Compound from magnolia tree bark found to impede SARS-CoV-2 replication in certain cells

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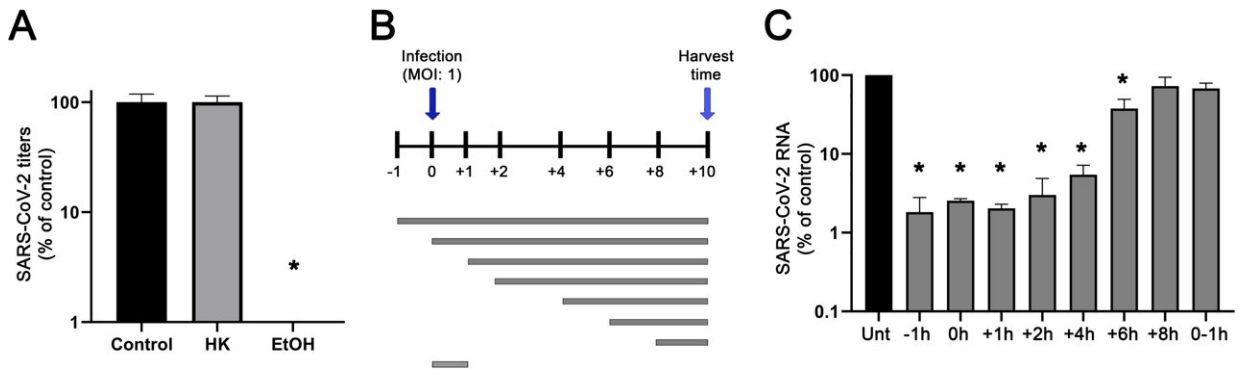

HK inhibits SARS-CoV-2 replication at a postentry step of the replication cycle. (A) Assessment of the virucidal potential of HK. A SARS-CoV-2 stock was incubated in medium (control) with 50 μM HK or 70% ethanol. The remaining infectious virus titers were determined by plaque assay and normalized to that of the untreated control (100%). The means ± SEM from 3 independent experiments are shown, and data were analyzed by one-way ANOVA and Bonferroni's post hoc test. (B) Schematic representation of the time-of-addition assay, depicting the different treatment intervals during which infected Vero E6 cells were exposed to 20 μM HK. (C) At 10 hpi, supernatants were harvested and viral load was determined by quantifying extracellular viral RNA copies by RT-qPCR. Copy numbers were normalized to the level of untreated infected cells (100%). The means ± SEM from 3 independent experiments are shown, and data were analyzed by one-way ANOVA and Bonferroni's post hoc test. Credit: *Microbiology Spectrum* (2023). 10.1128/spectrum.03273-22

A compound called honokiol, which is found in the bark of multiple species of magnolia tree, inhibits replication of SARS-CoV-2 virus in several types of cells, according to a team of researchers in the Netherlands. The research is published in *Microbiology Spectrum*.

The researchers found that honokiol inhibits replication of SARS-CoV-2 in several cell types, causing production of infectious SARS-CoV-2 particles in treated cells to fall to around 1,000th of the previous level.

The compound also inhibited replication of other highly pathogenic human coronaviruses, including MERS- and SARS-CoV. "This suggests that it has a broad spectrum of activity and would likely also inhibit novel coronaviruses that might emerge in the future," said Martijn J. van Hemert, Ph.D., Associate Professor, Department of Medical Microbiology, Leiden University Medical Center, Leiden, The Netherlands.

The motivation for the research was the lack of vaccines and treatments early in the pandemic, and the desire to be prepared for the next new coronavirus. To this end, van Hemert emphasized that his group, as well as others from around the world, responded to COVID-19 by testing many compounds for antiviral effects.

"If honokiol can be developed into a drug, possibly in combination with other compounds, stockpiling it would help us to increase our preparedness for the emergence of the next coronavirus," said van Hemert. "Broad-spectrum drugs could then be used to treat early patients and prevent spread, or they could be used prophylactically among healthcare workers, and in high-risk groups, such as among nursing home residents."

Honokiol also has anti-inflammatory properties, van Hemert noted. That, he said, could be helpful in cases where patients wait until a relatively

late stage of the disease to obtain medical treatment—a frequent occurrence—by which time the body's own inflammatory responses to the infection are causing symptoms. "At that point, inhibition of virus replication might no longer be helpful, but honokiol's anti-inflammatory response might mitigate the illness," van Hemert explained.

Honokiol inhibits a later step of the viral replication cycle—one that takes place after the virus has entered the cell. The investigators suspect that honokiol does so by triggering processes in the host cell that impede replication of the virus. It did so in the case of the original SARS-CoV-2 variants, and also in that of the more recent omicron variants.

At this early stage in the research, "Our study merely provides the basis for further research into potential therapeutic applications," said van Hemert. "It is important to mention that it is too early to claim that honokiol might be used in SARS-CoV-2 patients. This requires much more research and—if successful—properly conducted clinical trials."

Van Hemert learned about honokiol from Jack Arbiser, M.D., Ph.D., of Emory School of Medicine, during the early stages of the pandemic. Arbiser had been researching honokiol's anticancer properties, and he told van Hemert he thought that the effects of the compound on the host cell might be beneficial for treatment of COVID-19 patients as well.

Clarisse Salgado-Benvindo, a Ph.D. student in van Hemert's group, performed most of the experiments, using cultured cells that the researchers infected with SARS-CoV-2, or the highly pathogenic coronaviruses SARS-CoV and MERS-CoV. Experimenters worked inside a BSL-3 lab, which is a special high containment lab, while wearing protective suits with full-face masks to prevent infection.

More information: Clarisse Salgado-Benvindo et al, Honokiol Inhibits SARS-CoV-2 Replication in Cell Culture at a Post-Entry Step,

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