Could plant vaccines save the poultry industry?

The University of Pretoria (UP) and the Council for Scientific and Industrial Research (CSIR) have successfully developed a vaccine against avian influenza using tobacco plants, bypassing the many biosafety risks involved with using traditional live vaccine viruses.

In this world-first study, a virus-like particle (VLP) vaccine against bird flu in chickens was successfully produced and tested. This vaccine mimics an H6-subtype influenza virus, because a strain of H6N2 is endemic in South African chickens. H6N2 is the only influenza virus that the South African government allows vaccinations for.

The project was conceptualised by Professor Celia Abolnik, holder of the South African Research Chair Initiative in Poultry Health and Production in UP's Department of Production Animal Studies and the CSIR's Dr Maretha O'Kennedy, a lecturer in the same department. They co-supervised PhD candidate Tanja Smith in the laboratory and clinical study.

While avian influenza, or bird flu, is a virus that occurs naturally in birds, the virus spreads easily and rapidly. Poultry farmers need to ensure their flocks do not come into contact with wild birds in order to prevent outbreaks from occurring.

High costs of avian influenza

In 2017, a devastating outbreak of the H5N8 strain of avian influenza hit South Africa. Hundreds of thousands of poultry had to be culled, and according to the South African Poultry Association, this outbreak cost the poultry industry R954m. About 1,300 poultry farm workers lost their jobs as a result of the scourge. The effects on small-scale farmers and traders were devastating too. Food prices relating to poultry soared, with reports of egg prices in South Africa spiking by 16.9% from November 2016 to November 2017.

Shortly after the outbreak there was a decline in the production of eggs and chicken, forcing South Africa to rely on imported chickens to meet the demand for food. “Fortunately, the control measures that included culling infected flocks were able to contain and stop the spread of the virus in poultry in 2017, but there is always a chance that migratory birds could once again introduce a dangerous strain, and if the outbreaks became too widespread, vaccination may be the only way to protect the industry from total collapse,” said Prof Abolink.

She explained that the global avian influenza vaccine market remains dominated by live viruses grown in chicken eggs or cell cultures, subsequently inactivated using chemicals. Traditionally, vaccines are made from viruses that have been isolated from an outbreak and grown inside an egg or cell culture. The production of these vaccines is a lengthy process of adapting the viruses to grow to high concentrations in cells or eggs.

Mutations

Avian influenza, like most influenzas in both humans and animals, mutates at a rapid rate. Vaccines need to therefore be updated regularly in order for them to have effect. The World Health Organisation (WHO) advises that human influenza vaccines, for example, be updated annually, or their administration becomes ineffective. This is currently not happening with H6N2 vaccines available in the poultry industry.

Prof Abolnik said plants and bio-farming (a chemical-free method of farming that focuses on improving the microbiology as a way of increasing plant growth and produce yield) are, however, the future. Using plants eliminates many of the risks such as contamination that make current vaccines an issue. “No live virus is involved in any stage of our production of the plant-produced VLP vaccines.” The greatest advantages of producing poultry vaccines in plants is the safety and the speed with which new vaccines can be designed and produced to combat fast-evolving viruses like avian influenza.”

Plants are easily infiltrated with an agrobacterium which introduces the DNA to enable the plant to produce the proteins that are then used in the vaccine. “The plant isn’t permanently modified in any way, so it’s not as if we are creating a dangerous seed that could escape into the environment.” It is also scalable and can make a lot of vaccine. We demonstrated that just one kilogramme of plant leaf material can produce enough vaccine to immunise up to 30,000 chickens,” she said.

Less expensive

Apart from the scalability, safety and speed of the production of plant produced VLP vaccines, they are also far less expensive than traditional vaccine production. These vaccines can also be made quickly – only requiring the RNA sequence of the virus. This is an added benefit to the poultry industry, given vaccines need to be updated regularly.

Apart from these benefits, plant produced VLP vaccines are also more humane as it eliminates the need to inject a live virus into a growing chicken egg embryo. It is also difficult to source chicken eggs to make traditional vaccines as pathogen-free flocks are required. “There are not many companies that can provide the standard of eggs required to have a large-scale vaccine production facility,” said Prof Abolnik.

While facilities would be needed to cultivate the plants, it is a sustainable option of vaccine production with several large-scale bio-farms already in the planning phases in South Africa. “I honestly cannot think of any negatives to having a plant-based vaccine on the market,” she said.

Although there are no plans to market this particular vaccine, Prof Abolnik’s study is proof of concept, proving that it does work. This vaccine is based on a 2016 virus so she would need to do further tests to see if this strain is representative of what is currently circulating in the field. “The vaccine registration process is also a lengthy one in South Africa, so we would need an expert to assist with this.”

Securing licences

However, this study is the first step in getting this breakthrough technology out there. The next step would be securing the licences to use the vectors to produce these types of vaccines commercially. Prof Abolnik’s current licence is for research purposes only.

She continues to look to this type of technology as the answer for other avian viruses that mutate quickly. “We want to see how many other viral families we can optimise virus-like particles to produce outbreak-tailored vaccines, for example the coronavirus that causes infectious bronchitis in chickens.”

And while there are commercial vaccines on the market for strains like H5N8 that work well (one of these vaccines was tested at UP in 2017 for a large international vaccine manufacturer), mass-produced international vaccines would not be as effective as a vaccine that is exactly antigenically matched to the outbreak in a specific geographic region. Plant-produced vaccines can be highly tailored to a specific regional problem and scaled accordingly, she said. “This H6 vaccine was a proof of concept study, but the student successfully optimised the entire production process, which is invaluable for future vaccine production,” said Prof Abolnik.