

PERSPECTIVES

New Arthritis Foundation Guidelines On CBD Use Could Be First Of Many More To Come

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Murdoc Khaleghi, MD, Elevate CBD's Senior Medical Advisor, is passionate about explaining how natural interventions in combination with scientific rigor can be utilized to improve health, such as decreasing pain and inflammation, supporting mood, and stabilizing energy. Through research and testing, Dr. Khaleghi has developed an expertise on the endocannabinoid system, and the potential for treatments targeting this system. At Elevate CBD, Dr. Khaleghi works to educate the public on the safety and benefits of CBD. He also advises on the Elevate CBD's products, formulations and delivery platforms to help support solutions that can best serve consumers and their health needs.

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In addition to talking about health issues for Elevate CBD, Dr. Khaleghi is Chief Medical Officer at StemoniX and Medical Director at WellnessFX. He has authored eight books on health, wellness, prevention, and medical humor including Healthiest You Ever, The Everything Guide to Preventing Heart Disease, The Complete Idiot's Guide® to Boosting Your Immunity, The Everything Guide to the Mind Diet. Previous positions include Chief Executive Officer at Westfield Emergency Physicians, Chief Medical Officer at EverlyWell, and Chief Medical Information Officer at Baystate Noble Hospital.

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With 1 in 7 Americans using CBD to enhance their health,¹ it was only inevitable that the Arthritis Foundation issue guidelines for CBD use. And now that it has, we probably can expect more health agencies and medical organizations to do the same in the near future

The Arthritis Foundation's guidelines, issued in September, come at a time when CBD popularity is soaring with consumers in North America and globally. More than 50 million Americans report using CBD today, and the global

cannabidiol (CBD) market is predicted to grow 700% and be worth \$2.1 billion next year.²

In the same Gallup Poll that found 14% of Americans using CBD, some 40% of respondents said they took CBD for pain of various kinds and sources. In a survey of 2600 arthritis patients conducted this year, the Arthritis Foundation, itself, found that 80% of respondents use CBD, and that 94 percent of that number turn to CBD specifically for pain relief.²

Against such a backdrop of phenomenal CBD consumer popularity, it's not surprising that the Arthritis Foundation would issue guidelines like it did, becoming the largest health organization to date to do so. Though the foundation's response was not an outright recommendation of CBD use to treat arthritis, it was a meaningful acknowledgment of cannabidiol use as an alternative health therapy employed by many of its members and stakeholders. Because CBD is used by so many people to also treat other kinds of pain, anxiety and insomnia, it's likely that other health organizations will follow the Arthritis Foundation's action and issue their own guidelines for CBD use, safety and efficacy.

Admittedly, the Arthritis Foundation's CBD guidelines are generally expressed, and they most likely will have to be developed further as more research into CBD progresses. The guidelines convey. Even though rigorous clinical studies have yet to be performed, CBD may help with arthritis-related symptoms—especially pain—as well as insomnia and anxiety.

Though no major safety issues have been found with CBD when taken in moderate doses, users should be aware of potential drug interactions.

CBD should not be used to replace disease-modifying drugs that help prevent permanent joint damage experienced in inflammatory types of arthritis.

CBD USE SHOULD BE DISCUSSED WITH YOUR DOCTOR.

Because there are no established clinical guidelines on CBD usage, the foundation urges using initial low dosages before increasing cannabidiol's use in small, weekly increments.

CBD users should buy from reputable companies that test for purity, potency and safety by independent laboratories and provide certificates of analysis (COA) accordingly.

TYPICAL ARTHRITIS MEDICATIONS AND THEIR RISKS

Arthritis is a wide-ranging disorder, and there are more than 100 different forms of it and its related diseases. The most common types of arthritis include osteoarthritis, rheumatoid arthritis, psoriatic arthritis, fibromyalgia and gout. All forms cause pain for sufferers in different ways.

To address such an expansive physiological malaise as arthritis, multiple medication protocols can be engaged. Unfortunately, two of the medicines that are used the most carry with them some of the greatest risks.

