

Managing Chronic Pain with Medical Marijuana

Can medical marijuana help patients manage chronic pain? The jury is out, according to research, but it is an option for those unable to manage pain with other medications.

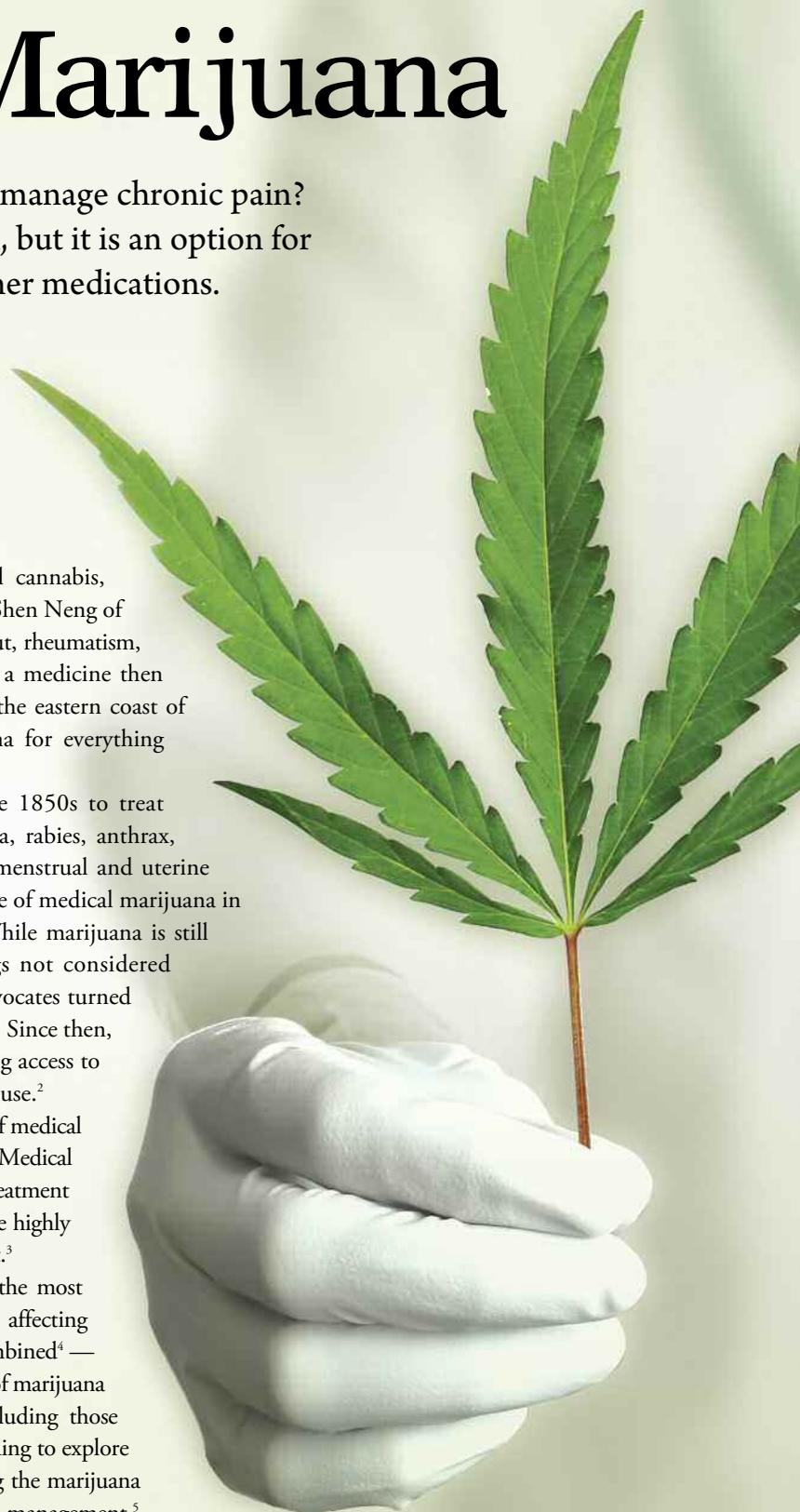
By Ronale Tucker Rhodes, MS

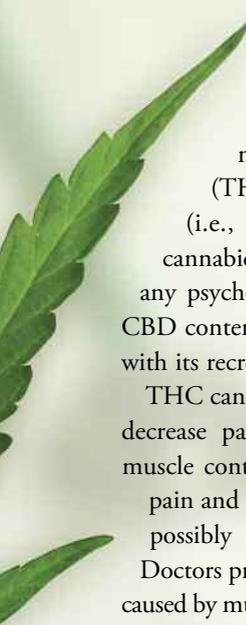
MEDICAL MARIJUANA, also known as medical cannabis, dates back to 2737 B.C., when the mystical Emperor Shen Neng of China prescribed marijuana tea for the treatment of gout, rheumatism, malaria and poor memory. The drug's popularity as a medicine then spread throughout Asia, the Middle East and down the eastern coast of Africa, with ancient physicians prescribing marijuana for everything from pain relief to earache to childbirth.¹

In the U.S., medical marijuana use began in the 1850s to treat afflictions such as neuralgia, tetanus, typhus, cholera, rabies, anthrax, leprosy, tonsillitis, dysentery, insanity and excessive menstrual and uterine bleedings. However, there was a prohibition on the use of medical marijuana in 1937 with the passage of the Marijuana Tax Act. While marijuana is still classified as a Schedule I drug (a category of drugs not considered legitimate for medical use), in 1996, patients and advocates turned to states for access to marijuana for medicinal purposes. Since then, voter initiatives in a host of states have passed, allowing access to medical marijuana, despite federal law prohibiting its use.²

According to surveys in recent years, public approval of medical marijuana has remained above 77 percent since 2011. Medical marijuana patients seem to also be satisfied with the treatment they experience, with a majority reporting they would be highly likely to recommend it to friends or family for treatment.³

