ÁREA PECUARIA

VACCINES FOR GASTROINTESTINAL PARASITES, A PILLAR OF PREVENTIVE MEDICINE IN VETERINARY PRACTICE: SYSTEMATIC REVIEW

VACUNAS PARA PARÁSITOS GASTROINTESTINALES, UN PILAR DE LA MEDICINA PREVENTIVA EN LA PRÁCTICA VETERINARIA: REVISIÓN SISTEMÁTICA

Vargas, Lina M.; Prieto, Laura D.; Baquero, Mónica M.; Corredor, Wilson; Alcantara-Neves, Neuza M.; Jaramillo-Hernández, Dumar A.

Lina M. Vargas
lina.vargas@unillanos.edu.co
University of the Llanos, Villavicencio, Meta, Colombia, Colombia

Laura D. Prieto
laura.prieto.prieto@unillanos.edu.co
University of the Llanos, Villavicencio, Meta, Colombia, Colombia

Mónica M. Baquero
mbaquero@uoguelph.ca
Ontario Veterinary College, University of Guelph, Ontario, Canada, Colombia

Wilson Corredor
wilson.c.95@gmail.com
Pontificial Javeriana University, Bogota, Colombia, Colombia

Neuza M. Alcantara-Neves
neuzalcantara@gmail.com
Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil, Colombia

Dumar A. Jaramillo-Hernández
dumar.jaramillo@unillanos.edu.co
Animal Sciences School, University of the Llanos, Villavicencio, Meta, Colombia, Colombia

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Abstract: Contextualization: The antiparasitic resistance caused by the indiscriminate use of anthelmintic drugs for the control of gastrointestinal parasites in production animals and pets, has become one of the biggest problems in animal health. For this reason, the use of vaccines could benefit animal health and welfare by controlling emerging zoonotic diseases and foodborne pathogens of animal origin, thus improving public health.

Knowledge gap: It is relevant for professionals in veterinary science to know the clinical trials of experimental vaccines for controlling certain gastrointestinal parasites. This way, they can be at the forefront of the next available technological products and so, be able to control this menace to the animal health and public health.

Purpose: To do a systematic review of clinical trials for experimental vaccines in production animals and pets for diseases caused by gastrointestinal parasites of relevance in animal production and/or public health. Furthermore, it presents the current gastrointestinal antiparasitic vaccines commercialized in different countries and their prophylactic efficacy.

Methodology: PRISMA protocols were followed for this systematic review. Articles were obtained from scientific databases with the following keywords: vaccines, clinical trials, commercial vaccines, parasites control, gastrointestinal nematodes, gastrointestinal cestodes, gastrointestinal protozoa, *Ascaris suum*, *Ancylostoma caninum*, *Cooperia oncophora*, *Echinococcus granulosus*, *Eimeria* spp., *Giardia lamblia*, *Haemonchus contortus*, *Osteortagia osteortagi*, *Taenia solium* and *Teladorsagia circumcincta*. Only clinical trials of gastrointestinal antiparasitic vaccines in birds, pets, pigs and ruminants were included in this analysis, as well as commercial vaccines currently available for these same parasites.

Results and conclusions: Even though there are important clinical trial studies of vaccines in these animal species (n=101) reported between 1964 to 2020, only five parasites can be prevented/controlled with commercial vaccines

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used in veterinary medicine: *Haemonchus contortus* and *Echinococcus granulosus* in ruminants, *Taenia solium* in pigs, *Eimeria* spp. in birds and *Giardia lamblia* in dogs (e.g., Cysvax™, Barbervax®, Providean® Hidatil EG95, CocciVac® and GiardiaVax™). It is expected that, with the development of bioinformatics and methodologies such as reverse vaccinology, this immunoprophylactic and immunotherapeutic range will be extended as to control these parasitic agents of great importance in human and animal health.

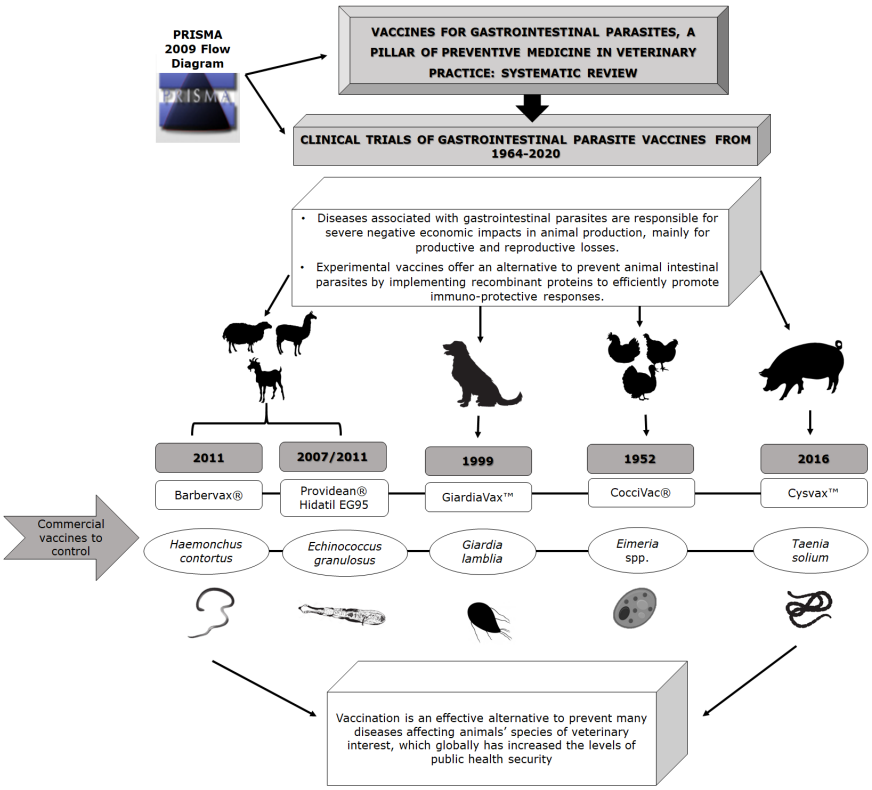
Keywords: clinical trial, immunoprophylaxis, gastrointestinal parasites, vaccination.

