Expert Panel on
Livestock Methane

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Potential of methane vaccines for reducing livestock emissions

Summary

This briefing summarises the latest science on the potential of methane vaccines as a mitigation tool in the livestock sector. Livestock accounts for up to 32% of methane emissions from human activity.

- Methane vaccines, which have been researched for almost three decades, aim to reduce methane emissions from ruminant livestock such as cows, goats and sheep.
- Specific microorganisms in the stomachs of cows, goats and sheep produce methane as a by-product of the breakdown of fibrous plant materials eaten by the animal. A methane vaccine would trigger the production of antibodies that suppress the activity of these microorganisms, resulting in less methane being expelled..
- While 'test-tube' studies have shown some promising results, consistent reductions in emissions have not yet been achieved in animal trials.
- Vaccine development faces a number of key challenges, including:
    - Triggering the production of specific antibodies that can substantially disrupt methane production
    - Ensuring that an adequate number of these antibodies reach the animal's stomach and are produced with sufficient frequency that they continuously reduce methane
    - Developing a vaccine that is effective across different animal species, diets and production systems.
- If successful, a vaccine could have advantages over other methane mitigation technologies due to its safety and convenience.
- It is likely to take between five and 10 years for a methane vaccine to become commercially available

How would a methane vaccine work?

Methane vaccines, which have been researched for almost three decades, aim to reduce methane emissions from ruminant livestock such as cows, goats and sheep. Microorganisms called methanogens, found in the stomachs of ruminants, produce methane through a process called enteric fermentation. Fibrous cellulose-rich plant materials are broken down by a variety of microbes into volatile fatty acids - which the animal uses for energy - and hydrogen, which the methanogens use to produce methane, which is expelled by the ruminant largely through belching. Methane is a potent greenhouse gas with significant near-term warming potential.

Unlike traditional vaccines that target bacteria or viruses to prevent disease, methane vaccines work by stimulating the animal's immune system to produce antibodies that attack methanogens in the stomach. By reducing the activity of methanogens, a vaccine could lower the amount of methane released into the atmosphere by the animal. An effective vaccine would target around a minimum 20% reduction in methane without impacting productivity. While ‘test-tube’ studies have shown some promising results, an appropriate level of methane reduction has not yet been achieved in animal trials.

Advancements in methane vaccine development have been reported in the scientific literature over the last two decades. However, because it is a new type of vaccine – targeting methanogenic microbes in the rumen rather than a typical pathogen – several steps in the vaccine development process, including antigen selection, immune response assessment and the delivery method, still need to be established and optimised. The lack of established frameworks and research for this kind of immunological intervention also makes it challenging to predict how long it may take for an effective vaccine to be produced.

What is needed to produce an effective vaccine?

The development of a vaccine requires a number of steps that are aimed at assessing its effectiveness, safety and scalability. The vaccine must target methanogens in livestock stomachs across different species and regions. A 2015 study found similar microbial communities in 32 ruminant and camelid animal species across 35 countries, suggesting a universal vaccine might work.

A key step in designing a methane vaccine is to identify specific molecules, called antigens, on the surfaces of methanogens that the animal’s immune system can recognise. These antigens – many of which are common across methanogens – should trigger the production of antibodies that disrupt methanogens when the animal is vaccinated. Only specific antigens will successfully stimulate the animal’s immune system. If a suboptimal antigen is chosen, the immune response may be weak, leading to insufficient reductions in methane production. While a range of possible antigens have been tested that show potential, selecting the right antigen remains a focus of methane vaccine development.

Another important step in developing an effective methane vaccine is to test whether the selected antigen produces sufficient antibodies in a vaccinated animal. As the cells in the stomach of ruminants do not deliver antibodies, they need to be delivered to the stomach via the animal’s saliva and must bind to the methanogens to stop them from producing methane. Studies have shown that while antibodies are produced in the saliva and plasma of vaccinated cattle, goats and sheep and delivered to the stomach via saliva, there may not be enough antibodies present in the saliva to have an effective result.

Once in the stomach, these antibodies may be quickly broken down by bacteria, reducing their ability to target methane-producing microbes. An effective vaccine would therefore also require the sustained release of enough antibodies to ensure long-term efficacy. The formulation of methane vaccines can be enhanced to ensure that sufficient levels of antibodies are supplied to the stomach, such as by adding ingredients – such as adjuvants – that improve the immune response.

Once it is confirmed that a selected antigen and adjuvant combination increases antibody production, the next step is test-tube or *in vitro* studies, whereby the antibodies’ impact on methane production is assessed. Test-tube studies have confirmed that vaccination can reduce methane production by up to 69%. However, a wide range of values have been recorded across studies, with some reporting reductions of as little as 12.8%, no reduction at all, or even increased methane production.