The medications used to treat arthritis include disease-modifying anti-rheumatic drugs (DMARDs), biologic response modifiers, interleukin, corticosteroids and more. By far, though, most arthritis sufferers typically rely on painkillers—either acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) or prescribed opioids. Not all have an effect on inflammation, a primary biological trigger of pain sensation.

Acetaminophen has been used for more than half a century, and it's the main ingredient in Tylenol. Though generally safe, it does carry with it the risk of liver. It does not reduce inflammation.

A drug that does reduce inflammation is of the class of medications known as nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs diminish both pain and inflammation. Over the counter NSAIDs include ibuprofen (used in Advil and Motrin) and naproxen (found in Aleve).

Though NSAIDs often are broadly effective in reducing inflammation, their side effects also carry substantial health risks and side effects, and especially for older populations of patients. NSAIDs can adversely affect kidney functions and lead to bleeding in the digestive system.

Opioid medications typically are not the first prescribed pharmaceutical response to arthritis symptoms, but they are used by many patients, and especially those who suffer from debilitating pain. But these controversially prescribed medications (such as oxycodone or hydrocodone) act on the central nervous system to mask — not alleviate — pain and are highly habit-forming. Equally troubling in their use is that opiates are one of the leading causes of accidental overdose death for people age 45-54⁴, a demographic that also possesses an almost 30% incidence rate of arthritis.⁵

With almost 50 percent of arthritis sufferers being older than 65,⁵ the adverse effects of these medications can bring even greater health risks and, therefore, reduce the pharmaceutical options available to older arthritis sufferers.

It is at the nexus of these challenges where CBD has prevailed, presenting a safe and potentially effective medical alternative to more risky medications commonly prescribed for arthritis pain. Cannabidiol use has little to no health risk or adverse side effects like those presented by NSAIDs and opioid medications. Though research into CBD use and efficacy have only begun in earnest, its overwhelming popularity has been driven by cannabidiol users committed to its use because of the positive health results they have

experienced. Clearly, this many people would not be so overwhelmingly dedicated to CBD today if they did not see health improvement in their lives.

CBD AND THE ENDOCANNABINOID SYSTEM (ECS)

To understand CBD's effect on humans, it's important to understand the body's endocannabinoid system (ECS). The ECS is a biological system in the human body that is expressed in both the central nervous system and the peripheral nervous system. It is made up of endogenous lipid-based retrograde neurotransmitters that bind to cannabinoid receptors that make up the ECS.

The ECS regulates an array of biological functions, most importantly through modulating homeostasis. The ECS and its endogenous cannabinoids were only recently discovered to exist in all vertebrates.

The ECS is populated by endogenous cannabinoids—or endocannabinoids, that are created within the body—the receptors to which the cannabinoids bind (categorized as CB₁ and CB₂), and the enzymes that help synthesize and degrade endocannabinoids.⁶

The CB₁ and CB₂ receptors present in the ECS are part of a class of G protein coupled receptors; CB₁ receptors are mostly present in the central nervous system, and most CB₂ receptors are found in the immune system.

CBD, or cannabidiol, is the active chemical compound in cannabis derived from industrial hemp, and it can have a profound effect on moderating anxiety, enhancing cognition, controlling appetite and—importantly for arthritis sufferers—reducing pain.

It is a phytocannabinoid, just like THC, or tetrahydrocannabinol, marijuana's euphoria-producing chemical compound. Unlike THC, though, hemp-derived CBD will not produce the euphoria associated with marijuana. CBD is not addictive and carries with it very little risk in its use. Further, it is legal in all 50 states as long as it contains less than 0.3 percent THC. Cannabidiol is one of the 113 phytocannabinoids found in the cannabis plant, and its interaction with the ECS already has been the focus of early research into possible arthritis therapies.

In 2014, researchers in Barcelona found increasing evidence from preclinical studies that pointed to the endocannabinoid system as a therapeutic target for osteoarthritis pain.⁷ Researchers called for further research into “the ubiquitous distribution of cannabinoid receptors, together with the physiological role of the endocannabinoid system in the regulation of pain and inflammation.” The study's authors also cited the antinociceptive effects of cannabinoids in different rodent models of osteoarthritis, too.