Resumen: Contextualización: La resistencia a los antiparasitarios provocada por el uso indiscriminado de antihelmínticos, para el control de parásitos gastrointestinales en animales de producción y mascotas, se ha convertido en uno de los mayores problemas en salud animal y pública. Por esta razón, el uso de vacunas podría beneficiar la salud y el bienestar de los animales al controlar las enfermedades zoonóticas y los patógenos de origen animal transmitidos por los alimentos.
Vacío del conocimiento: Es relevante para los profesionales en ciencias veterinarias conocer los estudios clínicos de vacunas experimentales para el control de ciertos parásitos gastrointestinales y de esta forma, estar a la vanguardia de próximos productos tecnológicos disponibles.
Propósito: Revisar sistemáticamente resultados de ensayos clínicos de vacunas experimentales en diferentes especies animales de producción y compañía, para parásitos gastrointestinales de relevancia en la producción animal y/o salud pública. Además, presentar el estado del arte de las vacunas antiparasitarias gastrointestinales comercializadas en diferentes países y su eficacia profiláctica respectiva.
Metodología: En esta revisión sistemática siguió la metodología del protocolo PRISMA. Se obtuvieron artículos de bases de datos científicas con las siguientes palabras clave: vacunas, ensayos clínicos, vacunas comerciales, control de parásitos, nematodos gastrointestinales, cestodos gastrointestinales, protozoos gastrointestinales, *Ascaris suum*, *Ancylostoma caninum*, *Cooperia oncophora*, *Echinococcus granulosus*, *Eimeria* spp., *Giardia lamblia*, *Haemonchus contortus*, *Osteortagia osteortagi*, *Taenia solium* y *Teladorsagia circumcincta*. En este análisis solo se incluyeron ensayos clínicos de vacunas antiparasitarias gastrointestinales en aves, mascotas, cerdos y rumiantes, así como vacunas comerciales actualmente disponibles para estos mismos parásitos.
Resultados y conclusiones: Aunque existen importantes estudios de ensayos clínicos de vacunas en estas especies animales (n=101) reportados entre 1964 y 2020, solo cinco parásitos pueden prevenirse/controlarse con vacunas comerciales utilizadas en medicina veterinaria: *Haemonchus contortus* y *Echinococcus granulosus* en rumiantes, *Taenia solium* en cerdos, *Eimeria* spp. en aves y *Giardia lamblia* en perros (por ejemplo, Cysvax™, Barbervax®, Providean® Hidatil EG95, CocciVac® y GiardiaVax™). Se espera que, con el desarrollo de la bioinformática y metodologías como la vacunología inversa, este abanico inmunoprofiláctico e inmunoterapéutico se amplíe en el

control de estos agentes parasitarios de gran importancia en la salud humana y animal.

Palabras clave: Ensayo clínico, inmunoprofilaxis, parásitos gastrointestinales, vacunación.

GRAPHIC ABSTRACT



authors

1. INTRODUCTION

Is urgent to develop vaccines against parasites for domestic animals because of: 1) resistance of parasites to conventional pharmacological treatments; 2) lack of effective anti-parasitic drugs and 3) the presence of chemical residues in products for human consumption (Emery et al., 1993; Woods et al., 2011).

Diseases associated with gastrointestinal parasites are responsible for severe negative economic impacts in animal production, mainly for productive and reproductive losses (Sharma et al., 2015). Parasitic infestations affect animal production in terms of health and welfare, for this reason, control measures should be implemented to reduce or mitigate this impact. The use of vaccines could benefit animal health and welfare by controlling emerging zoonotic diseases and foodborne pathogens of animal origin, thus improving public health (Corwin, 1997; Innes et al., 2011).

It is relevant for professionals in veterinary science to know the clinical trials of experimental vaccines for the control of certain gastrointestinal parasites and, in this way, to be at the forefront of the next available technological products to control this thread to the animal health and public health. On the other hand, the

usual veterinary medical practice has important gaps in the commercial offer of antiparasitic vaccines for the control of gastrointestinal parasites in production animals and pets.

Experimental vaccines offer an alternative to prevent animal intestinal parasites by implementing recombinant proteins to efficiently promote immuno-protective responses. These vaccines have been classified as 1) hidden antigens (i.e., those not recognized by the host's immune system), that are generally found in the parasite's intestine and 2) natural antigens, which are expressed during the infection process and identified by the host (Jenkins, 2001; Newton et al., 2003).

This manuscript aims to review results of clinical trials for experimental vaccines (in different production animals and pets) to prevent certain diseases caused by gastrointestinal parasites that affect animal production and /or public health. Furthermore, this research presents the state of the art of gastrointestinal antiparasitic vaccines commercialized in different countries and their prophylactic efficacy.

2. METHODOLOGY

This systematic review followed the PRISMA protocols (Moher et al., 2009). In general terms, a bibliographic search that identified possible articles for their inclusion, based on search keywords and pre-established inclusion criteria, was developed. This process is presented through the figure 1, PRISMA flow chart.