Once it is confirmed that methane is inhibited in a lab setting, animal-based, or *in vivo*, studies, where live animals are vaccinated, can be carried out. However, a positive result in a test-tube study does not necessarily guarantee a positive result in a live animal study – and several animal-based studies have reported unsuccessful results.

The best result reported thus far in a published scientific study is a 12.8% reduction in methane production in sheep at four to six weeks after immunisation. Once these results were corrected to account for differences resulting from the amount of food consumed by the sheep, the result was a 7.7% reduction in methane. A later analysis tested the same vaccine but did not detect any decrease in methane. Another vaccine, which was developed based on an assessment of the genetic diversity of methanogens in sheep, was tested in an animal-based trial but did not result in methane inhibition despite there being high levels of antibodies in the animals' saliva, stomach and blood.

Recently, US-based startup ArkeaBio reportedly developed a vaccine prototype that reduced methane emissions by 12.9% in 10 cows over a period of 105 days. In a radio interview, the CEO of ArkeaBio said the prototype is achieving a "13-15% reduction over an extended period but both the efficacy and the timeline that it remains in effect for aren't yet long enough". However, the experimental conditions and results have yet to be published in a scientific journal, making it difficult to assess their validity. More longer-term trials are needed to ensure that the methane reduction effects are long lasting.

Factors contributing to variability in results

A number of factors could explain the large variation in results among studies and the lack of reproducibility in animal trials of the vaccine, including:

- The type of methanogen species targeted
- Variability in immune response among different species at different locations
- The age of the animal
- The vaccine formulation and type of antigen used
- The vaccination schedule, including when vaccine boosters were administered
- The diet of the animal
- The method used to measure methane levels.

Potential advantages of a vaccine over other methane inhibition strategies

A major obstacle to rolling out other technologies for reducing methane emissions from livestock, such as feed-based methane inhibitors, is that the inhibitor needs to be constantly supplied, which is a challenge for animals raised on pasture. A methane vaccine could overcome this obstacle because it potentially would only need to be administered infrequently. Other methane reduction technologies may also require farmers to alter their farming practices, such as how they feed their animals, presenting a potential inconvenience as well as an additional expense. As farmers already routinely vaccinate their animals against various diseases, introducing an additional vaccine should not present a challenge. Vaccination is also an auditable practice that can be used in combination with other strategies. As methanogens are similar across different species, a single vaccine should also be applicable to different ruminants. Furthermore, vaccines are subjected to rigorous testing to ensure their safety, thereby reducing concerns around the use of other technologies, such as bromoform, which might be unsafe for animals.

How long do we need to wait for a methane vaccine?

The development of a typical veterinary vaccine - such as one based on well-known technology - from the lab phase, or preclinical development phase, to trials and regulatory approval typically takes three to six years. Once a vaccine has entered the clinical trial phase - which includes a series of systematic studies to ensure that a vaccine is safe and effective, and to determine the dose - regulatory approval can usually be obtained within two years. This approval rests on confirmation that the vaccine is safe and effective. For an atypical vaccine like a methane vaccine, this timeline could be longer due to the additional complexities discussed above.

Several organisations are researching a methane vaccine for livestock:

- The Pirbright Institute and Royal Veterinary College in the UK are working with New Zealand's AgResearch to improve the scientific understanding of antigens in order to provide a foundational understanding for vaccine development, though the institute is not developing a vaccine.
- The New Zealand Agricultural Greenhouse Gas Research Centre (NZAGRC) is also working with AgResearch and the Pastoral Greenhouse Gas Research Consortium (PGgRc) to identify suitable antigens and develop a vaccine.
- AgriZero and the New Zealand Agricultural Greenhouse Gas Research Centre (NZAGRC) are funding Lucidome Bio - a new venture aiming to produce a methane vaccine.
- ArkeaBio, a start-up backed by Breakthrough Energy Ventures, has developed a prototype vaccine that has reportedly reduced methane emissions by 12.9% in 10 cows over 105 days. A second trial is ongoing, according to scientific news portal Shining Science, although the company has not released any public information.

According to AgResearch scientists, once a suitable antigen has been found, the vaccine development process, including regulatory approval, could still take a further 10 years. By contrast, Arkea Bio's CEO Colin South said in an interview with Radio New Zealand that the company's prototype vaccine could be commercially ready within three to five years. The lack of available scientific data for the company's trials makes it difficult to evaluate the likelihood of vaccine deployment on such a short timescale.

The Expert Panel on Livestock Methane works together on a voluntary basis to bring the latest peer-reviewed science to the media and policy debate about livestock and climate change.