



A Briefing Paper on
The Evolution of Marijuana to Medicine and a
Closer Look at Charlotte's Web
January 21, 2014

Background:

Legalizing the crude marijuana plant is not necessary and not a scientific approach to providing safe and effective medicine. A number of modern medicines are derived from plant material, including the marijuana plant. Examples include: Taxol which comes from the yew tree (<http://www.research.vt.edu/resmag/1999resmag/taxol.html>); opiates which come from the poppy plant (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC46725/>); anesthesia which comes from the coca plant (<http://www.ncbi.nlm.nih.gov/pubmed/11895133>); aspirin which comes from the willow tree (<http://inventors.about.com/library/inventors/blaspirin.htm>); and dronabinol which is derived from the marijuana plant.

None of these medicines, however, are the raw plant rolled up and smoked. They are rather derived from specific extracts of the plant and delivered through a safe delivery system in a form that is stable where dosing is known and controllable. Some of these plants, such as the yew, actually contain some compounds that can be deadly so separating the specific compound that has medicinal value and has been shown to be more beneficial than harmful is extremely important. <http://www.nlm.nih.gov/medlineplus/ency/article/002877.htm>
<http://cal.vet.upenn.edu/projects/poison/plants/ppyew.htm>
<http://www.naturalmedicinalherbs.net/herbs/t/taxus-baccata=yew.php>

Marijuana contains hundreds of compounds, many of which are very harmful to one's health. Marijuana does, however, contain at least one compound, and possibly more, that are supported by science as being medicinal.

Decades ago, the tetrahydrocannabinol (THC) in marijuana was isolated after research proved it to be medically effective. After being isolated from the other compounds, it was synthetically replicated and produced in capsule form. Known as dronabinol generically, it is marketed in the United States under the brand name of Marinol. It is approved by the Food and Drug Administration (FDA) and typically prescribed for appetite stimulation and nausea control associated with chemo and radiation treatment. <http://www.drugs.com/pro/marinol.html> and <http://www.marinol.com/about-marinol.cfm>

Another compound in marijuana, cannabidiol (CBD), is currently undergoing research to determine its medical efficacy.

Sativex

Research is now underway by a European pharmaceutical company, GW Pharmaceuticals (GW), (www.gwpharm.com) to develop a THC-CBD product known as Sativex that is a natural extraction from two marijuana plant strains (one high in THC and one high in CBD), as opposed to a synthetic product. A distinction about the marijuana plants that are cultivated for this

research is that the plants are cloned, providing identical plants. GW has developed a safe delivery system rather than promoting the smoking of medicine.

Sativex is now approved in 24 countries. It is indicated as a treatment for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy. Sativex is also in Phase III clinical development for the treatment of cancer pain, the lead indication for the U.S. market.

Epidiolex

Following its work with Sativex, GW began to look at the other 99 non-psychoactive cannabinoids in marijuana. Research was conducted using CBD, a non-intoxicating cannabinoid in marijuana, that showed promising results in treating epilepsy. Once published, parents began contacting the researcher asking if they could use this for their children. The researcher then contacted GW Pharmaceutical. Extensive toxicology research had been done, as well as limited human trials.

Based on that research the therapeutic dose for CBD alone is likely to be 400-1500 mgs of CBD a day. The high-CBD strain developed for Sativex contains a very small amount of THC. GW was concerned that even this amount of THC might be harmful for a developing brain. **So, to get a purer CBD concentrate, GW uses a high tech machine to conduct an extra purification process, creating a product with pure CBD and an almost immeasurable amount of THC.** GW made the drug, known as Epidiolex, into a liquid form so that it would be easier to administer to children. **The FDA recently granted “orphan drug” designation for Epidiolex for use in treating children with Dravet Syndrome.** <http://www.gwpharm.com/Epidiolex.aspx>

According to a GW representative, two things are currently happening regarding access to Epidiolex:

- A physician can submit an “expanded access” IND (Investigational New Drug) application with the FDA to use Epidiolex to treat patients while the drug continues through the approval process. This would be for treatment purposes, not research. (no placebo –open label). Currently, 7 different physicians have been approved and five of those will have 25 patients and two are for individual patients. Two of the 25-patient INDs are supposed to start mid-January 2014; the other 3 are approved but have not started yet; the individual INDs are underway. **GW will be supplying the Epidiolex to these physicians for free so there is no cost to the families to participate.**
- In addition to these seven INDs, there will be a number of other physicians around the country who will submit INDs to FDA. There will be at least one in Florida.
- GW is also conducting its own clinical research. Their trial development program will begin in the next few months and we may soon see as many as 50 trial sites around the country.