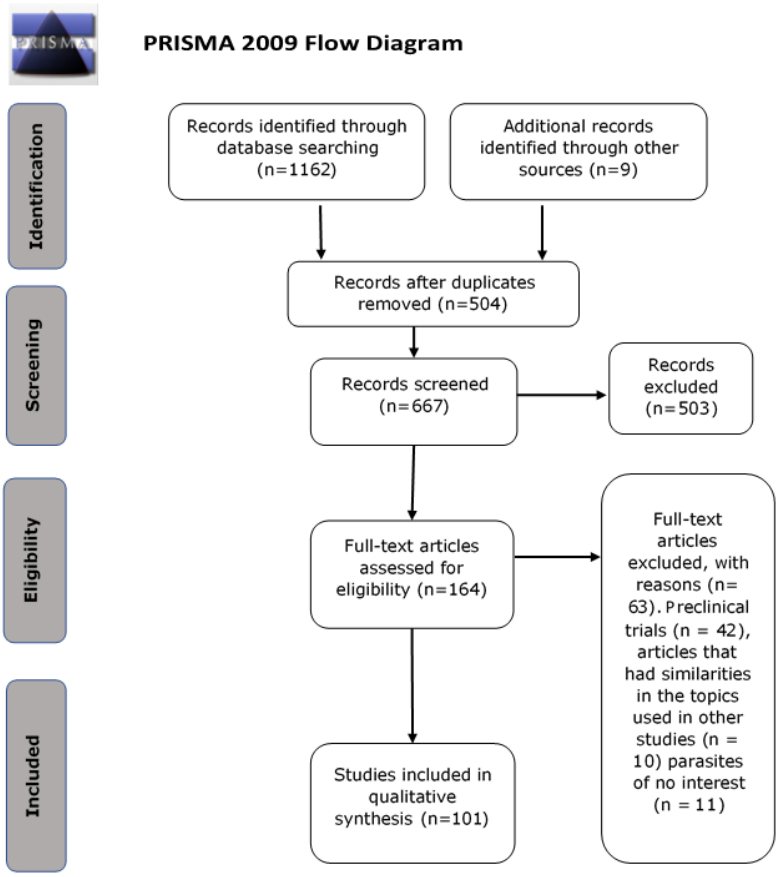


FIGURE 1
PRISMA flow diagram
authors

Search strategy for study identification

The search was based on four scientific platforms: PubMed (http://www.ncbi.nlm.nih.gov/pubmed/), Science Direct http://www.sciencedirect.com/), Scientific Electronic Library Online (SciELO: https://scielo.org/en) and Scholar Google (Scholar Google: https://scholar.google.com/). The keywords used for identifying the potential articles were: vaccines, clinical trials, commercial vaccines, parasites control, gastrointestinal nematodes, gastrointestinal cestodes, gastrointestinal protozoa, *Ascaris suum*, *Ancylostoma caninum*, *Cooperia oncophora*, *Echinococcus granulosus*, *Eimeria* spp., *Giardia lamblia*, *Haemonchus contortus*, *Osteortagia osteortagi*, *Taenia solium* and *Teladorsagia circumcincta*.

Eligibility criteria

We used the following inclusion criteria: 1. Only specific articles about these parasites that are harmful for production animals or pets, as well as their impact on public health: nematodes (*Haemonchus contortus*, *Teladorsagia circumcincta*, *Osteortagia osteortagi*, *Cooperia oncophora*, *Ancylostoma caninum* and *Ascaris suum*); cestodes (*Taenia solium* and *Echinococcus granulosus*); protozoa (*Giardia lamblia* and *Eimeria* spp.). 2. Clinical trials of gastrointestinal antiparasitic vaccines for the mentioned parasites in birds, pets, pigs, and ruminants; 3. Commercial vaccines currently available for these same parasites[1].

Data screening

The authors, divided in two working groups, read the titles, and in many cases, the abstracts of the articles retrieved from the databases consulted, according to keywords, and saved those that reported experimental studies of gastrointestinal antiparasitic vaccines in selected animal species (animal species for which the respective vaccine has been developed).

After the comparison of information between the two working groups, the articles chosen were read, then were included in the timeline reports of clinical trials (temporal analysis of the trials), and the data obtained by those in terms of levels of protection, for the parasitosis studied, were analyzed. It is important to clarify that, only two protozoa (*Giardia lamblia* and *Eimeria* spp.) were included in this study, given their importance for children's health and their drastic effects on poultry production (Bartelt & Platts-Mills, 2016; Gilbert et al., 2020). On the other hand, technical-commercial information is linked and extracted from the web pages of the pharmaceutical companies that produce the commercial antiparasitic vaccines discussed in this systematic review.

The other gastrointestinal parasites are mostly cestodes and nematodes. The last ones are the most studied because efficient mechanisms of prophylactic to control them, supported by vaccines, have been researched (Stutzer et al., 2018; Anvari et al., 2020; Britton et al., 2020; Ehsan et al., 2020; Sander et al., 2020). Regarding this, even though Toxocara spp. is a nematode with important effects on world public health in developed and developing countries, there are no clinical trials of vaccines for its control in canines (Jaramillo-Hernández et al., 2020).

3. RESULTS AND DISCUSSION

According to the search parameters initially proposed, a total of 1162 articles were found in the databases used in this study. Of those, 504 were repeated and were immediately separated. Subsequently, the remaining 667 scientific studies were reviewed to establish compliance with the inclusion and exclusion criteria pre-established. Only 164 articles, presumably, fulfilled some of the requirements.

After analyzing the results, it was established that 63 of these articles were studies about preclinical vaccine trials (e.g., using animal models of parasitic disease) or were studies in other parasites different from the interest of this study. So, in the end, a total of 101 articles about clinical phases of vaccine experimentation in poultry, pigs, ruminants, and pets (canines and felines) were included within the temporal analysis of experimentation and their antiparasitic protection. The period of the results reported is 1964 to 2020 (Figure 1).

The authors have presented these results by animal species or group of animal species (e.g., large and small ruminants), given the species-specific implications of the gastrointestinal parasites treated in this study. The results are organized under the subtitle "Advances in the development of vaccines for the control of gastrointestinal parasites in (...)". Likewise, the figure2 shows a time series of crucial experimental clinical studies that have determined the advances in prophylaxis and immunotherapy for the gastrointestinal parasite control in veterinary medicine. In the same way, under the subtitle "Gastrointestinal deworming vaccines currently commercialized in veterinary medicine", the existing commercial vaccines for the control of these gastrointestinal parasites were presented.