More importantly, at a time when chronic pain is the most common cause of long-term disability in the U.S. — affecting more people than cancer, heart disease and diabetes combined⁴ — a number of studies are exploring the medical properties of marijuana to manage chronic pain. And, many researchers, including those funded by the National Institutes of Health, are continuing to explore the possible uses of cannabinoids (chemicals comprising the marijuana plant) for medical treatment, including for chronic pain management.⁵





What Is Medical Marijuana

The term “medical marijuana” refers to using the whole unprocessed plant or the chemicals contained within it to alleviate symptoms of certain conditions or diseases. The marijuana plant is comprised of more than 100 cannabinoids (chemicals), each of which have different effects on the body. The two main cannabinoids used in its medicinal application are tetrahydrocannabinol (THC), the psychoactive compound in marijuana (i.e., the element that produces the high), and cannabidiol (CBD), the substance that does not produce any psychoactive effects (medical marijuana has a higher CBD content, so it doesn’t produce the euphoria associated with its recreational counterpart).⁶

THC can increase appetite and reduce nausea. It may also decrease pain, inflammation (swelling and redness) and muscle control problems. CBD may be useful in reducing pain and inflammation, controlling epileptic seizures, and possibly even treating mental illness and addictions.⁴

Doctors prescribe medical marijuana to treat muscle spasms caused by multiple sclerosis, nausea from cancer chemotherapy, poor appetite and weight loss caused by chronic illness such as HIV or nerve pain, seizure disorders and Crohn’s disease, among others.⁷ In addition, the California Medical Association states marijuana may also be used to help treat AIDS, anorexia, arthritis, cachexia, cancer, chronic pain, glaucoma, migraine, persistent muscle spasms, seizures, severe nausea and any other chronic or persistent medical symptom that limits a person’s ability to conduct major activities in life or can cause serious harm if not relieved.⁸

How Does Medical Marijuana Work?

