MedicalXpress

Developing a safe and effective alternative to medicinal marijuana

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In recent years, the use of cannabis in medical treatment has sparked a heated debate between state and federal governments. Although the federal government has banned marijuana—it is classified as a Schedule I Drug and a license is needed to possess it—some individual states have decriminalized it for medical use. A Schedule I Drug is defined as one with no currently accepted medical use and a high potential for abuse. As of July 2014, 23 states and Washington, D.C., have legalized medical marijuana and have set laws, fees and possession limits.

What if there were an alternative?

In time, there could be.

Researchers such as Aron Lichtman, Ph.D., professor of pharmacology and toxicology in the Virginia Commonwealth University School of Medicine, are studying cannabis-like chemicals called endogenous cannabinoids that are made by the human body and brain.

For more than 25 years, Lichtman has studied the effects of marijuana and THC on the brain, and the long-term consequences of exposure.

Below, Lichtman discusses misconceptions about marijuana, defines cannabinoids and delves into his field of research. Ultimately, he hopes his work will lead to the development of a medication that shares the medical benefits of cannabis, but has been scientifically proven to be safe and effective to reduce pain and suffering in patients.

One of the main reasons patients may obtain a prescription for medicinal cannabis is to manage pain due to headaches or diseases such as cancer or chronic conditions such as nerve pain. What are the issues with medical marijuana as it stands now?

The problem with cannabis is that where it has been made legal, state medical dispensaries can prescribe it for any medical condition. Unfortunately, there are few studies that prove that cannabis is actually effective at treating a particular medical issue, although there are many claims about it.

Further, cannabis is not regulated by the Food and Drug Administration, or any other federal agency. There are no standardized guidelines in place for its use, and there is a lack of scientific evidence to support its use and long-term effects.

The science that we have about marijuana should help guide those who are experts in public health policy. Delivering medication as a raw material that has to be smoked and contains a lot of toxins is not safe.

Health care professionals do not give patients opium to smoke—there are better ways of administering it. As scientists, we know its active ingredients, we're working on codeine and we have other opiates that chemists have synthesized.

I believe we can do the same thing for cannabis. We can do far better than cannabis.

What is the public perception of marijuana?

Many in the general public believe that marijuana is safe—and that's a problem. Cannabis is a drug, it contains THC, and yes, THC does have beneficial medical effects. But there is little known about the implications of long-term use of cannabis, and we're just starting to investigate this. It could produce problems in terms of learning and memory. We do not know how it effects the brains and bodies of juveniles.

While it is helpful for some people, there are others who can get into trouble with it in terms of dependency. A small percentage of people can have acute panic attacks with it—have a psychotic episode. This can land people in the ER/hospital.

What are cannabinoids?

Cannabinoids represent a class of drugs that are different in structure, but are most often thought about as being present in cannabis or marijuana.

There are three groups of cannabinoids: phytocannabinoids, synthetic or man-made cannabinoids and endogenous cannabinoids.

The most well-known cannabinoid is delta-9-tetrahydrocannabinol, or THC, which is the main constituent of cannabis responsible for most of the effects associated with marijuana. In addition to THC, there are more than 100 similarly structured chemicals. Some of them have THC effects, and some have effects of their own. These are called phytocannabinoids, which are plant-derived cannabis-like chemicals.

How did synthetic/man-made cannabinoids come to be? How potent are they?

Through the years, chemists have been involved with this research and once the structures of these naturally-occurring plant materials were elucidated, the chemists made modifications to these structures so they could add different chemical constituents to THC or change it around – and these are considered synthetic or man-made cannabinoids.

There are thousands of synthetic cannabinoids that have been developed. Some of these are equally as potent as THC, others are inactive. But there are some that are up to 100 times more potent than THC. Potency refers to the dose that delivers a given effect. When there is an increase in potency of these chemicals, there can be a lot of side effects.

THC is approved by the FDA in a capsule to be taken orally to treat nausea and vomiting associated with cancer chemotherapy and to stimulate appetite in AIDS patients. The dose range is between 5 and 90 milligrams. A synthetic cannabinoid in pill form called cesamet is also approved by the FDA which delivers a similar effect as marinol, but at a fraction of that dose. It can be done at 2-4 milligrams per day.

Your main area of research focus is the third type of cannabinoid—endocannabinoids. What is known about this group?

Endogenous cannabinoids are chemicals that naturally occur in our bodies and brains. They are lipids, so they are greasy and stick to cell membranes very well. When compared with THC and synthetic cannabinoids, endogenous cannabinoids differ in chemical structure – but they produce very similar effects. Much in the way endorphins (which occur in the body) mimic morphine and heroine, which are both opiates derived from plant matter, the endocannabinoids mimic THC.

Anandamide and 2-arachidonoylglycerol, or 2-AG, are examples of

endocannabinoids. 2-AG can be found in the central nervous system at a high concentration. These endocannabinoids work dramatically differently to the chemicals in marijuana. The body produces enzymes that very quickly break down these endocannabinoids. We and others have developed drugs that inhibit these enzymes, which when administered in preclinical models result in elevated levels of endocannabinoids and reductions in pain and anxiety, but without THC-like effects. Our bodies also have marijuana-like receptors called cannabinoid receptors. We have studied these, too.

Through your research, what are you hoping to learn? How could this research one day impact patients?

Our goal is to see if we can produce a medication that is targeted toward this naturally occurring marijuana-like system. To get there, we need to understand how the endogenous cannabinoid system works on the basic science level.

From there, we can eventually develop a medication that has decreased dependence liability and decreased addiction liability (so people are not going to crave it and become dependent on it), but it would reduce pain and make people more functional.

This work could possibly impact treatment for different disease states—from post-traumatic stress disorder to neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. The medications that may be developed could help reduce some of the symptoms of disease and improve a patient's quality of life.

There's not going to be a cure-all, but I think the potential is there to help with public health by understanding how the system works and developing target drugs and therapies. This is not developing another anti-

inflammatory drug that works like all the rest but in a new flavor. This is searching out brand new targets, finding different enzymes that regulate endocannabinoids that can produce a wide range of effects.

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