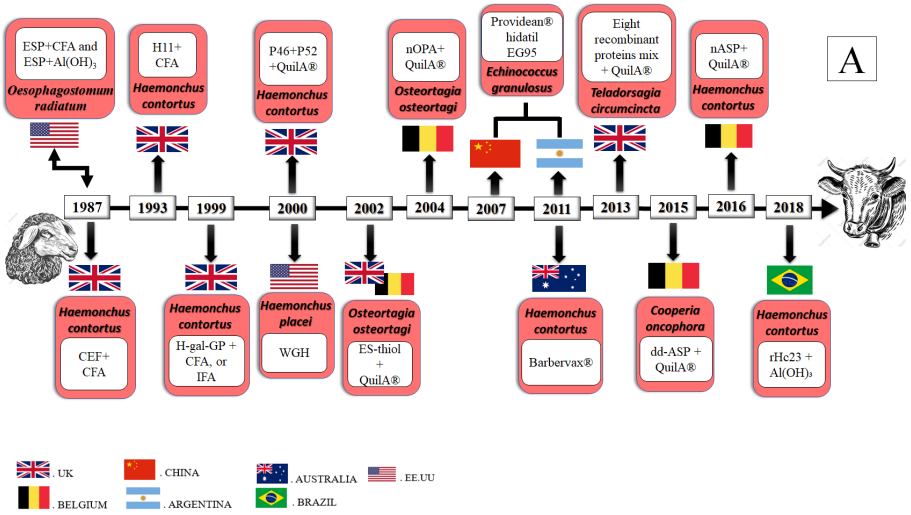


FIGURE 2

Timelines of clinical studies for the control of gastrointestinal parasites with their respective vaccines. This figure shows the animal species of interest; the year in which the study was executed; type of vaccine (antigen plus adjuvant) used; and the parasite to be controlled or eradicated and the country

Figure 2A: Timeline of the main clinical studies in large and small ruminant's main timeline.
Authors

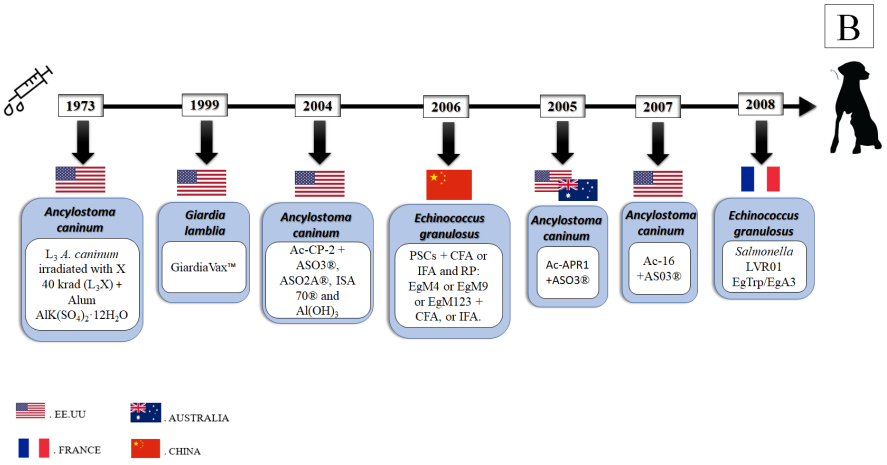


Figure 2B: Timeline of the main clinical studies in dogs.
Authors

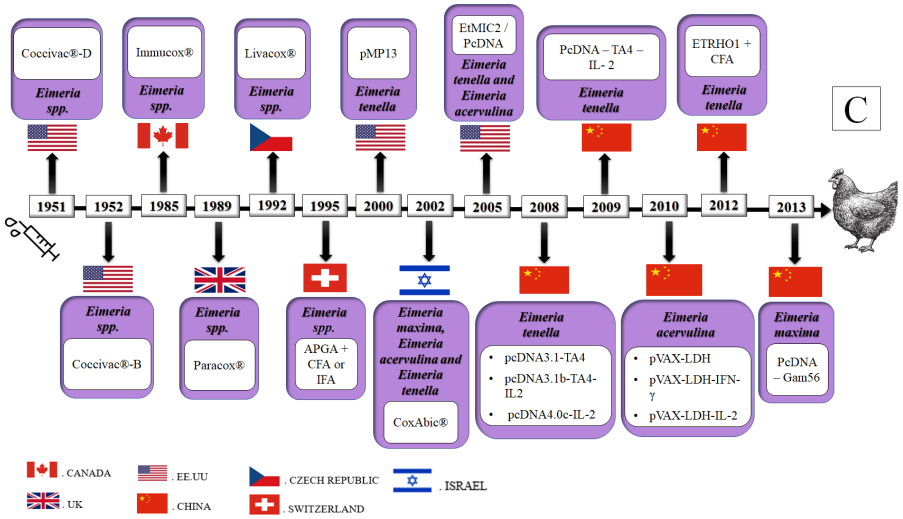


Figure 2C: Timeline of the main clinical studies in birds.
Authors

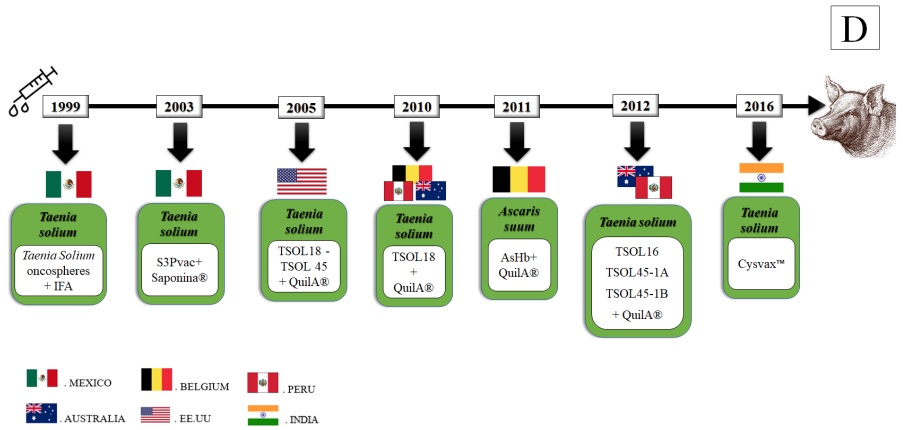


Figure 2D: Timeline of the main clinical studies in pigs.
Authors

Advances in the development of vaccines for the control of gastrointestinal parasites in domestic ruminants