THC is what causes people to feel high and also what gives cannabis some of its medicinal properties such as increased appetite. The human body produces endocannabinoids, its own natural version of cannabinoids. Studies show the endocannabinoid system (ECS) helps to regulate the body’s responses to a variety of stimuli. The body will produce endocannabinoids when needed, but sometimes the effect is very brief. Endocannabinoid receptors are found throughout the body, but are especially prominent in the brain. The cannabinoids in marijuana, like THC, bind to these receptors, producing various effects, some medicinal such as reducing pain or anxiety, but also the feeling of being high.⁹

CBD influences the body to use its own endocannabinoids more effectively. According to one study, this is because CBD does very little to the ECS. Instead, it activates or inhibits other compounds in the ECS. For example, CBD stops the body from absorbing anandamide, a compound associated with regulating pain. So, increased levels of anandamide in the bloodstream may reduce the amount of pain a person feels. CBD may also limit inflammation in the brain and nervous system, which may benefit people experiencing pain, insomnia and certain immune-system responses.¹⁰

Types Available

Medical marijuana comes in many forms: pills, oils, vaporized liquids, nasal sprays, food, dried leaves and buds, and plants. It can be smoked, vaporized (heated until active ingredients are released, but no smoke is formed), eaten (usually in the form of cookies or candy), taken as a liquid extract and rubbed onto the skin.^{7,11}

CBD influences the body to use its own endocannabinoids more effectively.

There is a distinction between medical marijuana, however, and cannabis extracts that are also made from CBD. CBD extracts are derived from hemp, while CBD products classified as medical marijuana are extracted from marijuana — even though the CBD used to make extracts is the same compound used to make medical marijuana. The laws governing CBD started with the Controlled Substances Act of 1970, which labeled all varieties of the cannabis plant, hemp included, a Schedule I drug. But a “hemp amendment” (Section 7606, Legitimacy of Industrial Hemp Research) in the Farm Bill of 2013 (signed into law in 2014) changed those rules. Previously, hemp could be imported but not grown in the U.S. The amendment allows states to create pilot programs to research and cultivate hemp, which the legislation defines as a cannabis plant containing 0.3 percent or less of THC by weight. (Marijuana plants grown today contain THC levels hovering around 20 percent.) The bill also allows hemp products to be marketed to the public.¹²

While not for the treatment of chronic pain, the U.S. Food and Drug Administration (FDA) has approved three drugs made from synthetic forms of ingredients found in marijuana to treat other conditions. These include dronabinol (Marinol, Syndros) and nabilone (Cesamet), which can be legally prescribed for the treatment of nausea and vomiting caused by chemotherapy when other treatments have failed. Dronabinol may also be used to treat anorexia associated with weight loss in people with AIDS.¹¹ The third FDA-approved medicine is a CBD-based liquid medication called Epidiolex to treat two forms of severe childhood epilepsy: Dravet syndrome and Lennox-Gastaut syndrome.⁵

In addition, FDA has approved two clinical research projects for new forms of marijuana ingredients.¹¹ One clinical trial is testing the drug Sativex for breast cancer pain. Sativex is a combination of chemicals from the marijuana

