Patented compound kills various human pathogenic fungi, may improve human health

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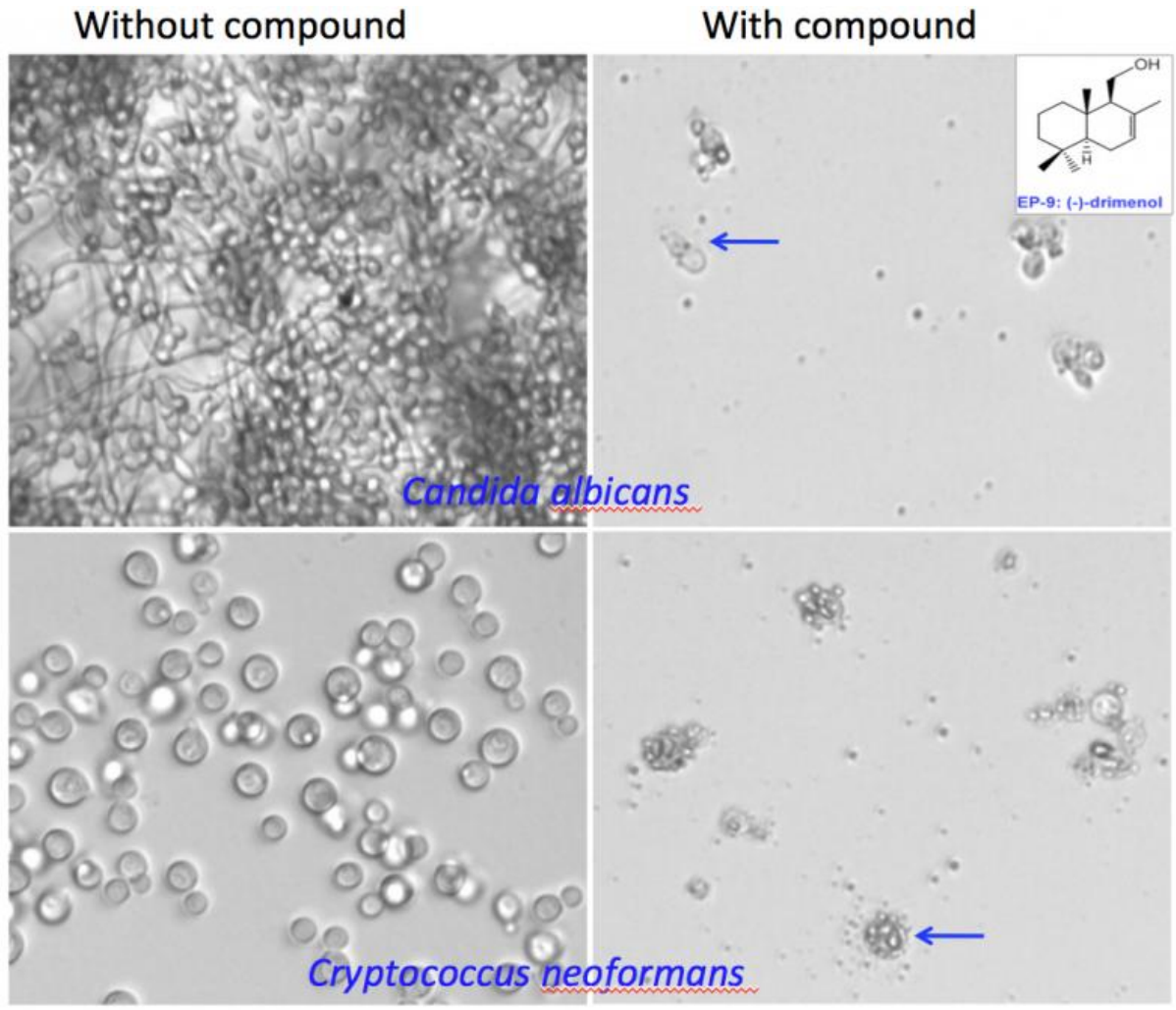

Antifungal resistant clinical Candida albicans and Cryptococcus neoformans without, on the left panel, and with drimenol, on the right panel, were tested in vitro. Some treated fungi showed blebbing and rupturing of fungal cells, depicted

with the arrows. Chemical structure of the tested compound is shown in top right corner. Credit: Govindsamy Vediyappan

A now-patented substance from two Kansas State University researchers may be an all-purpose solution for stopping fungus.

Govindsamy Vediyappan, assistant professor of biology, and Duy Hua, university distinguished professor of chemistry, received a U.S. patent for their invention "Sesquiterpenes for Antifungal Applications."

Vediyappan, who researches the microbiology of various bacteria and fungi, and Hua, who specializes in synthetic compounds, developed and identified a simple chemical compound that kills several major fungi that affect human health. The compound also may have applications for fungal diseases that affect wheat and rice plants.

The fungal cells are almost the same as human cells, which make it difficult to develop drugs that kill a fungus without damaging human cells, Vediyappan said. Similarly, most antifungal drugs that exist are for one specific cellular target, such as the cell wall or cell membrane of the fungus.

The compound developed at Kansas State University may be an exception. In tests, researchers discovered the compound was very effective against numerous fungi.

"We found that this compound kills lots of different pathogenic fungi—from ones that severely affect human health to ones that are not life-threatening but are annoying," Vediyappan said. "We also saw that it only takes a small amount of the compound to affect a broad spectrum of fungi."

Researchers tested the compound on the following fungi, killing most of the cells in each fungus sample:

- *Candida albicans*, including with drug resistance—A common resident fungus in our mouth and gut that can get into the blood stream, kidneys, liver and spleen. The fungus is persistent in immune suppressed patients, such as those with cancer or HIV. Once inside the organ, it continues to multiply and invade, making it difficult to kill.
- *Cryptococcus neoformans*—A fungus common in bird feces. When inhaled, it travels to the lungs and leads to the development of respiratory diseases and fungal meningitis.
- *Trichophyton equinum*, a dermatophyte—The fungus often responsible for ringworm fungal disease in animals and in humans. It lives in plant debris and decaying materials.
- *Aspergillus fumigatus*— A fungus that causes respiratory disease in people who have had organ transplants.

Positive results did not stop at the number of species the compound was effective on.

"Normally, fungi make mutations in their genes to become resistant to antifungals and sequester them via their secreted polysaccharide substances," Vediyappan said. "From our preliminary results, we found that the fungi were not able to develop resistance to our compound. We're thinking that may be because the compound is affecting multiple mechanisms or pathways in these fungi rather than a single pathway that can easily be modified for resistance development."

Some of the gene expression studies were conducted in collaboration with a research colleague in Canada.

While the research has focused on human health, Vediyappan said the

compound also may be beneficial for food plants. Rice and wheat, for example, are susceptible to fungi such as Magnaporthe oryzae and Fusarium graminearum, which causes rice blast and fusarium head blight.

Researchers hope to work with the National Institutes of Health to conduct more studies with the compound. These tests would build off of ones with a worm model of Candidiasis that showed that the compound killed most of the fungi while not harming the worms.

The patent was issued to the Kansas State University Research Foundation, a nonprofit corporation responsible for managing technology transfer activities at the university.

The discovery was made possible through support from the Kansas IDeA Network of Biomedical Research Excelence, or KINBRE; Kansas State University's Johnson Cancer Research Center; and funding for Hua's research and for Vediyappan's research.

The results were presented in meetings, and the researchers will publish their findings with the compound in the near future.

Provided by Kansas State University