What can a parent do that has a child suffering from Dravet or Lennox Gastaut Syndromes where other medications may not be helping?

- Talk to their child’s neurologist and ask a referral into one of the INDs.
- Have their child’s neurologist contact GW pharmaceuticals to take part in their clinical trials. According to a representative of GW, even if a child receives placebo (which is

added to his/her current anti-epileptic drugs; existing medications are not taken away), in a few months, after the trial is over, the child will be offered the option of receiving Epidiolex in a subsequent long term “open label” study.

How can parents and lawmakers help expedite the approval process?

- Contact the FDA and urge that Epidiolex be fast-tracked for approval in the U.S.
- All clinical trial sites have to be licensed by the Drug Enforcement Administration (DEA); for Sativex this was a lengthy process. Contact the DEA and urge them to make this a priority. http://firstclinical.com/journal/2011/1112_DEA.pdf

We have heard advocates use the term “nutraceutical” when describing smoking pot as a medicine or using Charlotte’s Web. What do they mean?

- Nutraceutical means dietary supplement. An analogy would be hemp oil capsules. Hemp oil capsules can be found in a health store and are used as a dietary supplement. However, they do not contain CBD, THC, or any other cannabinoids because it would be illegal if they did. Marijuana oil or smoked cannabis cannot be a dietary supplement because it contains cannabinoids.
<http://www.justice.gov/dea/pubs/pressrel/pr100901.html> In addition, the law requires dietary supplements to be oral. Nutraceuticals, by law, cannot be smoked. (21 U.S.C. , United States Code, 2010 Edition, Title 21 – Food and Drugs Chapter 9 – Federal Food, Drug, and Cosmetic Act, Subchapter IV, – Food, Sec. 350 - Vitamins and minerals)

What is Charlotte’s Web?

Charlotte’s Web most often refers to oil extracted from marijuana plants that are bred with the representation that the plants are low in THC (the intoxicating compound in marijuana) and high in CBD content (a non-intoxicating compound in marijuana). The ratio in Charlotte’s Web varies, however, and “low in THC” is an uncertain term since it has been reported to have levels of 4-6% and sometimes even higher.

The product getting most of the publicity refers to one of the many marijuana strains cultivated and sold by the Stanley brothers, Joel, Jesse, Jon, Jordan and Jared, in Colorado. It is described as a shorter plant that grows slower than other marijuana plants cultivated at their dispensary. Although the ratio has not been disclosed, it is said to be high in cannabidiol (CBD) and low in tetrahydrocannabinol (THC). How high, and how low is unknown. In their process, they report that the marijuana is soaked in grain alcohol to extract the cannabinoids and then the resulting liquid is put through an evaporator to remove the alcohol. The Stanley brothers report that they named the strain after one of their customers, Charlotte Figi, a young girl with Dravet Syndrome. Others report that the name Charlotte’s Web comes from the web-like leaves that are distinct to this plant breed.

The Stanley brothers promote Charlotte’s Web for use by children through their foundation known as Realm of Caring (<http://realmofcaringfoundation.org/aboutus/>). Their website, while portraying compassionate photos and personal stories of sick children who they claim have been provided a “better quality of life” through the use of their product, acknowledges that: *“The statements have not been evaluated by the Food and Drug Administration (FDA). These products and statements are not intended to diagnose, treat, cure or prevent any disease. Any and all of Realm of Caring representatives, are not doctors in any way or claim to be.”*

In addition to the product marketed by the Stanleys, several other dispensaries and on-line stores market products under the name of Charlotte's Web. Marijuana labeled as "Charlotte's Web" varies and consumers have no way of knowing exactly what they are getting.