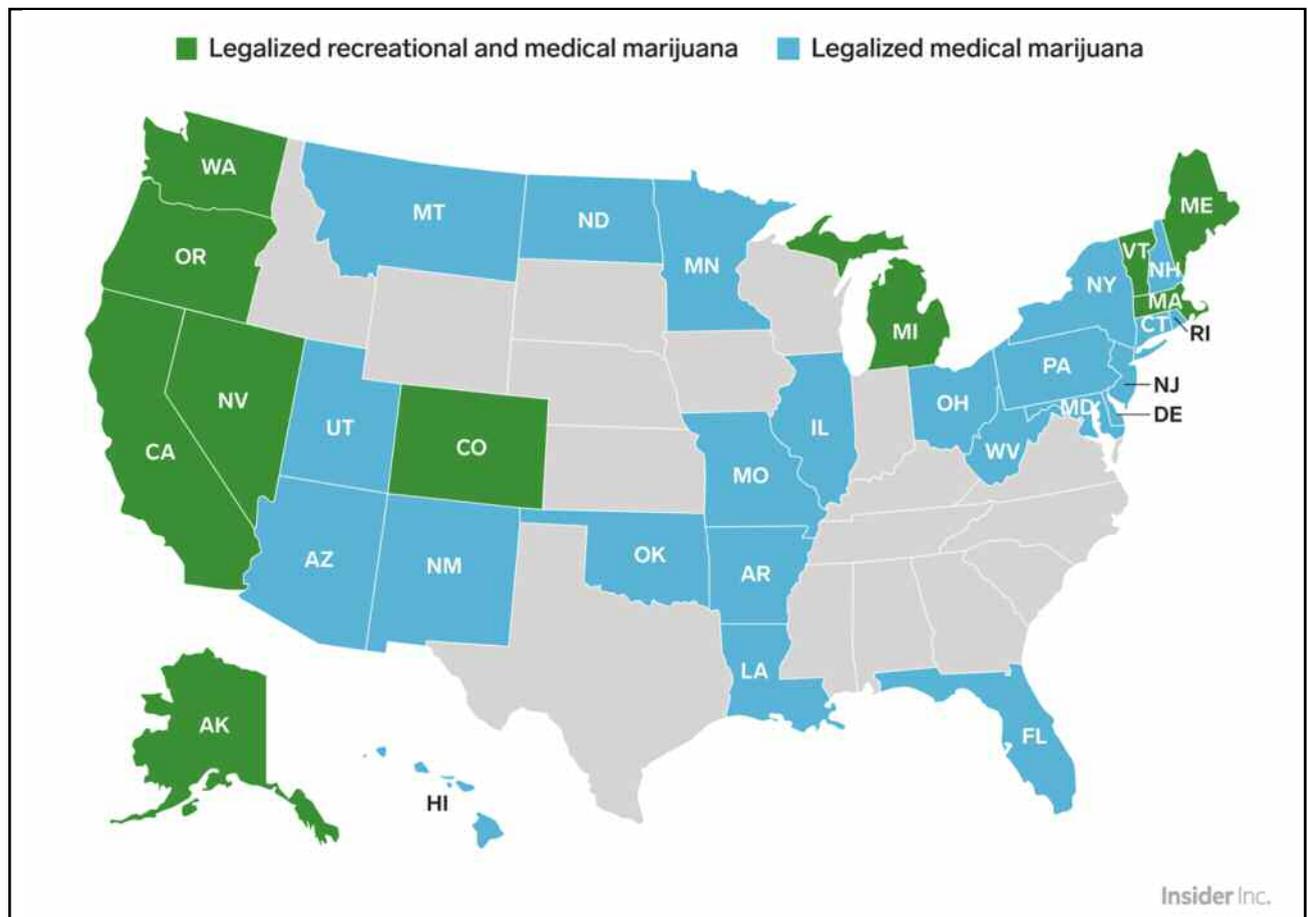
herb and is sprayed into the mouth. It is approved in more than 20 countries to treat muscle spasms from multiple sclerosis and cancer pain.¹³

It's important to note there are side effects of marijuana that usually don't last long, including dizziness, drowsiness, short-term memory loss and euphoria. More serious side effects include severe anxiety and psychosis. In addition, only people 18 years and older can be prescribed medical marijuana. Further, its use is advised against in people with heart disease, pregnant women and people with a history of psychosis.⁷

Where Can Medical Marijuana Be Purchased?

The FDA does not approve or recognize marijuana as a medicine. However, medical marijuana is legal in many states today. California became the first state to legalize it in 1996, and since then, 33 states have followed suit (Figure).^{1,14}

Figure. States Where Marijuana Is Legal¹⁴



Medical marijuana laws, usage and prices vary from state to state. Not only do prices differ dramatically by state, there are also significant differences in prices between cities within the same state. In addition, the number of medical marijuana dispensaries in each state varies, as do the number of medical marijuana patients and caregivers. For example, while New Mexico had a legal medical marijuana patient rate of 25 per 1,000 residents in May 2018, Illinois had a rate of under two per 1,000 residents.³

To get medical marijuana, you need a written recommendation from a licensed doctor in states where it is legal. And, a person must have a condition that qualifies for medical marijuana use. Each state has its own list of qualifying conditions. Some states may also require an individual to get a medical marijuana ID card. With that card, medical marijuana can be purchased at a store called a dispensary.¹⁵

CBD extracts can be purchased over the counter at drug stores and through online retailers with no state or federal oversight.¹²

Studies Pertaining to Chronic Pain

Many studies show medical marijuana is effective in managing chronic pain; however, there are other studies showing no beneficial effect. Indeed, more than 45 studies have looked at marijuana and pain related to chronic diseases such as cancer, diabetes, fibromyalgia, multiple sclerosis, HIV, rheumatoid arthritis and spinal injuries. The studies have included smoked marijuana, along with herbal and man-made forms, the majority of which showed improvement in pain relief in comparison to a placebo or to other traditional pain medications. However, about a quarter of the studies showed no improvement.¹³

