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NUS scientists develop oral vaccine to protect farmed fish from deadly virus

Method useful for fish larvae, fingerlings, which are hard to vaccinate through jabs

Chin Hui Shan

To prevent fish from being killed by a deadly disease, National University of Singapore researchers have come up with an oral vaccine that can be mixed into their feed.

This is especially useful for fish larvae and fingerlings, which are the most susceptible to the virus and are difficult to vaccinate through injections.

The nervous necrosis virus (NNV) attacks the nervous system of the fish and has a high mortality rate, especially among fish larvae and juvenile fish. Widely considered a major aquaculture threat, it is highly contagious and has been reported in dozens of marine fish species worldwide.

Currently, vaccination mostly involves injecting the fish individually, which is not only a mammoth task but also may not be suitable for fish larvae and juvenile fish due to their small size, said Yang Daiwen, a professor from the Department of Biological Sciences at the NUS Faculty of Science who led the research team of six, who included researchers from Temasek Life Sciences Laboratory.

The oral vaccine can be used on species such as grouper, as well as European and Asian sea bass, he said. Asian sea bass, also known as barramundi, and groupers are farmed in Singapore.

Noting that the virus is not a major issue here, he said it remains a significant problem in other places like China and the Mediterranean, and is still a serious concern as the virus can disappear and then re-emerge quickly.

The research findings for the study, which began in 2021, were published in the journal, Fish & Shellfish Immunology, earlier in 2026.

"Most of the time, people do not care too much for the young fish. The reason is that economic loss is less significant... But I think if we are able to save the fish from this infection during the nursery stage, this will enhance fish survival and improve overall production efficiency," said Yang.

The disease has a near 100 per cent mortality rate for fish in the larval stage, he pointed out, adding that the growth of the fish will be reduced even if they survive the virus.

Bigger and older fish are less susceptible, although different species have different mortality rates.

The oral vaccine has two main components – a particle to train the immune system of the fish and a carrier to safely deliver this particle into its bloodstream.

The scientists created virus-like particles (VLPs) using the outer shell of the virus but without its genetic material. While these hollow particles resembling the virus cannot actually infect the fish, they trigger an immune response in them.

To safely deliver the particles through the fish's digestive system, a carrier is needed to protect them from the stomach, which has a very acidic environment and could erode the particles.

The scientists packed the VLP into a bacterium called *Lactococcus lactis*, which acts as a protective capsule to deliver the particles to the intestines and later into the bloodstream. The bacterium can resist the acidic environment in the stomach for some time.

Without the bacterium, most VLPs may not be able to survive in the stomach, said Yang.

After being safely delivered to the bloodstream, the VLPs induce an immune response in the fish, which generates antibodies against the virus.

"Now, the fish will have the antibodies and so when the real virus hits, they will recognise this virus immediately and eliminate it," he said.

Yang said the oral vaccine doubled the levels of antibodies and neutralising antibodies compared with feeding the fish VLPs with no protective capsules. Neutralising antibodies are specific antibodies that block the virus from infecting the host.

The vaccine also proved effective in reducing brain viral load by about 300 times after the fish had been exposed to the virus for seven days, he said.

This means the vaccine dramatically reduced the amount of virus replicating in the fish, effectively protecting them from the lethal effects of the disease.

One limitation of the oral vaccine, however, is that it is less effective than injectable vaccines and requires a higher dose.

Yang said the oral vaccine was evaluated in Asian sea bass and grouper under laboratory conditions. Each trial lasted about two months. At least three trials for the Asian sea bass were conducted and showed that the vaccine induced neutralising antibodies and suppressed viral replication and dissemination, he said.

In the grouper, which was studied once, the oral vaccine boosted survival rates to about 95 per cent in the vaccinated fish, compared with 60 per cent in unvaccinated fish.

The research team has filed three patents for the vaccine and plans to collaborate with industry partners for field trials on grouper and other types of fish.

It also hopes to develop a similar oral vaccination for scale drop disease virus, a deadly virus that causes fish to shed scales and develop skin lesions. The virus affects fish like the Asian sea bass and yellowfin sea bream.

