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# HIV drugs may help fight deadly fungal infection, study finds

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(From left) Ehab Salama and Yehia Elgammal work in Mohamed Seleem's lab at the Center for One Health Research. Photo by Andrew Mann for Virginia Tech. Credit: Virginia Tech

Antiviral drugs can make antifungals work again.

That, at its simplest, is the approach Mohamed Seleem's lab at the Center for One Health Research has found may be a key treatment strategy in the battle against Candida auris, a frighteningly deadly fungal pathogen discovered in 2009 that is considered an urgent threat by the Centers for Disease Control and Prevention (CDC).

Candida auris, first discovered in Japan as an ear infection, has a staggering 60 percent mortality rate among those it infects, primarily people with compromised health in hospitals and nursing homes.

Recently, Seleem and Ph.D. students Yehia Elgammal and Ehab A. Salama published a paper in the American Society for Microbiology's *Antimicrobial Agents and Chemotherapy* journal detailing the potential use of atazanavir, an HIV protease inhibitor drug, as a new avenue to improving the effectiveness of existing antifungals for those with a Candida auris infection.

A perfect storm of antimicrobial resistance, global warming and the COVID-19 pandemic has resulted in the rapid spread of Candida auris around the world, said Seleem, director of the center, a collaboration between the Virginia-Maryland College of Veterinary Medicine and the Edward Via College of Osteopathic Medicine.

"We don't have lots of drugs to use to treat fungal pathogens. We have only three classes of antifungal drugs," said Seleem, the Tyler J. and Frances F. Young Chair in Bacteriology at Virginia Tech. "With a fungal pathogen, it's often resistant to one class, but then we have two other options. What's scary about Candida auris is it shows resistance to all three classes of the antifungal.

"The CDC has a list of urgent threats, but on that list there is just one fungal pathogen, which is Candida auris. Because it's urgent, we need to deal with it."

Widespread use of fungicides in agriculture, in addition to the three classes of antifungal drugs used widely in medicine, has contributed to fungal pathogens developing more resistance, particularly Candida auris.

Also, its rise has been linked to rising global temperatures and to easier spread through hospitals filled with COVID-19 patients in recent years during the global pandemic.

Atazanavir, an HIV protease inhibitor drug, has been found by Seleem's lab to block the ability of Candida auris to excrete antifungals through its efflux pumps.

Think of a boat taking on water and hoses siphoning that water out of the boat to keep it afloat. Atazanavir stops up the hoses.

That allows the azole class of antifungal drugs to not be expelled as easily and perform better against Candida auris, the Seleem lab's research has found.

The research on atazanavir builds on work three years ago by Seleem's lab, then at Purdue University, finding potentially similar benefit in lopinavir, another HIV protease inhibitor.

HIV protease drugs are already in wide use among HIV patients, who can also be extra susceptible to Candida auris. Some HIV patients have likely been taking HIV protease drugs and azole-class antifungals in tandem for separate purposes, providing a potential source of already existing data that can be reviewed on whether those patients had Candida auris and what effects the emerging pathogen had on them.

Repurposing drugs already on the market for new uses can allow those treatments to reach widespread clinical use much more rapidly than would happen with the discovery of an entirely new drug, as existing

drugs have already been tested and approved by the Food and Drug Administration and have years of further observation of effects in prescriptive use.

**More information:** Yehia Elgammal et al, Atazanavir Resensitizes Candida auris to Azoles, *Antimicrobial Agents and Chemotherapy* (2023). DOI: 10.1128/aac.01631-22

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