A study conducted in 2015 that reviewed the pharmacology, indications and laws related to medical marijuana use found marijuana for chronic pain, neuropathic pain and spasticity due to multiple sclerosis is supported by high-quality evidence. The study looked at six trials that included 325 patients examined for chronic pain, six trials that included 396 patients with neuropathic pain and 12 trials that included 1,600 patients with multiple sclerosis. While several of these trials had positive results, suggesting marijuana or cannabinoids may be effective for these indications, the authors noted there are also many that do not.¹⁶

In 2018, *The New England Journal of Medicine* published a case vignette of a 31-year-old woman with a long history of complex regional pain syndrome in her right leg and foot.

After being treated with several opioids, regional and sympathetic nerve blocks, transcutaneous nerve stimulation, lidocaine and compounded salves, behavior modification, acupuncture and alendronate infusions, she continues to suffer what she calls excruciating pain. Two physicians were asked to comment, based on published literature, experience, recent guidelines and other sources of information, as appropriate, about which option they would recommend: 1) Prescribe medical marijuana, or 2) Discourage the use of medical marijuana.

Benjamin Caplan, MD, chose option one: “Cannabis added to her regimen could alleviate emotional distress and provide a more direct route to pain relief... Cannabis has been shown to contribute, through cannabinoid-receptor and non-cannabinoid-receptor mechanisms, to anti-inflammatory and neuroprotective effects that may alleviate chronic pain. These effects appear to be dose-dependent with respect to synaptic transmission within the dorsal horn of the spinal cord, and inhibition of this communication may play a role in the development of chronic pain associated with local inflammation or nerve injury. For example, in a murine model of neuropathic pain, administration of cannabis significantly reduced allodynia [a rare type of pain, generally on the skin] in a dose-dependent manner. Furthermore, in a recent study of refractory pain, cannabis showed efficacy in patients for whom traditional treatment options had failed.”

Edgar Ross, MD, who chose option two, explained: “Literature reviews on the efficacy of medical marijuana are cautionary about effectiveness and side effects. Although the cannabinoid compounds are almost certainly safer than long-term opioid therapy, studies in humans that suggest efficacy are limited in quality and scope... Since the mechanism underlying cannabis-associated psychosis is unknown, establishing a safe dose for routine use is difficult. Controversy about the addictive potential of cannabis and the risk of cannabis withdrawal syndrome is also ongoing.”¹⁷

But, there have been studies that show medical marijuana is safe for chronic pain, at least among people with some experience using the drug. In one study, the first and largest of the long-term safety of medical marijuana use by patients with chronic pain in seven pain treatment centers across Canada, researchers followed 215 adult patients with chronic pain who used medical marijuana for one year and compared them with a control group of 216 chronic patients who didn't use medical marijuana. Participants who used medical marijuana were provided leaf marijuana containing 12.5

percent THC from hospital pharmacies. The researchers found there was no difference in serious side effects between the two groups, but the marijuana users did have a 73 percent increased risk of minor side effects, including headache, nausea, sleepiness and dizziness. “In terms of a side effect profile, we felt the drug had a reasonably good safety profile if you compare those effects to other medications,” said study lead author Mark Ware, MD, director of clinical research for the Alan Edwards Pain Management Unit at McGill University Health Center in Montreal. And, while the study focused on medical marijuana’s safety, Dr. Ware reported participants also appeared to experience some pain relief with its use, as well as improvements in mood and quality of life.¹⁸

Still, despite an abundance of research, some say that while “most states in the U.S. that have legalized medical cannabis include chronic pain or painful conditions among the accepted indications for use, ... these same states also note that research supporting medical cannabis for chronic pain is thin.” For instance, Minnesota accepts intractable pain as a reason for prescribing medical marijuana, but says “the literature assessing the effects of medical cannabis treatments for non-cancer chronic pain is sparse and patchy.” Similarly, the California Medical Association’s “Physician Recommendation of Medical Cannabis” states the approved list of 12 serious medical conditions cannabis can be used for “is broad and, in most cases, not supported by solid clinical research.” In addition, a review of two dozen clinical trials published in the journal *Pain Physician* found “the majority of studies did not show an effect.” Yet, the review concludes

