

Review Article

SMART DELIVERY OF ANTIPARASITIC VACCINES OF VETERINARY IMPORTANCE-A REVIEW

**S.T. Bino Sundar^{1*}, T.J. Harikrishnan², Bhaskaran Ravi Latha¹,
G. Sarath Chandra³ and T.M.A. Senthil Kumar⁴**

¹Department of Veterinary Parasitology, Madras Veterinary College, Chennai-7, India

²Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Madhavaram Milk
Colony, Chennai-51, India

³Pharmacovigilance Laboratory for Animal Feed and Food Safety, TANUVAS

⁴Department of Animal Biotechnology, Madras Veterinary College, Chennai-7, India

E-mail: binosundar.s.t@tanuvas.ac.in, microfilbino@gmail.com (*Corresponding Author)

Abstract: Protection of domestic animals and human beings against parasitic infections remains a major challenge in most of the developing countries, especially in the surge of drug resistant strains. In this circumstance vaccination seems to be the sole practical strategy to combat parasites. Potent delivery systems can tremendously improve the effectiveness of vaccines by accelerating the immune responses and use of smart or “needle-free technologies” pave way for successful vaccine delivery.

Keywords: Antiparasitic vaccines, smart delivery systems.

Introduction

Vaccines play a major role in the control of parasitic diseases. Delivery systems of vaccines are very much important in order to induce an effective protective immunity by the vaccines especially to ensure the slow release of vaccines. Several vaccine delivery systems include the use of gene guns, in-ovo vaccines, gel spray vaccines, trans dermal patches, emulsions, microparticles, nanoformulations, immune-stimulating complexes, liposomes and edible vaccines to name a few. This article reviews the various delivery systems available for the smart delivery of antiparasitic vaccines with their commercial uses, advantages and limitations including the methods which are still in research and experimental trials.

Desirable qualities of a smart vaccine delivery system include the following

A smart vaccine delivery system should have the desirable qualities like Less labor intensive, User friendly design, Speed, Painless or Needle free, Low adverse reactions, Sustained release/Pulsatile release, Less stress to animals, birds or human, Effective delivery of

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antigens, Better stimulation of immune responses, Abolition of the “Fear factor” about vaccines, Improved shelf life, Environment friendly, Cost effective, Non toxic and Readily biodegradable nature. Following are the various smart delivery strategies for vaccines against parasites of veterinary importance.

1. In ovo vaccination

It is an automated method that can deliver vaccines to a chick while it is still in the egg. Vaccines are injected directly into the eggs in hatchery by machines at embryonation day 18. In ovo vaccines are available for chicken coccidiosis. Inovocox® (Pfizer) is a live vaccine containing oocysts of *Eimeria acervulina*, *Eimeria maxima* and *Eimeria tenella*. It offers protection to the bird in a single dose against three of these most common species of coccidia. Handling Capacity of fully automated machine is 70,000 eggs/hour and semi automated machine is 12,000-20,000 eggs/hour. Advantages include Early generation of Immunity against coccidiosis, Minimal interference from maternally derived antibodies, Reliable and accurate delivery of vaccine under carefully controlled and hygienic conditions, Stimulates innate and adaptive immune responses, Less labour intensive and less prone to human error, Chick handling is minimised, reducing bird stress and improving bird health, Quick transfer of birds out of hatchery and Use of this technique to deliver recombinant DNA vaccines is under way

2. Gel Spray vaccines

In this method vaccine is evenly dropped on day old chicks kept in crates in a gel form by automated dispenser machines. The vaccine is absorbed when the birds ingest the coloured gel droplets containing the vaccines. Vaccine is dispensed uniformly on the crate contributing to good vaccine take. Gel Spray vaccines are available for chicken and turkey coccidiosis (Ceva, France). They are live vaccines containing oocysts. Immucox I® - *E. acervulina*, *E. maxima*, *E. necatrix*, *E. tenella* and Immucox II® - *E. acervulina*, *E. maxima*, *E. necatrix*, *E. tenella*, *E. brunette* for chicken and Immucox-T® - *E. adenoeides*, *E. meleagrimitis* for turkeys. Once the vaccine is sprayed over the chicks, they become quite wet and start pipping and rubbing against each other and this brings the vaccine into contact with the upper digestive and mucosal tissue including the eyes, nostril and mouth. Vaccine enters body by absorption and ingestion. Since pecking is a natural behavior of chicks, the coloured gel droplets are preened off within minutes and the oocysts suspended in the gel droplets are ingested. Advantages include Unique gel dispenser system and uniform suspension, Accurate dosage and easy consumption, Precise droplet size and volume for best vaccine uptake,

Constant flow rate and pressure, Speed, User friendly design, Oocysts are kept in suspension by the gel diluent, All coccidian species are evenly distributed during application, Visibility to chicks and Will not soak feathers. Disadvantages include Vaccine wastage (on feathers and crate floor), Quick drying of vaccine, Chances of uneven vaccine distribution, Chicks missed the vaccine have a chance of getting infected, Sometimes drop in temperature of chicks after vaccination. Vaccine candidates incorporated in gelatin beads is also used for intestinal coccidiosis

