

Researchers recommend clinical trials for CBD to prevent COVID-19 based on promising animal data

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CBD reduces viral replication in vitro compared to other cannabis compounds. Credit: Nguyen et al., Science Advances, 2022

An interdisciplinary team of researchers from the University of Chicago has found evidence that cannabidiol (CBD), a product of the cannabis plant, can inhibit infection by SARS-CoV-2 in human cells and in mice.



The study, published on January 20, 2022, in *Science Advances*, found that CBD showed a significant negative association with SARS-CoV-2 positive tests in a national sample of medical records of patients taking the FDA-approved drug for treating epilepsy. The researchers now say that clinical trials should be done to determine whether CBD could eventually be used as a preventative or early treatment for COVID-19. They caution, however, that the COVID-blocking effects of CBD come only from a high purity, specially formulated dose taken in specific situations. The study's findings do not suggest that consuming commercially available products with CBD additives that vary in potency and quality can prevent COVID-19.

Scientists have been looking for new therapies for people infected by the coronavirus and emerging variants, especially those who lack access to vaccines, as the pandemic continues across the country and world and as breakthrough infections become more common.

CBD: An unexpected avenue for fighting COVID-19

The idea to test CBD as a potential COVID-19 therapeutic was serendipitous. "CBD has anti-inflammatory effects, so we thought that maybe it would stop the second phase of COVID <u>infection</u> involving the immune system, the so-called 'cytokine storm.' Surprisingly, it directly inhibited viral replication in lung cells," said Marsha Rosner, Ph.D., Charles B. Huggins Professor in the Ben May Department of Cancer Research and a senior author of the study.

To see this effect, the researchers first treated human lung cells with a non-toxic dose of CBD for two hours before exposing the cells to SARS-CoV-2 and monitoring them for the virus and the viral spike protein. They found that above a certain threshold concentration, CBD inhibited the virus's ability to replicate. Further investigation found that CBD had the same effect in two other types of cells and for three variants of



SARS-CoV-2 in addition to the original strain.

CBD did not affect the ability of SARS-CoV-2 to enter the cell. Instead, CBD was effective at blocking replication early in the infection cycle and six hours after the virus had already infected the cell.

Like all viruses, SARS-CoV-2 affects the host cell by hijacking its gene expression machinery to produce more copies of itself and its viral proteins. This effect can be observed by tracking virus-induced changes in cellular RNAs. High concentrations of CBD almost completely eradicated the expression of viral RNAs. It was a completely unexpected result.

"We just wanted to know if CBD would affect the immune system," Rosner said. "No one in their right mind would have ever thought that it blocked viral replication, but that's what it did."

The researchers showed that the mechanism by which CBD blocks SARS-CoV-2 replication involves CBD activation of one of the host cell stress responses and generation of interferons, an antiviral cell protein.

Real world data: Patients taking CBD test positive for COVID-19 at lower rates

The researchers wanted scientific data to show that CBD prevents viral replication in live animals. The team showed pretreatment with CBD for one week prior to infection with SARS-CoV-2 suppressed infection both in the lung and the nasal passages of mice. "These results provide major support for a clinical trial of CBD in humans," said Rosner.

And the success of CBD wasn't limited to the laboratory: An analysis of 1,212 patients from the National COVID Cohort Collaborative revealed



that patients taking a medically prescribed oral solution of CBD for the treatment of epilepsy tested positive for COVID-19 at significantly lower rates than a sample of matched patients from similar demographic backgrounds who were not taking CBD.

The potential for CBD to treat patients recently exposed to or infected by SARS-CoV-2 does not precede the first lines of defense against COVID-19, which are to get vaccinated and follow existing public health guidelines for masking in indoor spaces and social distancing. But the published results offer a potential new therapeutic, something still needed as the pandemic rages on.

"A clinical trial is necessary to determine whether CBD is really effective at preventing or suppressing SARS-CoV-2 infection, but we think this may have potential as a prophylactic treatment," said Rosner. "Maybe you're in a hot spot or you think you might have been exposed or you've just tested positive—that's where we think CBD might have an effect."

Not your dispensary's CBD

The research team emphasized that the COVID-blocking effects of CBD were confined strictly to high purity, high concentrations of CBD. Closely related cannabinoids such as CBDA, CBDV and THC, the psychoactive element enriched in marijuana plants, did not have the same power. In fact, combining CBD with equal amounts of THC actually reduced the efficacy of CBD.

"Going to your corner bakery and buying some CBD muffins or gummy bears probably won't do anything," said Rosner. "The commercially available CBD powder we looked at, which was off the shelf and something you could order online, was sometimes surprisingly of high purity but also of inconsistent quality. It is also hard to get into an oral



solution that can be absorbed without the special, FDA-approved formulation," Rosner said.

Furthermore, CBD use is not without potential risks. It appears to be extremely safe when consumed in food or drink, but methods of use such as vaping can have negative side effects, including potential damage to the heart and lungs. It's also not well studied in certain populations, such as pregnant people, and so should be used only under the supervision of a physician and with caution.

While the study's results are exciting, additional study is needed to determine the precise dosing of CBD that is effective at preventing SARS-CoV-2 infection in humans as well as its safety profile and any potential side effects.

"We are very eager to see some <u>clinical trials</u> on this subject get off the ground," Rosner said. "Especially as we are seeing that the pandemic is still nowhere near the end—determining whether this generally safe, well-tolerated, and non-psychoactive <u>cannabinoid</u> might have anti-viral effects against COVID-19 is of critical importance."

Rosner was also pleased that this research project was a case study in the power of scientific collaboration by bringing together a highly interdisciplinary group of researchers. Senior authors listed on the paper came from three different research universities and from departments as diverse as microbiology, molecular engineering, cancer biology and chemistry.

"This was truly a team-science effort, and that's something that really excites me," said Rosner. "From clinicians to David Meltzer's group who did the patient analysis to virologists like Glenn Randall, and it goes on and on. This is the way science should be carried out."



More information: Long Chi Nguyen et al, Cannabidiol inhibits SARS-CoV-2 replication through induction of the host ER stress and innate immune responses, *Science Advances* (2021). <u>DOI:</u> <u>10.1126/sciadv.abi6110</u>

Provided by University of Chicago Medical Center

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