Large and small grazing ruminants are continuously exposed to nematode infections. On the other hand, nematodes develop resistance to medicines, due to continuous anthelmintic treatments; this limits livestock production and represents a constant threat to animal welfare (Knox, 2000; Knox et al., 2003). The most important gastrointestinal parasites in ruminants are *Haemonchus contortus* (*H. contortus*) and *Teladorsagia circumcincta* (*T. circumcincta*) in sheep; *Osteortagia osteortagi* (*O. ostertagi*) and *Cooperia oncophora* (*C. oncophora*) in cattle. Due to the high cost of treatments and the potential anthelmintic resistance, a significant effort has been carried out in the discovery of vaccine candidates for parasite control (Dalton et al., 2001; Matthews et al., 2016). Table 1 summarizes a series of clinical trials in different experimental or production stages for gastrointestinal parasite control in ruminants.

TABLE 1
Clinical trials of experimental vaccines for the gastrointestinal parasites control in large and small ruminants

Parasite	Vaccine	Protection %		Vaccination schedule	Ref.
		Worm	Eggs (EPG)		
Osteortagia osteortagi	nASP + Quil-A®	-	59	Cattle 6-8 months old were immunized three times with 30 µg of nASP + 750 µg QuilA®, (IM at 3 weeks intervals). The control group received 750 µg of Quil-A®.	(Vlaminck et al., 2015)
Haemonchus contortus	rHc23 + Al(OH)3	70	80	6-month-old lambs divided into: group 1 and 2 received 50 µg and 200 µg of rHc23, respectively; + 1 mL Al(OH)3 (IM, on days 42, 28 and 14 before the challenge). Group 3 received 1 mL of Al(OH)3. Group 4 received QuilA® + rHc23 200 µg (IM on days 49, 28 and 7 prior to the challenge). Group 5 received QuilA® on the same days.	(González-Sánchez et al., 2018)
Haemonchus contortus	Contortin + CFA	78	-	Lambs between 60-150 days of age were distributed in different subgroups and treated with 20 mg of CEF + CFA (IM). Immunized at different time intervals. Control group received PBS + CFA.	(Munn et al., 1987)
Haemonchus contortus	H11 + CFA	74.2	>90	44-day-old lambs were divided in two groups. Group 1: received 3 doses of 70 µg of HII + 2 mL of PBS emulsified with 2 mL of CFA (at intervals of 3 to 4 weeks).	(Smith & Smith 1993)
Haemonchus contortus	P46+P52 + QuilA®	33	78	5-month-old sheep received 3 doses of 1 mL of 100 mg P46 + P52 + 5 mg of QuilA® (IM at 3-week intervals). The control group received PBS + QuilA®.	(Smith et al., 2000)
Haemonchus contortus	H-gal-GP + CFA, or IFA	40	69.7	5 - 6-month-old lambs applied 3 immunizations with H-gal-GP as follows. 1st: 4 doses of 0.5 mL of 100 µg of H-gal-GP + CFA (SC). 2nd and 3rd: 1 mL of 100 µg of H-gal-GP + IFA (IM at 3- and 6-weeks interval).	(Smith et al., 1999)
Osteortagia osteortagi	nOPA + QuilA®	-	60	8-month-old calves. They received three immunizations with 100 µg of nOPA + 750 µg of QuilA®. (IM at 3-week intervals). The control group received 750 µg of QuilA®.	(Vercauteren et al., 2004)
Osteortagia osteortagi	ES-thiol /QuilA®	18	60	7-month-old calves immunized three times with 100 µg ES-thiol + 700 µg QuilA® (IM, at 3-week intervals). Control group: Tris buffer + QuilA® (IM).	(Geldhof et al., 2002)
H. placei	WGH	53-72	>90	12-week-old calves were immunized with two doses of 100 µg WGH + 4 mL DS 5% in PBS (SC at 27-day interval). The control group received 4 mL of PBS.	(Siefker & Rickard, 2000)
Teladorsagia circumcita	8 recombinant protein + QuilA®	75	92	Lambs of 204-206 days of age got divided in 2 groups. Group 1: 3 doses of 400 µg Tci-ASP-1 + Tci-MIF-1 + Tci-TGH-2 + Tci-APY-1 + Tci-SAA-1 + Tci-CF1 + Tci-ES20 + Tci-MEP-1; + 10 mg of QuilA® (SC at 3 weeks intervals). Group 2: 3 doses of Urea + PBS + 10 mg of QuilA® (at the same interval as above).	(Nisbet et al., 2013)
Coopearia oncophora	dd-ASP + QuilA®	-	91	7-month-old cattle were divided into 2 groups. Group 1: 3 doses of 30 µg dd-ASP + 750 µg QuilA® (IM at 3 weeks interval). Group 2: 3 doses of 750 µg QuilA®.	(Vlaminck et al., 2015)
Oesophagostomum radiatum	ESP + CFA and ESP + Al(OH)3	23		Calves from 8-18 weeks of age were splitted in 2 groups. Group 1: 2 mg ESP + FCA (IM). 2 weeks later they received 2 mg ESP + Al(OH)3 (PI). Group 2: NaCl + CFA.	(Gasbarre & Douvres 1987)
Oesophagostomum radiatum	Soluble extract L4 + CFA	↓ 81 ↑ 99	↓75 ↑100	Calves immunized 2 times with soluble extract of L4 at low dose (↓) 520 µg or high dose (↑) 2600µg always + PBS/CFA (SC at 4 weeks interval). Additionally, they received a new low dose (↓) 130 µg or high dose (↑) 650 µg + PBS, on day 56. The control group received PBS/CFA.	(East et al., 1988).