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ENHANCING FISH SURVIVAL

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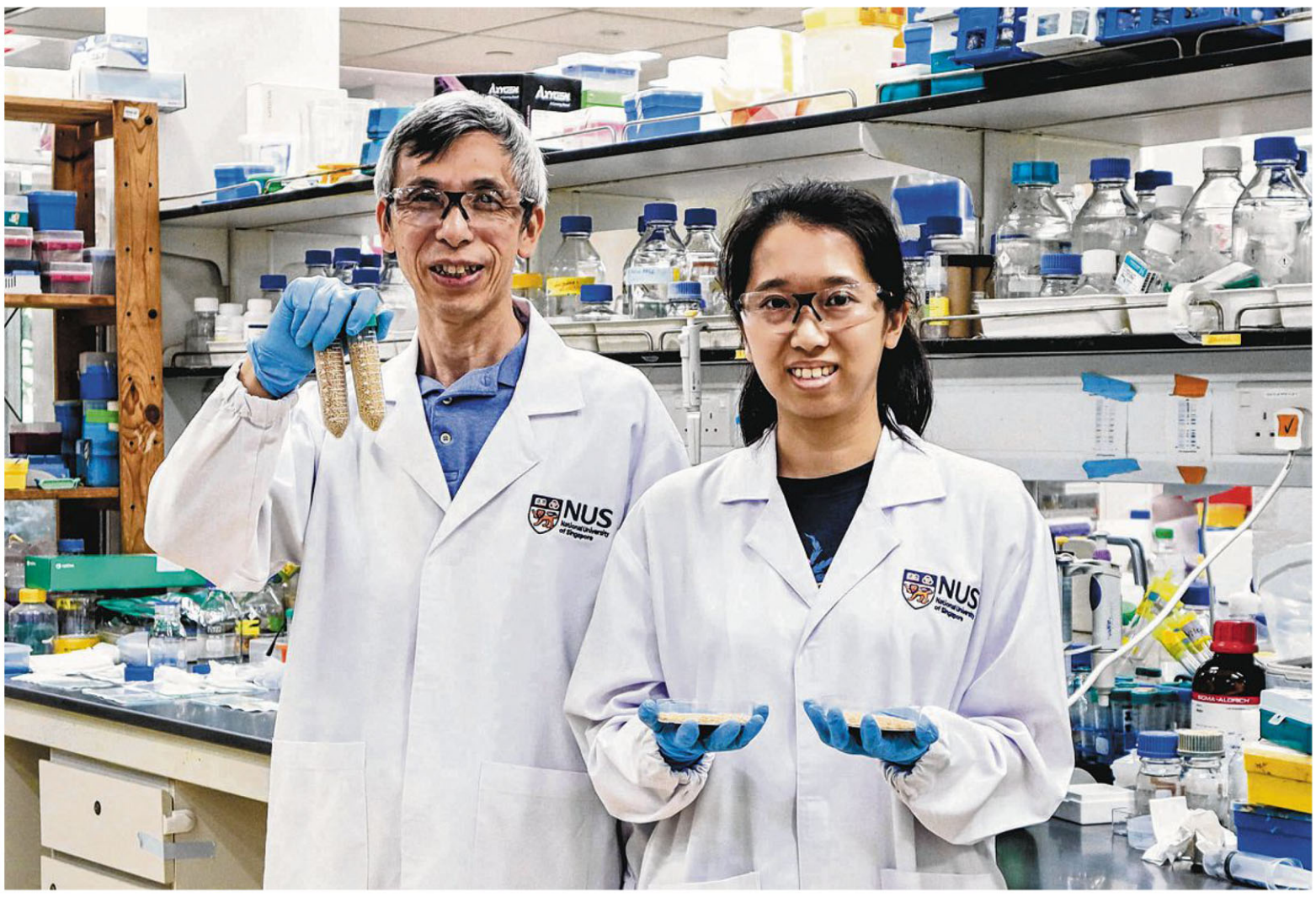
YANG DAIWEN, professor from the Department of Biological Sciences at the NUS Faculty of Science.



Yang Daiwen (far left) and Hong Hui Yee from the NUS Department of Biological Sciences and their research team developed an oral vaccine that can be mixed into fish feed to protect farmed fish from the nervous necrosis virus. PHOTO: NATIONAL UNIVERSITY OF SINGAPORE