## Is CBD a wonder drug or waste of money? Here's what the evidence says

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Claims about the health benefits of cannabidiol have outpaced credible research, but CBD does show some real promise



HAND lotion, dog treats, deodorant. Pillows. Beard oil. Sports bras. The range of CBD products now available is as broad as the health claims these products are marketed with. Items containing CBD, or cannabidiol – the non-intoxicating compound derived from cannabis plants – are touted to stave off wrinkles, improve sleep, reduce anxiety, ease menstrual cramps, prevent hair loss and more.

Celebrities are in on the action. Jennifer Aniston champions CBD for reducing pain and stress. Mike Tyson

has a line of CBD dog chews. And business is booming: around 1 in 7 adults in the US say they use products containing CBD, while in the UK a quarter of adults say they would try it and 1 in 10 people under 24 already have, according to polls. In 2020, people in the US spent \$4.6 billion on such products. Next year, that could balloon to more than \$20 billion. In the UK, the CBD market was valued at £690 million in 2021.

Early evidence hints at many potential medical applications, for issues ranging from arthritis to addiction. But as the skyrocketing popularity of CBD leaves researchers and regulators scrabbling to catch up, we are left with an overwhelming number of products on the market, some of which may work, others whose claims are baseless.

Thankfully, we are starting to get some answers that can help us navigate through the confusion, enabling us to figure out what CBD really does, how it can benefit our health and what products are just a waste of money.

CBD is one of more than 130 compounds found in the cannabis plant known as cannabinoids. It is perhaps the second best known after THC, or tetrahydrocannabinol. THC creates the marijuana "high"; CBD won't get you stoned. "You couldn't get high with it if you tried," says Peter Grinspoon, an internist at Massachusetts General Hospital.

Researchers have known about CBD since the compound was first isolated from a cannabis plant in the 1940s, but, until recently, it has been far less closely studied than intoxicating THC. However, a handful of policy changes in the past decade have made it easier to produce and sell CBD in the US, UK and elsewhere – and set the stage for the current proliferation of products that contain it (see "The CBD explosion").

Regulators and researchers are struggling to keep up. The US Food and Drug Administration (FDA) acknowledged earlier this year that it isn't currently equipped to successfully regulate the compound. "The claims of benefits for CBD have soared so far above the evidence base," says Grinspoon, who is the author of the recent book Seeing Through the Smoke: A cannabis specialist untangles the truth about marijuana.

To date, the FDA has approved just one CBD drug. In 2018, the agency authorised the use of Epidiolex – also available in the UK, other parts of Europe and several other countries – for treating seizures caused by Lennox-Gastaut syndrome and Dravet syndrome, severe forms of childhood epilepsy. In Canada, Australia, Europe and the UK, the oral spray Sativex has also been approved to ease symptoms of multiple sclerosis, including muscle spasms and nerve pain. It hasn't yet been authorised by the FDA, however, after disappointing results in a late-stage clinical trial in 2022.

Although dozens of clinical trials are under way in the US alone – investigating CBD to manage everything from insomnia to symptoms of Alzheimer's disease – most of that research is at an early stage.

The appeal of effective CBD-based therapies is huge. The compound is comparatively cheap and easy to come by, has been shown to be safe even at high doses and isn't habit-forming. The pharmaceutical industry is certainly paying attention. A 2021 analysis by cannabis market research firm Brightfield Group noted that, even with just one CBD-based drug available in the US, CBD pharmaceutical sales were worth \$470 million in 2020. By 2026, with fair winds and further FDA approvals, the firm expects that to more than quadruple to over \$2 billion.



Most clinical trials of CBD are still in early stages

As the opioid overdose crisis continues in the US, many are hopeful that any new CBD-based drugs will include urgently needed options for pain management. Pain treatment isn't only a leading area of CBD research, but it is the reason most people give for using the compound.

There are promising signs. Beyond its potential to treat painful symptoms of multiple sclerosis, it can also help with other forms of chronic pain, according to a recent review of a dozen high-quality studies. Survey results from 2021 echo this: of people who attended special clinics for treating chronic pain, two-thirds said they had tried CBD. Of those, the majority said it reduced their pain and enabled them to cut back on medications, including opioids.

