Researchers identify three drugs as possible therapeutics for COVID-19

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Researchers at the University of Tennessee Health Science Center working with colleagues at the University of New Mexico have identified three drugs, already approved for other uses in humans, as possible therapeutics for COVID-19, the illness caused by the SARS-CoV-2 virus.

Based on virtual and in vitro antiviral screening that began in the earlier months of the COVID-19 pandemic, the researchers led at UTHSC by Colleen Jonsson, Ph.D., identified zuclopenthixol, nebivolol, and amodiaquine as promising therapeutics for the virus in its early stages.

Dr. Jonsson is a professor and the Endowed Van Vleet Chair of Excellence in Virology in the College of Medicine at UTHSC. She also directs the UTHSC Regional Biocontainment Laboratory (RBL), where this research was conducted. The university's RBL is one of roughly a dozen federally funded labs authorized to safely study contagious pathogens.

In a paper published in *ACS Pharmacology & Translational Science*, the researchers propose the drugs as possible candidates for testing in future clinical trials to improve immune response to the virus. Amodiaquine is an older antimalarial, zuclopenthixol is an antipsychotic, and nebivolol is a blood pressure medication.

"Particularly in the context of this pandemic, there is a stringent need for high-quality studies that can provide critical knowledge concerning the COVID-19 disease and reliable treatment proposals," the paper states. "With these caveats in mind, we conceived a computational workflow that included independent in vitro validation, followed by assessing emerging candidates in the context of available clinical pharmacology data with the aim of proposing suitable candidates for clinical studies for early stage (incubation and symptomatic phases) patients infected by SARS-CoV-2."

"Given the need for improved efficacy and safety, we propose zuclopenthixol, nebivolol, and amodiaquine as potential candidates for clinical trials against the early phase of the SARS-CoV-2 infection," the researchers wrote.

Comparing the drugs to hydroxychloroquine, the anti-malarial drug most-frequently studied in clinical trials for use as a COVID-19 therapeutic, the researchers examined 4,000 approved drugs and found these three to act similarly to the hydroxychloroquine, and in some cases, more safely. The research indicates they may also improve efficacy when combined in lower doses with remdesivir, an anti-viral given an emergency use authorization by the United States Food and Drug Administration as a therapeutic for COVID-19.

"Think of it as a whack-a-mole game," said Tudor Oprea, MD, Ph.D., professor of Medicine and Pharmaceutical Sciences, chief of the UNM Division of Translational Informatics, and corresponding author on the paper. "Instead of having one hammer, you have two hammers, which

is more effective. We're trying to give the scientific community two hammers, instead of one."

Dr. Jonsson added, "This is a very exciting discovery and we are following up on the potential use of zuclopenthixol, nebivolol, and amodiaquine in additional research studies."

More information: Giovanni Bocci et al, Virtual and In Vitro Antiviral Screening Revive Therapeutic Drugs for COVID-19, *ACS Pharmacology & Translational Science* (2020). DOI: 10.1021/acsptsci.0c00131

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