acting route)
• Oral: less than 6% due to first pass metabolism
• Topicals: 30-40%
• Oil is the most potent form.
• Tinctures are alcohol-based and very popular.
• Oils are best for topical use in targeted areas.
• Oral products are best for pain over.
CBD is metabolized by CYP 450, so it matters how you take it.

- Sublingual or topical has negligible metabolism.
- 10 mg a day is recommended orally up to 80 mg a day.

Literature review on CBD found studies that it can treat:

- Anxiety, depression, acne, heart disease, nausea vomiting and distress of cancer, chronic pain, multiples sclerosis symptoms such as pain and muscle spasm, epilepsy, insomnia, opiate addiction, IBS, autism, endometriosis, medication overuse headaches, pediatric complex motor disorders, wound pain with pyoderma gangrenosum, dysautonomic syndrome, post HPV vaccine pain, lupus, low grade ovarian cancer with concomitant Laetrile treatment, PTSD, corneal pain, post kidney transplant pain, sleep behaviors associated with Parkinson’s disease, fibromyalgia
- Decreases resting blood pressure, drug-seeking behavior, spread of tumors, diabetes incidences, surgical incision pain, addiction to marijuana, gastric inflammation, joint damage
- Acts as an antipsychotic, protects nerves, enhances facture healing, and produces high volume eyelashes
• Acetaminophen and CBD given to mice caused liver injury, reproductive toxicity and impaired fertility in males.
• A study at the University of Arkansas found liver damage with high doses of CBD and death within 3 to 4 days.
• It is known to cause sleepiness, sedation, lethargy, increase liver function tests, decreased appetite, diarrhea, rash, fatigue, malaise, weakness, poor sleep quality, insomnia, suicidal ideation, suicide attempts, agitation, increased depression, and panic.
• Oils are not likely to cause liver damage because of low dose and often used topically.
• Might interfere with effectiveness of anti-inflammatories and some cancer drugs

TASTE OF THE LITERATURE

• 57 healthy males given 50, 300, 600 mg of CBD vs. a placebo in a double-blind study to determine level of anxiety while giving speech.
• 300 mg had significant reduction in anxiety but no changes noted with higher doses or placebo

• CBD and imipramine were given to mice
• CBD showed an antidepressant-like effect equal to that of imipramine
• Studied by using a forced swimming test.
• Mechanism of action believed to be by activating 5-HT1


• CBD induced cell death in cancer cells


• CBD showed lipostatic and anti-proliferative anti-inflammatory effects in sebaceous gland function and is promising for acne

• Case series with Parkinson’s patients with REM sleep behaviors. CBD show substantially reduced paroxysmal loss of muscle atonia and nightmares.


• Single dose of CBD caused a 5 mmHG decrease in blood pressure and healthy individuals from resting rate in nine males. Heart rate increased 10 bpm and stroke volume decreased by 13 mL.


• CBD prevents social recognition memory deficits in Alzheimer’s disease in transgenic mice. CBD given orally over eight months. Substantial impact noted on inflammatory response, cholesterol, and phytosterol retention. May be a preventative for social withdrawal and facial recognition issues. CBD did not change amyloid load or oxidative damage. There was no impact on anxiety or associative learning.

CBD attenuates oxidative stress, inflammation and cell death impacting left ventricular hypertrophy function and biochemical markers in mice model of type I diabetes-related cardiomyopathy.


CBD reduced incidence of diabetes 86% in treated mice versus 30% in untreated mice. Showed reduction of pro-inflammation cytokines.


CBD meta-analysis of 14 studies related to impact on opiate, cocaine, and nicotine use. Nine animal and five human studies reviewed.

CBD showed less severe diarrhea and shakes in mice post intoxication.

CBD failed to show decrease drug-seeking behavior in heroin addict model mice.

CBD had no impact on cocaine reward effect in mice.

CBD did not show clear impact on marijuana users.

In humans a CBD case report showed possible reinforcing behavior of marijuana users.

In humans a study of 24 smokers showed nicotine reduction with use of CBD.

A study of 10 human alcoholics showed no difference in addictive behaviors.

THE BEST RESEARCH SUPPORTS...

Epilepsy treatment

CONCLUSIONS

- Caveat Emptor-Buyer Beware
- You get what you pay for
- Read product labels
- Read research with analytical eye- remember journal club days?
- “Give someone who has faith in you a placebo and call it a hair growing pill, anti-nausea pill or whatever, and you will be amazed at how many respond to your therapy.” Bernie Siegel
- May not be harmless
- May be found in drug screens