Some promotions of the Charlotte's Web strain of marijuana make it sound more like a recreational drug than a medicine. Charlotte's Web is described at <http://www.strainbrain.com/marijuana/sativa/charlottes-web> as:

Charlotte's Web Plant:

Charlotte's Web is a Sativa medical marijuana strain that is named after the popular children's novel Charlotte's Web by E.B. White. This is a strain that is recognized for its strong and exceptionally pine-like smell. Although the name of this strain is unknown as to why it was named after a children's novel, it could be because there are so many resin covered buds that it almost appears as if they are forming spider webs of crystals.

Charlotte's Web Effects:

These particular Sativa medical marijuana strains that produces a buzz for patients where all they want to do is play around and listen to music, preferably with a loved one. You can enjoy a mild sense of euphoria, and your senses are heightened when you smoke this strain as it would be with most Sativas. The high takes about ten to fifteen minutes to reach its full potential, but once it is reached you become somewhat entranced. Some patients have even said that you can nod in and out of consciousness.

Charlotte's Web Uses:

This specific medical marijuana strain has been known to provide relief and comfort for patients who are suffering from conditions such as severe anxiety, mood disorders, chronic stress, insomnia, pain associated within the body and muscle spasms that are associated with multiple sclerosis.

Charlotte's Web Cons:

Unfortunately, patients who have smoked this strain have complained about a mild sense of dizziness but that is only because of this strain's strong Sativa properties. Other than that, patients have experienced the most common side effects of dry mouth and dry eyes. Please note that each patient is different and may experience a different side effect.

Conclusion:

Overall, this is a great strain and that's easily recognizable by taking notice of the spider-web like crystal glands all over the buds. It has a strong smell, a delightful taste and can provide Sativa-lovers with that cerebral and euphoric high that they've been dying to achieve. If you love Charlotte's Web and wish to dive into it, this is the strain to lose yourself in.

Potential dangers of using Charlotte's Web:

- There is no standardized dose.
- A patient who takes 600 mg of CBD a day would also be taking 24 mg. of THC, if the plant is 5% THC (20:1 CBD:THC). This is almost the same amount of THC that a person would get by smoking an average joint containing 10% THC marijuana, given what is lost in burning and side-stream smoke! (Math calculation based upon DHHS/DEA eight factor analysis <http://www.gpo.gov/fdsys/pkg/FR-2011-07-08/pdf/2011-16994.pdf>)
- This marijuana product could have molds and microbes that are not removed by the ethanol process that converts it into a non-smokable form.

<http://www.foxnews.com/health/2013/12/02/university-to-test-marijuana-for-contaminants/>

- Physicians in Colorado attending a conference on epilepsy, reported during a side meeting with GW Pharmaceutical officials to discuss setting up clinical trials that some children have shown up with bacterial infections, presumed to be from the medical cannabis they are using
- There is no way to standardize or purify the CBD in Charlotte's Web. In fact no one knows what the exact THC-CBD ratio is, and the labs that "test" their product are not FDA and DEA registered. They do not put the ratio on their website, or invite registered labs to replicate their testing. The growers would not be able to assure batch-to-batch consistency because the plant material is variable, and the manufacturing process itself can affect the CBD-THC ratio.
- We have no way of knowing which patients (ages, diagnoses) have benefited, what side effects they might have experienced, and which patients have gotten no benefit. Only a few "selected" cases, such as Charlotte Figi's, are known to have been publicized. All the cases should be reported (without names, of course).
- The product could have harmful chemicals in it that were used in the cultivation (pesticides, herbicides) or extraction processes.
<http://www.hindawi.com/journals/jt/2013/378168/>

Conclusion

Legalizing the marijuana plant - even the strain known as Charlotte's Web - and allowing open access to it is not necessary and may even create a public health danger for seriously ill patients.

The THC in marijuana, which science demonstrates has medicinal value, is already available in prescription form as a synthetic medication. A non-synthetic medication containing pure THC is also available in 21 countries and is in Phase III clinical development in the United States. A non-synthetic medication containing pure CBD is now in clinical trials in the United States and available to patients desiring to try the drug.

While GW Pharmaceuticals has obviously led the way in the development of Sativex and Epidiolex, other research is ongoing and it is anticipated that we will see other similar medications brought to market. Efforts should focus on supporting the research and development of modern medicines rather than circumventing our nation's established process for protecting the public from harmful human experiments with substances that could prove to be more harmful than helpful.

This document was prepared by Drug Free America Foundation, Inc. (www.dfaf.org). For more information, please contact us at 727-828-0211.