Unfortunately, the evidence around pain relief is still far from conclusive. For instance, in a 2021 study, when volunteers submerged their hands in icy water, CBD provided no benefit over placebo in increasing pain tolerance and even increased pain on some measures. There are also mixed results when it comes to studies looking at the use of CBD for treating pain associated with arthritis, and while CBD may help ease pain linked to fibromyalgia, it appears to provide the most relief when THC is also present.

With a compound that is now so popular – and has the added bonus of a wellness halo thanks to its natural origins and bold claims about its benefits – expectations may also make a big difference. It turns out believing that CBD reduces anxiety may be powerful in its own right. In a study where people were given CBD-free hemp seed oil but told it contained the compound, participants' heart rates lowered and they reported a drop in stress levels – but only if they believed CBD had the power to produce these effects.

## **Relaxation and rehabilitation**

There does seem to be more than expectation at work when it comes to using CBD to treat anxiety, however.

In 24 people with generalised social anxiety disorder who had never tried CBD, a single 600-milligram dose helped reduce anxiety before a public speaking task, for instance. In a larger study published this year, people given a 300mg dose each day for two weeks reported a significant reduction in worries and anxiety compared with those given a placebo. In a 2019 study, people who struggled with anxiety and related sleep disruption were given 25mg of CBD daily. After a month, 79 per cent reported less anxiety and 67 per cent said they had slept better.

Researchers are confident that such work will lead to useful treatments, yet are under no illusions about what limitations there will be. "The future for CBD-based products is incredibly promising,

but that doesn't mean it's right for all people for all things," says psychiatrist Staci Gruber at Mclean Hospital in Massachusetts.

Another area of particular interest is in treating substance misuse, including addictions to opioids and cannabis. Last year, a review of the existing research on CBD and opioid withdrawal found evidence that the compound can reduce cravings. In 2019, a study of 42 people with heroin addiction found that ingesting 400mg or 800mg of CBD also markedly reduced physiological measures of stress around these urges, such as increased heart rate and levels of the hormone cortisol.

In a month-long trial of 82 people classified as "severely addicted" to marijuana, some took either a high, medium or low dose of CBD while trying to quit using the drug. Others received a placebo. Those who got the middle dose of CBD – 400 milligrams per day – consumed around half the amount of marijuana as those given the placebo.

Yet for all of these encouraging results, a major challenge in figuring out what conditions CBD might be useful for is that, even for approved treatments, we don't have a clear idea of exactly why it is working.

"CBD is what's called a promiscuous molecule. It interacts with dozens of different receptors," says Grinspoon. We know, for instance, that CBD binds with some nerve cell receptors that also bind with capsaicin, the molecule that makes chillies spicy. Capsaicin affects neurotransmitters that relay pain signals to the brain, which may be how CBD eases chronic pain for some people. CBD also binds to some types of receptor for the neurotransmitter serotonin, which plays a role in regulating mood, and could be a way by which it helps to relieve anxiety.

We also know that CBD interacts with receptors in our endocannabinoid system, a complex and ancient signalling network in the body that regulates many key functions, including pain control and immune responses. For instance, clinical trials have shown that CBD can boost the amount of anandamide, an endocannabinoid that produces feelings of delight, perhaps explaining the "bodily high" or deep sense of relaxation many users report.

Yet we are still working to pin down which receptors are involved and to what extent. "We're just beginning to learn what [CBD] does and how it does it," says Grinspoon.

Further complicating matters, even when we start to pin down how the molecule can ease pain or anxiety, it doesn't follow that any CBD products will offer those benefits. The CBD doses that are starting to show therapeutic effects in clinical trials are frequently in the hundreds of milligrams – far more than what is in most off-the-shelf goods.

"Three-hundred milligrams of oral CBD might show some slight signal that it could reduce anxiety, but whether that would also translate to taking 10 milligrams of CBD in your coffee, no one really knows the answer to that yet," says Tory Spindle at Johns Hopkins University in Maryland.