The ECS and its role in pain and inflammation also was analyzed in a more recent study that focused on rheumatic disease. In 2017, health researchers in Sydney found that endocannabinoids—the endogenous organic compounds produced in our bodies—have an effect on both pain modulation and inflammation.⁸

EXPANDING OUR UNDERSTANDING OF CBD AND PAIN

U.S. marijuana prohibition laws during the past half century may have done little to end the use of cannabis, but they have hampered scientific research until only recently. Since the early 1970s, the DEA's schedule 1 classification of cannabis has constricted research into cannabis—both marijuana and CBD-producing industrial hemp—because of the prohibitions of federal funding for any cannabis-related research. That has begun to change, though, and especially with the recent approval of the 2018 U.S. Farm Bill, the landmark legislation that substantially and broadly legalized the cultivation of hemp nationwide.

This is not to suggest there is no scientific literature on the general topic of cannabis and pain control in arthritis. Even with cannabis research funding affected by federal prohibition, there have been some important studies and surveys conducted into the medical efficacy of cannabis. Not surprisingly, much of the existing research focuses on how cannabis can diminish pain, especially the kind indicative of arthritic conditions.

One of the earliest published reports on cannabis and pain, from 2006, studied the efficacy, tolerability and safety of the cannabis-based medicine (CBM) called Sativex,⁹ used to treat rheumatoid arthritis. That CBM extract (also known as Nabiximols) contains both THC and CBD, and it was designed to alleviate neuropathic pain, especially the kind experienced by patients with multiple sclerosis. In the first ever controlled trial of a CBM in rheumatoid arthritis, the study saw a significant analgesic effect and even indications that disease activity was significantly suppressed following the use of Sativex.

Other published scientific inquiries have found similar connections between overall cannabis use and the reduction of chronic pain. Two published studies have explored the role of cannabis in specifically treating fibromyalgia, a chronic pain condition that shares many aspects of rheumatoid arthritis. Many RA sufferers also grapple with fibromyalgia simultaneously.

This year, a study published from the Netherlands found that fibromyalgia patients responded to the drug Bediol, which contains high doses of both THC and CBD, with a decrease in spontaneous pain by 30%.¹⁰ Additionally, research conducted at the Kennedy Institute of Rheumatology in London almost 20 years earlier showed the therapeutic potential of CBD in murine collagen-induced arthritis (CIA), a condition induced in laboratory rats and mice to study rheumatoid arthritis. That early study found that CBD's combined immunosuppressive and anti-inflammatory actions have a strong anti-arthritic response to counter CIA effects.¹¹

Interestingly, another research effort involving lab animals and collagen-induced arthritis found that topical use of cannabidiol often can be the most effective way of attenuating inflammation and pain.¹² The 2016 University of Kentucky study suggested that transdermal CBD is an effective treatment for reducing inflammation and hypersensitivity associated with the so-called rodent adjuvant-induced monoarthritis model. Adjuvant arthritis is an experimental

form of immunopathology that is thought to share aspects of human rheumatoid arthritis. Today, it is one of the most widely used models for studying the anti-inflammatory effects of compounds. Also of note regarding CBD and arthritis: Research is ongoing into CBD's therapeutic use for psoriatic arthritis and osteoarthritis in the hands.¹³

WHAT ARTHRITIS PATIENTS NEED TO KNOW NOW

The research cited above is just a sampling of the continuing scientific inquiry into CBD and cannabis' effect on arthritis symptoms. No doubt, more research lies ahead as cannabis legalization and acceptance increases in North America and beyond.

Meanwhile, though, as the popularity of CBD grows unbounded—JAMA reported this past month that “CBD” was one of the most-Google searched items of 2019¹⁴—it's important for health practitioners to know that at least one survey has concluded what many healthcare professionals already know: People are learning about CBD from the internet, friends or family—not healthcare professionals.¹⁵

So, guidelines like those issued by the Arthritis Foundation can—even if generalized—offer a good starting point for CBD users who have questions about safety and dosage, but what else should CBD users consider?

Foremost, CBD users should ensure that they consume only hemp-based products if they want to avoid the legalities and euphoric effects of marijuana-based CBD products. Hemp-based CBD can be carried and used anywhere in the U.S., unlike with marijuana products that have more than 0.3 percent THC.