Authors

nASP: Native secreted protein associated with ASP1 activation, QuilA®: Adjuvant saponin, Al(OH)3: Aluminum hydroxide, DS: Dextran sulfate, H-gal-GP: Digestive protease glycoprotein complex, H11: Hc isolated integral intestinal membrane protein, CEF: Contortin-enriched fraction, rHc23: Recombinant somatic Hc protein, P46+P52: Hc apical intestinal surface protein, nOPA: Native purified antigen of Osteortagia osteortagi polyprotein, ES-thiol: Cysteine proteinase enriched fraction, EPG: Eggs for gram feces; IM: Intramuscular, SC: Subcutaneous, PBS: phosphate buffered saline, dd-ASP: double domain ASP protein, ESP: larval excretory-secretary products of Oesophagostomum radiatum, IP: Intraperitoneal, L4: Larval stage 4 of Oesophagostomum radiatum, WHG: H. placei whole gut homogenate, EPG: eggs per gram of feces, CFA: Complete Freund's adjuvant, IFA: Incomplete Freund's Adjuvant. (↓) : low dose, (↑) : high dose, (-): not data available.

Several hidden intestinal antigens have been found in animals to confer protection against *H. contortus*. The hidden intestinal antigen digestive protease glycoprotein complex (H-gal-GP) was effective in protecting sheep against *H. contortus*, by decreasing parasitic loads in 70 %, with a decrease in fecal egg count (FEC) of 90 %, in several clinical trials (Smith et al., 1994; Smith & Smith, 1996; Knox & Smith, 2001). Another *H. contortus* antigen, that has played an important role in clinical studies, is in the hidden integral intestinal membrane. This protein was isolated from *H. contortus* (H11 antigen). This antigen has proved to bind specific antibodies that disable the enzymatic activity of the antigen, showing a 90 % reduction in FEC and

a 75 % drop in the presence of adult *H. contortus* in the abomasum of immunized sheep (Newton & Munn, 1999).

Based on these results and with new technologies available to obtain antigens, (Vercruysse et al., 2018), it seems that vaccines composed by several antigens of the same nematode species promote a more intense and long-lasting protection against the specific parasite, avoiding a potential adaptation of these parasites to the administered vaccine (Claerebout & Geldhof, 2020).

In the last decade, efforts have been made to develop vaccines for *T. circumcincta*, an important parasite that affects small ruminants, causing gastroenteritis, and a reduction in weight gain (Nisbet et al., 2013; Matthews et al., 2016). An immunoprophylactic study against this nematode was performed in sheep in the last third of gestation and in grazing lambs (*in-situ*), where they were inoculated with a combination of recombinant proteins (Tci-ASP-1; Tci-MIF-1; Tci-TGH-2; Tci-APY-1; Tci-SAA-1; Tci-CF1; Tci-ES20; Tci-MEP-1), resulting in a 45 % decrease in the FEC (Nisbet et al., 2016).

The parasite of abomasum, *O. ostertagi*, and the small intestinal parasite, *C. oncophora*, are the nematodes that affect prevalently grazing cattle in the tropics. The vaccines studied against these parasites has showed the following results: Calves that were vaccinated with an *O. ostertagi* excretory-secretory antigen fraction, enriched with cysteine proteinase (ES-thiol) activity, and the adjuvant Quil-A®, indicated that a protective immune response against *O. ostertagi* was induced, which was reflected by a reduction in FEC from 56 to 60 % (Geldhof et al., 2004; Meyvis et al., 2007). The administration of an ASP-based vaccine against *O. ostertagi* (a double-domain ASP protein-dd-ASP, purified from excretory/secretory material of C. oncophora larvae) showed successful results and has been considered a vaccine candidate (Borloo et al., 2013).

Echinococcus granulosus (*E. granulosus*), a canine intestinal cestode, is the causative agent of human hydatidosis, which also affects several intermediate hosts (such as sheep, cattle, camelids, and horses). This zoonotic disease causes significant economic losses and public health concerns in many countries (Lightowlers et al., 1999; Dalimi et al., 2002). To advance in the control of this parasitic agent, a vaccine that contains a recombinant antigen belonging to the oncosphere of the *E. granulosus*, called EG95, has been developed (Larrieu et al., 2015; Larrieu et al., 2019). With this antigen, a protection of 96-98 % with respect to the parasitic load was obtained (Lightowlers et al., 1996).

A study was executed in which cattle were immunized with EG95, and with Quil-A® as adjuvant, finding a protection of 90 % of the immunized animals for 12 months (Heath et al., 2012). These results suggest that the vaccine from the EG95 antigen could have a wide applicability as a tool to control hydatidosis (Lightowlers et al., 1999). However, it cannot be overlooked that the vaccine should be used in combination with other control measures, such as health education, control of slaughter, and canine deworming; for more favorable results (Anvari et al., 2020).

Advances in the development of vaccines for the control of gastrointestinal parasites in pets (dogs and cats)

Some of the parasitic diseases of pets (dogs and cats) are highly zoonotic. For this reason, a significant effort for developing clinical trials, to find a solution that prevents high rates of animal-human contagion has been done (Hotez et al., 1996). Table 2 presents several clinical immunoassays for the control of gastrointestinal parasites in pets, especially against the hookworm *Ancylostoma caninum* (*A. caninum*), one of the main causative agents of anemia and malnutrition in dogs and in humans in the less developed countries of the tropics (Ghosh et al., 1996).

In 1973, a vaccine prepared from larvae (L3) of *A. caninum*, irradiated with Roentgen rays, was commercialized, resulting in 90 % of protection (associated to the reduction of the parasitic load). The distribution of this vaccine was interrupted two years later, due to limitations that included price, supply, and stability of protection (Miller, 1964; Boag et al., 2003). After that, a clinical trial with dogs immunized with Ac-ASP-2 (catalytically active cysteine protease [Ac] and proteins secreted from *Ancylostoma larvae* [ASP])

showed a significant reduction in the FEC and in the load of adult hookworm parasites in the intestine (Fujiwara et al., 2006).