The market for products that contain CBD is booming

Another big unknown is how much of the stuff you are really ingesting. To begin with, how you consume CBD affects how much you absorb. When it is taken in a food or drink, people absorb around 15 per cent. A CBD patch or under-the-tongue tincture is closer to 30 per cent. With pillows or eye masks, who knows?

Tests of off-the-shelf items show that the amount of CBD on the label may not be accurate anyhow. Last year, a study of 105 topical CBD products available in stores and online in the US found that only around a quarter were correctly labelled. More than half the products contained more CBD than advertised, while 18 per cent contained less. A similar 2019 study in the UK tested 29 store-bought CBD goods and found one item, an oil selling for £90, contained no CBD whatsoever.

Inaccurate labelling may result in people taking more CBD than expected, but the risk of deadly consequences is close to zero. People can tolerate doses of up to 1500mg of pure CBD without major issues, though very high doses can cause nausea, diarrhoea, drowsiness or confusion for some people.

There is also the issue that these goods may contain unwanted ingredients. The study of topical CBD products found that more than a third of those tested had small traces of THC, including four that were explicitly labelled as THC-free.

## **Hidden ingredients**

Testing also takes time and money, and studies have shown that some manufacturers skip testing protocols required by consumer protection agencies. The volume of products on the market has made it easier for questionable ones to slip through as well. A 2022 report on 188 North American CBD companies found that 1 in 5 provided no evidence of purity testing. That is a worry: some products tested in the US and UK have been shown to contain surprise contaminants like pesticides, heavy metals and potentially harmful microbes.

For those reasons, Spindle says that people who want to try CBD or are already regular users should buy from licensed retailers. "That would be the only way to ensure there's some degree of quality control." Legitimate products sold in the US and UK will have a certificate of analysis and be tested by a third-party lab, which buyers can ask to see. If you only want CBD, look for the terms "CBD isolate" and avoid "full spectrum" or "broad spectrum", which can include other cannabinoids.

Gruber says you should also talk to your doctor. Just as grapefruit juice can affect how some medications are metabolised by the body, so can CBD. Especially when taken orally, CBD can compete for enzymes involved in drug metabolism in the liver, changing the amount and timing of delivery for some drugs. "If you happen to be on a blood thinner, CBD interacts pretty significantly with some of these anticoagulants," says Gruber.

She and others acknowledge that, even with limited oversight, many people want to try CBD, particularly if they think it might help where other treatments have failed. But studying the products available on store shelves isn't straightforward. In many countries, researchers are barred from testing real-world CBD products for medical purposes, relying instead on CBD samples with origins and purity guaranteed by their government. In the US, for decades the only option was to use CBD from approved hemp grown by a single institution, the University of Mississippi.

"Consumers will go down to a dispensary and have a staggering array of products available to them, but I can't use one drop of any of those products in a clinical trial, because if I do, legally, they're being evaluated as a [medical] drug," says Gruber.

Thanks to a law introduced in the US in 2016, that is starting to change, albeit slowly: other growers are now approved to cultivate marijuana for research and product development. "CBD is more readily accessible, and it's cheaper and easier for us to do research now," says Ryan Vandrey at Johns Hopkins University.

That means, despite the overwhelming unknowns about CBD right now, experts are optimistic we will have a much better understanding of its potential benefits within the next decade, if not sooner. "We're definitely headed in the right direction," says Grinspoon. "We will get the answers that we're looking for."

## The CBD explosion

In nations with legal CBD, it comes almost exclusively from hemp – a kind of cannabis plant that has scarcely any THC. A US law change in 2018 that made it legal to grow hemp really kicked off CBD's rapid rise in popularity.

Legalising hemp made it easier to add CBD to foods, beauty products and more without much oversight, and the US Food and Drug Administration has yet to make a coherent plan for regulation beyond issuing occasional warning letters to manufacturers making unsubstantiated health claims.

The UK, Canada, Australia and other countries where CBD is legal have more coherent monitoring and authorisation systems in place, but the rising volume of products is making it difficult for regulators to keep up (see main story). CBD is also catching on in other nations that have loosened legal restrictions, such as Belgium, France, Germany and Poland.

Support for cannabis more broadly has surged too, particularly in the US, where it is now legal for either medicinal or recreational use in 38 states.