Many patients and studies can attest to medical marijuana’s management of chronic pain.

cannabis-based medications “might be effective for chronic pain treatment, based on limited evidence, primarily for neuropathic pain patients.” And, a systematic review of the efficacy of cannabis in patients with neuropathic pain or multiple sclerosis or receiving chemotherapy concluded “there is incomplete evidence of the efficacy and safety of medical use of cannabis” and that “confidence in the estimate of the effect was again low or very low.”¹⁹

Caution Is Advised

Clearly, some studies show there are many beneficial properties of medical marijuana, while others do not. And, currently, it is not an approved FDA medicine because FDA requires clinical trials in hundreds to thousands of human subjects to determine the benefits and risks of a possible medication. According to FDA, researchers have not conducted enough large-scale clinical trials that show the benefits of the marijuana plant (as opposed to its cannabinoid ingredients) outweigh its risks in patients.⁵

Still, many patients and studies can attest to medical marijuana’s management of chronic pain. However, it’s important to note that medical marijuana is not monitored like FDA-approved medicines. In fact, there are many unknowns, including its potential to cause cancer, its purity, potency or side effects. Considering these risk factors, only people who have a prescription from a doctor should use medical marijuana.⁷ ■

RONALE TUCKER RHODES, MS, is the editor of *IG Living* magazine.

References

1. Stack, P, and Suddath, C. A Brief History of Medical Marijuana. *Time*, Oct. 21, 2009. Accessed at content.time.com/time/health/article/0,8599,1931247,00.html.
2. U.S. Legal. Medical Use Of Marijuana-History. Accessed at medicalmarijuana.uslegal.com/medical-use-of-marijuana-history.
3. Statista. Medical Marijuana in the U.S. — Statistics & Facts. Accessed at www.statista.com/topics/3064/medical-marijuana-in-the-us.
4. Leonard, J. What Are the Best Cannabis Strains for Chronic Pain? *Medical News Today*, Aug. 3, 2018. Accessed at www.medicalnewstoday.com/articles/322051.php.
5. National Institute on Drug Abuse. Marijuana as Medicine. Accessed at www.drugabuse.gov/publications/drugfacts/marijuana-medicine.
6. What Is the Difference Between Medical and Recreational Marijuana? DocMJ, June 5, 2017. Accessed at docmj.com/2017/06/05/difference-medical-recreational-marijuana.
7. Harding, A. Medical Marijuana. Accessed at www.webmd.com/pain-management/features/medical-marijuana-uses.
8. Healthline. Medical Marijuana. Accessed at www.healthline.com/health/medical-marijuana.
9. Silverman, J. How Medical Marijuana Works. Accessed at science.howstuffworks.com/medical-marijuana.htm.
10. Johnson, J. Does CBD Oil Work for Chronic Pain Management? *Medical News Today*, March 16, 2018. Accessed at www.medicalnewstoday.com/articles/319475.php.
11. Mayo Clinic. Medical Marijuana. Accessed at www.mayoclinic.org/healthy-lifestyle/consumer-health/in-depth/medical-marijuana/art-20137855.
12. Gaines, LV. Why Are CBD Products Sold Over the Counter Some Places and Tightly Regulated in Others? *Chicago Reader*, March 23, 2017. Accessed at www.chicagoreader.com/Bleader/archives/2017/03/23/why-are-cbd-products-are-sold-over-the-counter-some-places-and-tightly-regulated-in-others.
13. Vaida, B. Medical Marijuana: What the Research Shows. Accessed at www.webmd.com/pain-management/features/medical-marijuana-research-web#1.
14. Berke, J, and Gould, S. This Map Shows Every U.S. State Where Pot Is Legal. *Business Insider*, Jan. 4, 2019. Accessed at www.businessinsider.com/legal-marijuana-states-2018-1.
15. WebMD. How Do You Get Medical Marijuana? Accessed at www.webmd.com/a-to-z-guides/qa/how-do-you-get-medical-marijuana.
16. Hill, KP. Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems: A Clinical Review. *Journal of the American Medical Association*, 2015 June 23-30;313(24):2474-83. Accessed at www.ncbi.nlm.nih.gov/pubmed/26103031.
17. Cautley, L, Caplan, B, and Ross, E. Medical Marijuana for Chronic Pain. *The New England Journal of Medicine*, Oct. 18, 2018; 379:1575-1577. Accessed at www.nejm.org/doi/full/10.1056/NEJMclde1808149.
18. Thompson, D. Medical Marijuana Seems Safe for Chronic Pain. WebMD, Oct. 7, 2015. Accessed at www.webmd.com/pain-management/news/20151007/medical-marijuana-seems-safe-for-chronic-pain-patients-study-finds#1.
19. Chriss, R. Little Evidence Cannabis Can Treat Chronic Pain. *Pain News Network*, Jan. 8, 2018. Accessed at www.painnewsnetwork.org/stories/2018/1/8/little-evidence-supports-cannabis-in-treating-chronic-pain.

