



Two Cannabis Compounds Inhibit COVID-19 Infection in In Vitro Study

CBDA and CBGA bind to the SARS-CoV-2 spike protein, according to a team of Oregon State University researchers.

By CBD Inside & Out Staff

Two compounds found in cannabis, cannabigerolic acid (CBGA) and cannabidiolic acid (CBDA), were shown in a recent *in vitro* study to bind to the SARS-CoV-2 spike protein, blocking a critical step in the process the virus uses to enter cells, according to a team of researchers at Oregon State University (OSU). Results were published in the *Journal of Natural Products*.

Led by Richard van Breemen, a researcher with Oregon State's Global Hemp Innovation Center, College of Pharmacy, and Linus Pauling Institute, the team concluded that because these hemp compounds target the same spike

proteins as COVID-19 vaccines and antibody therapies, they could theoretically serve as an adjunctive therapy to thwart infection or disease progression.

INHIBITING CELL ENTRY

Effectiveness was determined using human endothelial cells in an *in vitro* setting. CBDA and CBGA both targeted the spike protein and prevented entry of the virus into cells.

"These cannabinoid acids are abundant in hemp and in many hemp extracts," van Breemen said. "They are not controlled substances like THC, the psychoactive ingredient in marijuana, and have a good safety profile in humans. And our research showed that hemp compounds were equally effective against variants

of SARS-CoV-2, including the variant B.1.1.7 which was first detected in the United Kingdom, and variant B.1.351, first detected in South Africa."

These two variants are known as the alpha and beta variant, respectively. Currently, the omicron variant (B.1.1.529) is the dominant variant of the virus, according to the Centers for Disease Control (CDC) and the World Health Organization (WHO).

"Any part of the infection and replication cycle is a potential target for antiviral intervention, and the connection of the spike protein's receptor binding domain to the human cell surface receptor ACE2 is a critical step in that cycle," van Breemen said. "That means cell entry inhibitors, like the acids from hemp, could be used to prevent SARS-CoV-2 infections and also to shorten infections by preventing virus particles from infecting human cells. They bind to the spike proteins so those proteins can't bind to the ACE2 enzyme, which is abundant on the outer membrane of endothelial cells in the lungs and other organs."

“Any part of the infection and replication cycle is a potential target for antiviral intervention, and the connection of the spike protein’s receptor binding domain to the human cell surface receptor ACE2 is a critical step in that cycle. That means cell entry inhibitors, like the acids from hemp, could be used to prevent SARS-CoV-2 infections and also to shorten infections by preventing virus particles from infecting human cells. They bind to the spike proteins so those proteins can’t bind to the ACE2 enzyme, which is abundant on the outer membrane of endothelial cells in the lungs and other organs.”

—Richard van Breemen, *Researcher at Oregon State University’s Global Hemp Innovation Center, College of Pharmacy, and Linus Pauling Institute*

SCREENING FOR SOLUTIONS

The two cannabis compounds were singled out via a mass spectrometry-based screening technique invented in van Breemen’s laboratory, which was described in detail in an earlier paper appearing in the *Journal of the American Society for Mass Spectrometry*.

The technique, affinity selection mass spectrometry, involves incubating a drug target like the SARS-CoV-2 spike protein with a mixture of possible ligands (things that might bind to it) such as botanical extracts. “After incubating a complex mixture like a hemp extract with the immobilized spike protein, we simply wash away unbound molecules while retaining the beads with spike protein and bound hemp compounds with a magnet. Then, we release the ligands from the protein with alcohol and measure them with a mass spectrometer.”

The team screened a range of botanicals used as dietary supplements, including red clover, wild yam, hops, and three species of licorice. In the process, van Breemen said that licochalcone A, found in licorice, also bound to the SARS-CoV-2 spike protein, however, this compound has not yet been tested against the live virus.

“These compounds can be taken orally and have a long history of safe use in humans,” van Breemen said. “They have the potential to prevent as well as treat infection by SARS-CoV-2. CBDA and CBGA are produced by the hemp plant as precursors to CBD and CBG, which are familiar to many consumers. However, they are different from the acids and are not contained in hemp products.”

MORE ANALYSIS NEEDED

Van Breemen said the rapid spread of successive variants is concerning, and research will need to continue past spike proteins from early versions of the virus. However, he said that vaccinations and CBDA/CBGA combined could be a much more

challenging environment for SARS-CoV-2 than vaccinations in isolation.

Van Breemen told *CBD Inside & Out* that what would make a CBDA/CBGA formulation unique is the synergy between these two compounds. “CBDA and CBGA can bind simultaneously to the spike protein and can work synergistically,” he said. “Whether they can function synergistically with antibodies against the spike protein is still unknown. Antibody therapy has been used to clinically treat COVID. Clinical studies of CBDA and CBGA are still needed to prove efficacy.”

What we do know about the development of a potential therapeutic, van Breemen said, is that the two hemp compounds can be absorbed through ingestion and reach the bloodstream. While clinical data is limited so far, there is evidence that CBGA and CBDA doses bioequivalent to those used *in vitro* have been used by humans before, he said.

UNDERSTANDING EXTRACTION

While most consumers may recognize cannabidiol (CBD), the less familiar cannabidiolic acid (CBDA) is the natural form of CBD found in the hemp plant. This phytocompound was previously thought to be inactive and unstable, noted NeXtraction Inc., a leading manufacturer of CBDA and CBGA.

However, recent research has shown that CBDA extracted in particular ways, such as with water, is stable and bioavailable in the body. Water-based methods, such as NeXtraction’s proprietary H2Only technology, appear to keep the structure of CBDA intact and allow for optimal absorption both through skin and blood.

CBDA contains an extra chemical group called a “hydroxyl” group. When CBDA is exposed to high heat and chemicals it degrades into CBD, which is less available in the body. The natural hydroxyl group attached to CBDA increases bioavailability for better absorption in the body. ■