TABLE 2
Clinical trials of experimental vaccines for the control of gastrointestinal parasites in companion animals

Parasite	Vaccine	Protection %		Vaccination schedule	Ref.
		worm	Eggs (EPG)		
Ancylostoma caninum	Ac-16 + AS03®	25.3	63.4	Canines of 4 to 62 days old received 3 immunizations, in days 21 and 42, with 0.5 mL of 100 µg Ac-16 + AS03® (IM). The control group received ASO3® in PBS.	(Fujiwara et al., 2007)
Echinococcus granulosus	*Salmonella* LVR01 EgTrp/ EgA3	79	-	Canines were divided in 3 groups. Group 1: 2 doses of 5 × 1010 Salmonella LVR01, expressing EgTr/EgA3 + PBS (PO at 21 days interval). Group 2: 2 doses of Salmonella without *E. granulosus* genes + PBS (PO at 21 days interval). Group 3: (control) PBS 0.1 mM.	(Petavy et al., 2008)
Ancylostoma caninum	Ac-CP-2 + ASO3®, ASO2A®, ISA 70® and Al(OH)$_3$	-	62-75	Canines of 8 weeks old received three immunizations with 0.5 mL doses of 100 mg µg of one vaccine: Ac-CP-2 + ASO3®, ASO2A®, ISA 70®, Al(OH)3 (IM at 21day intervals). The control group received Al(OH)3 in PBS.	(Loukas et al., 2004)
Ancylostoma caninum	L$_3$ *A. caninum* irradiated with X 40 krad (L$_3$X) + Alum AlK(SO$_4$)$_2$·12H$_2$O	53	87	Canines received 3 doses of 1000 L3X (SC at 21-day intervals). The control group was treated with Alum-AlK(SO4)2-12H2O.	(Fujiwara et al., 2006)
Ancylostoma caninum	Ac-APR1 + ASO3®	33	70	Canines of 62 days old were immunized 3 times with 0.5 mL of 100 µg Ac-APR-1 + ASO3® (IM at 21 days intervals). The control group received AS03® with PBS.	(Loukas et al., 2005)
Echinococcus granulosus	PSCs + CFA or IFA and RP: EgM4 or EgM9 or EgM123 + CFA, or IFA.	PSCs, 55 and RP, 99		Canines from 1-3 years old were distributed in 5 groups. Group 1: 3 doses of 0.25, 0.125 and 0.125 mg PSCs + FCA or + IFA (SC at 3-week intervals). Group 2: 3 doses of 0.5, 0.25, and 0.25 mg PSCs + CFA or IFA (SC at 3 weeks intervals). Group 3: (control) CFA or IFA in PBS. Group 4: (received one of the following) 80 mg EgM4, EgM9, EgM123 + CFA or + IFA (SC at 3-week intervals). Group 5: (control) PBS + GST.	(Zhang et al., 2006)

Authors
Ac-16: Immunodominant antigen of A. caninum, ASO3®: Oil in water emulsion, EgTrp+EgA3: Recombinant adult A. caninum worm proteins, Ac-cp-2: Catalytically active cysteine protease, ASO2A®: Oleaceous emulsion of L3 irradiated with X (irradiated larvae of A. caninum), Ac-APR1: Aspartate protease of A. caninum, EPG: Eggs for gram feces; IM: Intramuscular, SC: Subcutaneous, EgM4, EgM9 and EgM123: Recombinant purified soluble fusion proteins of E. granulosus. CFA: Complete Freund's adjuvant; IFA: Incomplete Freund's Adjuvant, GST: Glutathione S-transferase, PO: Per os, PSCs: Soluble proteins from E. granulosus protoscolls, RP: Recombinant protein, (-): not data available.

Cystic echinococcosis caused by the cestode *E. granulosus*, also called hydatidosis, represents a concerning problem in public health and livestock, mainly in developing countries (Budke et al., 2006; Petavy et al., 2008). During its adult stage, this parasite locates in the small intestine of dogs, where it grows and can migrate to other organs such as liver and lungs (Grosso et al., 2012). In a classical vaccination study, a new approach for the immunization of dogs against E. granulosus was performed using secretory antigens derived from adult tapeworms grown in-vitro, which induced a significant decrease in the FEC of *E. granulosus* in immunized canines (Herd et al., 1975).

Advances in the development of vaccines for the control of gastrointestinal parasites in birds

The poultry industry has evolved significantly around the world, and the first-generation of experimental vaccines have been developed against diseases caused by protozoa, such as *Eimeria* spp. coccidiosis diseases (Vercruysse et al., 2004). These diseases affect intestinal epithelial cells, causing considerable weight reductions due to reduced food consumption and malabsorption. In addition, the continuous administration of coccidiostats generates adaptation of the parasites, making it a constant problem in the poultry industry (Jenkins, 2001; McDonald & Shirley, 2009). In Table 3, a series of clinical immunoassays for the control of gastrointestinal parasites (specifically for *Eimeria* spp.) in birds are summarized.

TABLE 3
Clinical trials of experimental vaccines for gastrointestinal parasites control in birds

