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Novel drug repurposing method reveals two drugs effective for bacterial, fungal infections

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A Purdue University researcher has developed a novel strategy on identifying antimicrobial drugs to better treat bacterial and fungal infections, which could produce significant impacts that leapfrog the drug development process and save years of expensive research.

Mohamed Seleem, an associate professor of microbiology in Purdue's College of Veterinary Medicine, has used novel drug repurposing methods to discover two drugs that could have significant promise as a potent antimicrobial agent for treatment of both superficial and invasive infections.

Seleem said that bacterial resistance to conventional antibiotics as well as invasive fungal infections, has become a burgeoning global health epidemic that necessitates urgent action.

"In the United States alone more than two million individuals are stricken each year with infections caused by multidrug-resistant pathogens," he said. "Invasive fungal infections afflict millions of patients annually, resulting in nearly one-and-a-half million deaths. The demand for antifungals is at an all-time high because current antifungal treatments aren't working very well and can't be administered very conveniently."

Seleem said that approximately 30 percent of newly approved FDA

drugs and vaccines have been repurposed. However, not a single drug has been thoroughly investigated and repurposed for use as an antibacterial or antifungal.

Finding new ways to repurpose drugs for antimicrobials outside of their current scope could allow companies many benefits, he added.

"Repurposing existing approved drugs allows companies to bypass much of the preclinical work and early-stage clinical trials required for new compounds, thus cutting the cost associated with bringing a drug to the marketplace by as much as 40 percent," he said. "Given these drugs have already been tested in human patients, valuable information pertaining to their chemical parameters are known. This permits a better understanding of the overall pharmacology of the drug, potential routes of administration, and establishing an appropriate dosing regimen for patients."

Seleem and his team are currently screening 3,200 of the 4,000 available approved drugs to test, which involves identifying those that have shown activity against bacteria and fungi and determining which ones are most promising.

"We take a drug that is being used for, say, heart disease and we re-use it as something like a topical ointment over the skin. The drug hasn't changed, but the method of application and purpose has," Seleem said. "We have ready information about the drugs from previous research for its initial purpose, but we conduct tests in the new model since they have never been used as an antifungal or antimicrobial, to reveal any additional information we may need. We plan on buying the additional 800 drugs for testing."

Seleem said that through his research and studies he has identified two drugs, auranofin and ebselen, as a potent antimicrobial agent that is

capable of killing intracellular Methicillin-resistant Staphylococcus aureus (MRSA), a bacterium responsible for several difficult-to-treat infections in humans. In addition, auranofin and ebselen also are exhibiting novel antifungal mechanisms.

"Through our trials we have found that these two drugs have the ability to disrupt adherent staphylococcal biofilms, the most frequent cause of infections originating in hospitals. We've found also that they suppress toxin production and key resentment factors and reduce excessive host-inflammatory responses associated with these toxins, significantly reducing bacterial load and enhancing wound healing," he said. "In addition, both drugs have many advantageous qualities including oral bioavailability, potent bactericidal activity in a clinically achievable range, very low frequency of resistance, and synergistic activity with conventional antibiotics."

Seleem said he plans to research two other drug repurposing applications that would be of interest to the market: acne and toenail fungus.

"Approximately 85 percent of people age 12-24 suffer from at least minor acne, and current treatments aren't always effective. Toenail fungus is prevalent in about 10 to 20 percent of the world population, and current treatment, which can take for up to three years, is only effective in about 10 percent of those people," he said. "So we want to start screening the causative agent of these conditions and hopefully find a treatment that is safe and effective that is already being used in other approved drugs to fast track its availability to the market."

Seleem initially received funding from startup and university incentive grants, which allowed him to purchase the library of drugs he has been testing. He also received a one-year, $250,000 grant from the National Institutes of Health and is seeking additional funding to expand his research. He is also open to partnerships with companies that could use

his research to move the drug into clinical trials for its new purpose.

Provided by Purdue University