Cannabidiol to Treat Chronic Pain: *A Physician's Perspective*

CANNABIDIOL (CBD) has been touted for its beneficial effects for managing chronic pain. But, with no large-scale clinical trials, it is still not an approved medicine by the U.S. Food and Drug Administration. Nevertheless, CBD products cultivated from hemp are allowed to be marketed to the public. But, because research results are mixed on whether CBD is beneficial for improving pain, it can be difficult for consumers to decide whether using it is the correct choice. For a professional perspective, we discussed the use of CBD with Lisa Allen-Khalil, MD, an internal medicine specialist in Brooksville, Fla., who is a proponent of CBD.

IG Living: What led you to recommending CBD to manage pain?

Dr. Allen-Khalil: Cannabis has been used medicinally for more than 3,000 years, beginning in the 19th century when Western medicine recognized its benefits for treating pain and spasms. Just recently, medical cannabis has become available in my state of Florida. In my internal medicine practice, I have seen patients with chronic pain issues who have not responded to conventional treatment modalities. Either the side effects of these modalities were unacceptable or the efficacy was poor.

IG Living: Is there any particular research you are familiar with that has led you to believe in CBD's benefits for pain management?

Dr. Allen-Khalil: There isn't a lot of research regarding the efficacy of using CBD for chronic pain. But, what is available is promising, and more research is being conducted. So, we will learn more as results become available. Studies published in the *Journal of American Medicine*¹ and *Annals of Internal Medicine*² give moderate evidence and low-quality evidence, respectively, supporting the use of cannabinoids for chronic pain, particularly neuropathic pain, spasticity, sleep problems, HIV-associated wasting, chemotherapy-related nausea and vomiting, and Tourette syndrome.

IG Living: Tell us about your personal experience with CBD?

Dr. Allen-Khalil: I have used CBD myself to treat pain as a result of sports-related injuries with fair results.

IG Living: What factors have you found determine which CBD products are the most effective for managing pain?

Dr. Allen-Khalil: Since CBD is currently not regulated by the U.S. Food and Drug Administration (FDA), finding a standardized formulation is very difficult. As such, the efficacy of the many preparations is hard to gauge. I have recommended to my patients who want to try CBD to talk with their pharmacist to find a reputable company that makes a quality CBD product. Having stated this, until CBD is regulated by FDA, people may not be entirely sure they are getting what they pay for.

IG Living: Have you prescribed CBD to your patients, and if so, what has been their experience?

Dr. Allen-Khalil: The few patients for whom I've recommended CBD have had mixed results. This is due to the lack of availability of standardized preparation and the uniqueness of each patient's physiology.

IG Living: What advice would you give to chronic pain sufferers who are unsure if they should try CBD?

Dr. Allen-Khalil: I would advise them to obtain a consultation with a pain management specialist familiar with CBD who can make sure they are prescribed the proper formulation and dose of CBD to treat their specific conditions.

References

1. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. *JAMA*, 2015 Jun 23-30;313(24):2456-73.
2. Nugent SM, Morasco BJ, O'Neil ME, et al. The Effects of Cannabis Among Adults with Chronic Pain and an Overview of General Harms: A Systematic Review. *Annals of Internal Medicine*, Sep. 5, 2017.