3. Tick Bite Patch™: Transdermal delivery system for anti-tick vaccines

It is a biopolymer based, user-friendly, sustained release, programmable transdermal vaccine delivery system based on the phenomenon of acquired tick resistance. In this mode of vaccine delivery initially peptide antigens (small portions of proteins) present in tick saliva that can be used as a vaccine are identified. The identified tick salivary gland gene sequences are screened using a computer-based process called immunoinformatics to predict their interaction with human T-cells and stimulate an immune response. Results have indicated that some of the tick spit proteins have antigenic properties and can be used as potential vaccine candidates (>500 tick spit proteins identified). Some of them also induces immediate hypersensitivity reactions that alert and help people to get rid of biting ticks. The potential proteins/peptides are embedded into a programmable patch can mimic the natural salivation-sucking cycle that ticks use while feeding, all while delivering synthetic peptides. These antigens stimulate effective immunity in people so that when they encounter a tick bite, their body reacts to reject the tick and combat any disease-causing microbe that the tick may transmit. Component of tick saliva stimulates an immune response and that the tick-bite site became inhospitable to the entering pathogens, preventing infection. Tick Bite Patch contains a microchip, tiny battery and elusive vaccine molecules as a cocktail. These patches are called smart patches because they can be programmed to switch on and off – to mimic the intermittent spit and suck process of tick blood feeding, and effectively deliver the synthetic tick peptides. Lyme disease, babesiosis and anaplasmosis are covered in this patch.

4. Gene Guns

A gene gun or a biolistic particle delivery system, a device for injecting cells with genetic information intradermally. This technique is often simply referred to as bioballistics or biolistics. This device is able to transform almost any type of cell and is not limited to genetic material of the nucleus, it can also transform organelles, including plastids. Gene guns are used to deliver DNA vaccines into the body of human or animals in a split second. DNA

dissolved in salt water is atomized into fine droplets that find their way into the cells. Gene gun vaccination has successfully been used to prevent infection of mice with the rodent malaria strain *P. berghei* and has been employed in a macaque model of human *P. falciparum*. The *Schistosoma mansoni* nucleic acid vaccine, Sm23 has been successfully administered to mice using gene gun. A merozoite surface protein-1 cDNA with IL-12 expression plasmid confers protection against lethal *Plasmodium yoelii* in A/J mice using gene gun. A single protein-producing gene from *Cryptosporidium parvum* tailored with a regulatory gene was injected into the mammary glands of pregnant sheep and antibodies were produced in milk. These are expensive, chances of cellular damage and insertion of DNA into undesired cells are problems.

5. Microseeding/Microneedles/Coated Microtines

It is a method of vaccine delivery wherein plasmid DNA solution is delivered directly to the target cells of the skin by a set of oscillating solid microneedles driven by a modified tattooing device. It is a simple and effective method. This is a new needle free vaccine-delivery patch based on hundreds of micron-scale needles made of sugar or carboxymethylcellulose that dissolve into the skin in 5 min and deliver the vaccine. Solid microneedles pierce through the outermost layers of the skin leaving open pores after which the vaccines are delivered into the skin. Various types of microneedles include solid microneedles, coated microneedles, dissolving microneedles and hollow microneedles. Mice were immunized with Sm23, an integral membrane protein of *Schistosoma mansoni* by microseeding. Antibody isotypes analysis revealed that microseeding elicited mainly IgG2a and IgG2b antibodies, with relatively low levels of

IgG1 and IgG3. Advantages include Dried live vaccine within the microneedles remains stable and effective at room temperature, Overcoming issues concerning vaccine transportation, Vaccine could be self-administered, As the needle simply dissolves, the technology also overcomes the concerns over safe disposal, Potential for more of the public to be open to vaccination- a potentially painless alternative to hypodermic needles. But this is limited to skin dwelling or intracellular parasites

6. Nanovaccines

Nanovaccines contain nano-sized particles of a biodegradable polymer, which encapsulates an antigen. Nanoparticles (NPs) such as dendrimers, polymeric NPs, metallic NPs, magnetic NPs and quantum dots have emerged as effective vaccine delivery systems. Malarial vaccines are delivered using this technology and dendrimer based delivery is used for *Schistosoma*

japonicum. Nanogels, Nanospheres, Nanocapsules, Micelles, Dendrimers, Nanoclays, Nanopowders, Nanofibres and Nanotubes are other forms of nanoparticle based delivery systems.

7. Edible vaccines/Green vaccines for parasitic diseases

Plants are a promising system for the development of edible vaccines as they can be genetically engineered to express parasitic antigens and to produce vaccines against various diseases. In *Fasciola hepatica* the candidate antigen is Cysteine Protease, a 981 nucleotide cDNA fragment encoding the catalytic domain of the cysteine protease of *F. hepatica* transfected into lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). In *Schistosoma japonicum*, candidate antigen is Sj23 gene of *S. japonicum*, transfected into *Medicago sativa* (Alfaalfa) through Agrobacterium. In *Taenia solium*, candidate antigens are three synthetic peptides, KETc1, KETc12 and GK1 consisting of 12, 8 and 18 amino acids, respectively (designated S3Pvac-the only field tested vaccine). Papaya was selected to express S3Pvac. In *Echinococcus granulosus*, candidate antigen is EG95, a highly immunogenic oncosphere antigen and the only field trial-tested vaccine candidate against hydatidosis (99% protection in sheep and goats).EG-95 expressed in Alfa alfa leaves. In *Ascaris suum*, candidate antigen is 16-kDa antigen (As16) of *A. suum* L3.This antigen was expressed as a chimeric fusion protein with B subunit of cholera toxin (CTB) in rice endosperm under the control of endosperm-specific glutelin-GluB-1 promoter. In *Eimeria tenella*, candidate antigens are EtMIC1 and EtMIC2. One of the microneme proteins, EtMIC2 of *E. tenella* is expressed in tobacco leaves.

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