

PRESS RELEASE

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Plant based compound Peruvoside could prevent spread of diverse medically important viruses: NUS Medicine

Researchers from NUS Medicine found that inhibiting a human protein that is essential for building the virus factories within the body, may be the answer to fighting a range of virus infections, such as SARS-CoV-2, Hand, Foot and Mouth Disease and Influenza.

Singapore, 22 June 2023 — Peruvoside, a plant-based compound that is commonly used to treat heart failure, has been discovered to be able to prevent up to 12 medically important viruses, all originating from different virus families. These viruses are of medical significance as they cause prevalent viral diseases, such as SARS-CoV-2, Hand, Foot and Mouth Disease (HFMD) and Influenza. When modified, Peruvoside acts on GBF1, a protein that is crucial for the replication and production of virus in the body, by disabling its functionality so that production of more virus is stopped.

Led by Associate Professor Justin Chu from the Infectious Diseases Translational Research Programme and Department of Microbiology and Immunology at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), the study aimed to find a therapeutic that is effective in killing a wide range of viruses. Thousands of compounds were screened using a high-throughput screening test, normally used in drug discovery processes. Peruvoside was identified as the ideal candidate and was found to possess broad-spectrum antiviral properties to prevent the replication of a number of infectious viruses, with minimal side effects.

In their study, the team evaluated the efficacy of Peruvoside in fighting Enterovirus, the virus that causes HFMD. At a treatment dosage level of 0.5 milligrams, the results showed 100% efficacy in protection with no detectable traces of virus in tissues, the region usually affected by the Enterovirus.

The team also measured the toxicity of the Peruvoside drug using the LDH assay, which is revealed based on the level of liver enzymes in the blood stream. An inflamed liver or damage to liver cells would lead to elevated levels of liver enzymes in the blood test. In the study, a very low level of toxicity was detected following the administration of Peruvoside at different concentrations.

In the field of infectious diseases, there are typically two ways to target the intruding virus. The first method is targeting the virus particles using antibodies, at the start of the infection process. The second method is targeting the infected cells where the virus replicates itself, which is known as the viral factories. The virus begins its infectious stage at the entry point of the cell.

Once the virus gets to the entry point, it releases its genetic material into the cells to form viral factories, that replicate and produce more copies of the virus, developing into an infectious disease within the body.

Many commonly-known viruses of medical importance such as SARS-CoV-2, Dengue virus, Zika virus, Chikungunya virus and Enterovirus are known as positive-sense RNA viruses. For this group of viruses, the virus replication cycle takes place exclusively in the cytoplasm of the cell, instead of the cell nucleus. The virus decodes and releases its genome to be replicated, building up viral factories within the cytoplasm to ensure virulence. Surprisingly, the team found that Peruvoside also has the ability to prevent virus replication of other viruses that cause Herpes Cold Sores, H1N1 Human Influenza A and the common flu, with minimal side effects. These viruses are not in the same positive-sense RNA virus group that the team initially set out to test.

Associate Professor Justin Chu is confident of the benefits of Peruvoside as the next effective drug to fight against existing and emerging viruses. Speaking as Principal Investigator of the study, Assoc Prof Chu said, "This study shows great significance for Peruvoside to be considered as a general cellular target and an anti-viral therapeutic for medically important virus-mediated diseases, especially when no vaccine and therapeutic is available. For the next stage of this study, the team aims to modify and improve the pharmacological and safety profile of Peruvoside so that it can be eligible for clinical trials and safe for consumption."

This study is published in <u>Acta Pharmaceutica Sinica B</u>.

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The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2023 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2022).

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