It's also vitally important that health consumers turn to products that have undergone some form of independent validation testing to ensure that the CBD they use is safe and is made from trusted and advertised ingredients. As beneficial as CBD might be, not all CBD products provide the ingredients and effects of what the labels might promise.

Additionally, new CBD users should dose optimally, which has several components. First, people taking CBD should do so for several weeks to better determine its effect on their health. It simply is unrealistic for consumers to use CBD one or a few times and expect consistent beneficial outcomes, which often don't manifest until a week or more after CBD use begins.

Also, CBD users should experiment with the different forms of CBD treatments to find the one with the greatest efficacy for their individual needs. For example, many arthritis sufferers might find that topical (transdermal) CBD products provide the best relief, while other individual arthritis sufferers might get their best results from oral or sublingual forms of CBD instead.

Regardless of the form used, CBD generally offers an attractive alternative to other medications, especially those with high health risks and substantial side effects like those exhibited in NSAID and opioid therapies. As such, guidelines like those presented by the Arthritis Foundation can help consumers better trust the safety of CBD and explore its use for their own beneficial health results.

REFERENCES

1. 14% of Americans Say They Use CBD Products. available at <https://news.gallup.com/poll/263147/americans-say-cbd-products.aspx>
2. CBD use is Dramatically Rising in Popularity Globally. available at <https://www.pnewswire.com/news-releases/cbd-use-is-dramatically-rising-in-popularity-globally-300816181.html>
3. Arthritis Foundation: Patients Tell Us About CBD Use. available at http://blog.arthritis.org/news/patients-tell-us-cbd-use/?_ga=2.42539884.817872563.1572317518-505791750.1572317518
4. CDC: Drug overdose deaths in the U.S. available at <https://www.cdc.gov/nchs/products/databriefs/db294.htm>
5. CDC: Arthritis related statistics. available at https://www.cdc.gov/arthritis/data_statistics/arthritis-related-stats.htm
6. Distribution of the Endocannabinoid System in the Central Nervous System. <https://www.ncbi.nlm.nih.gov/pubmed/26408158>
7. La Porta C, Bura SA, Negrete R, Maldonado R. Involvement of the endocannabinoid system in osteoarthritis pain. *Eur J Neurosci*. 2014 Feb;39(3):485-500. doi: 10.1111/ejn.12468.
8. Barrie N, Manolios N. The endocannabinoid system in pain and inflammation: Its relevance to rheumatic disease. *Eur J Rheumatol*. 2017;4(3):210-218. doi:10.5152/eurjrheum.2017.17025
9. Blake DR, Robson P, Ho M, Jubb RW, McCabe CS. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology (Oxford)*. 2006 Jan;45(1):50-2. Epub 2005 Nov 9.
10. van de Donk T, Niesters M, Kowal M, Olofsen E, Dahan A, van Velzen M. An experimental randomized study on the analgesic effects of pharmaceutical-grade cannabis in chronic pain patients with fibromyalgia. *PAIN*: April 2019 - Volume 160 - Issue 4 - p 860-869 doi: 10.1097/j.pain.0000000000001464
11. Malfait AM, Gallily R, Sumariwalla PF, et al. The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritis therapeutic in murine collagen-induced arthritis. *Proc Natl Acad Sci U S A*. 2000;97(17):9561-9566. doi:10.1073/pnas.160105897
12. Hammell DC, Zhang LP, Ma F, et al. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. *Eur J Pain*. 2016;20(6):936-948. doi:10.1002/ejp.818
13. CBD Treatment in Hand Osteoarthritis and Psoriatic Arthritis. available at <https://clinicaltrials.gov/ct2/show/NCT03693833>
14. Leas EC, Nobles AL, Caputi TL, Dredze M, Smith DM, Ayers JW. Trends in Internet Searches for Cannabidiol (CBD) in the United States. *JAMA Netw Open*. 2019;2(10):e1913853. doi:10.1001/jamanetworkopen.2019.13853
15. Corroon J, Phillips JA. A Cross-Sectional Study of Cannabidiol Users. *Cannabis Cannabinoid Res*. 2018;3(1):152-161. Published 2018 Jul 1. doi:10.1089/can.2018.0006