Parasite	Vaccine	Protection % Oocyst decrease	Vaccination schedule	Ref.
Eimeria máxima	PcDNA-Gam56	53.7	1-week old broilers divided into 6 groups. Group 1: not immunized or challenged. Group 2: not immunized. Group 3: pcDNA3. Group 4, 5 and 6: doses of 25, 50 and 100 µg pcDNA-Gam56, respectively, with reinforcements at 14 and 21 days of age.	(Xu et al., 2013)
Eimeria tenella	pcDNA–TA4–IL-2	72.67	14-day-old chickens divided into 7 groups. Group 1 and 2: controls, they are given sterile (TE). Group 3, 4, 5 and 6: 2 doses of 25, 50, 100 and 200 µg of DNA pcDNA3.1b-TA4 - IL-2, respectively (IM at 7-day intervals). Group 7: (control) 100 µg pcDNA3.1b.	(Song et al., 2009)
Eimeria tenella	pcDNA3.1-TA4 pcDNA3.1b-TA4-IL2 pcDNA4.0c-IL-2	68.2 75.1 66	14-day old chickens distributed in 5 groups. Group 1, 2 and 3: 2 doses of 100 µg of pcDNA3.-1b-TA4-IL2, pcDNA4.0c-IL-2, and pcDNA3.1-TA4, respectively (IM at 7-day intervals). Group 4 and 5: (controls) sterile TE.	(Xu et al., 2008)
Eimeria tenella *Eimeria acervulina*	EtMIC2 / pcDNA	45-70	Immunization in ovo. They were immunized with 25 or 50 µg EtMIC2 / pcDNA / egg, with a booster at 7 days after hatching of 100 µg EtMIC2 / chicken. The control group received PBS or pcDNA.	(Ding et al., 2005)
Eimeria Tenella	pMP13	50-60	Day-old chickens were immunized twice with 5, 10, 50 or 100 µg doses of pMP13 DNA (IM or SC at 2-week intervals). The control group received only the plasmid pBK-CMV.	(Song et al., 2000)
Eimeria acervulina	pVAX-LDH pVAX-LDH-IFN-γ pVAX-LDH-IL-2	53.29 56.82 57.59	2-week-old chickens divided into 8 groups. Group 1, 2, 3, 4 and 5: 2 doses of 100 µg pVAX-LDH, pVAX-LDHIFN-c, pVAX-LDH-IL-2, LDH and inclusion bodies (IM at 1-week intervals). Group 6: control) plasmid pVAX1. Group 7 and 8: sterile TE buffer.	(Song et al., 2010)
E. tenella *E. máxima* *E. acervulina*	APGA + CFA or IFA	45-63	Chickens were divided into 8 groups. Group 1 and 2: 2 APGA doses, 1st 100000 or 400 000 gametocytes + CFA and 2nd 100000 or 400000 gametocytes + IFA. Group 3: 1 mg Gex. Group 4: 40 µg Mex. Group 5: 150 µg OoNex. Group 6: 150 µg OoSex + FCA. Group 7: (control) PBS + FCA. Group 8: no immunization.	(Wallach et al., 1995)
Eimeria tenella	ETRHO1 + CFA	77.3	Day-old chickens divided into 3 groups. Group 1: (3 doses) 1st. and 2nd: 100 µg of WHT1 + CFA (IM). 3rd: 100 µg of WASTE1 + CFA (IM days 7 and 21). Group 2: (control) PBS. Group 3: (control) no immunization.	(Li et al., 2012)

Authors

PcDNA-TA4-IL-2: DNA fusion vaccine co-expressed in E. tenella, PcDNA: DNA fusion vaccine, Gam56: Recombinant plasmid from E. maxima, EtMIC2: Recombinant microneme gene from E. tenella, pMP13: Preserved antigen of E. tenella, pVAX-LDH-IFN-γ: Recombinant antigen plasmid of E. acervuline, Raw gametocyte extract, IM: Intramuscular, SC: Subcutaneous, APGA: gametocyte antigens purified by affinity, RHMR1: rhomboid-like gene, CFA: Complete Freund's adjuvant, IFA: Complete Freund's adjuvant, PBS: phosphate-buffered saline, TE: buffer solution commonly used in molecular biology, Mex: raw extract of merozoite, OoNex: raw extract of non-sporulated oocysts, OoSex: crude extract of sporulated oocysts.

During the 1950s, the first vaccines against *E. tenella* were marketed using live sporulated oocysts (Soutter et al., 2020). Due to the economic relevance of avian coccidiosis, a series of commercial vaccines from different companies have been commercialized (Williams, 2002). In the last decades, a special focus has been made to manipulate recombinant DNA antigens from different stages of growth of the *Eimeria* spp., based on the fact that metabolic and reproductive processes are essential for its permanence in their hosts change

during the life cycle of the parasite (Jenkins, 1998; Vermeulen, 1998).Likewise, the identification of different antigens with a high potential for its use in these vaccines is increasingly important for the target market (Blake et al., 2017; Soutter et al., 2020).

Advances in the development of vaccines for the control of gastrointestinal parasites in pigs

A major advance has been made by the pig industry over the past five decades, supported by genetic improvement. The continuous treatments for the control of gastrointestinal parasites remains conventional, and thus developing anti-parasite resistance and worsening public health problems. Therefore, several research groups have made important efforts to develop vaccines for the control of the main parasites of pigs with public health implications (Table 4).

An example of these advances is the control of *Taenia solium* (*T. solium*), which is a common cestode in pig breeding areas and is the main cause of human cysticercosis, an important neurological disease of global public health, with the pig as the intermediate host. This zoonotic pathology is associated with human population areas of scarce economic resources where pigs roam freely, consolidating the transmission of the parasite from pigs to humans. Most attempts to control the parasite transmission have been ineffective and unsustainable (Verastegui et al., 2002; Gauci et al., 2012) with some exceptions of success in specific geographic areas, which have linked comprehensive community actions based on vaccination schemes and conventional antiparasitic management (Garcia et al., 2016).

TABLE 4
Clinical trials of experimental vaccines for the gastrointestinal parasites control in pigs.

Parasite	Vaccine	Protection %	Vaccination schedule	Ref.
Taenia solium	TSOL18 + QuilA®	99.3 - 100	Piglets 2 to 3 months old received 3 doses 1 mL of 200 µg TSOL18 + 5 mg QuilA® (IM at 4 weeks interval), second dose: + 30 mg/kg Oxfendazole (PO), and 3 months for the third dose. Control group received 30 mg/kg Oxfendazole (PO).	(Assana et al., 2010)
Taenia solium	TSOL18 TSOL 45	99.98 98.6	Three-month-old pigs distributed in 4 groups. Group 1: 2 doses of 200 µg TSOL18 + GST, at 4-week intervals. Group 2: 3 doses. 1st and 2nd: 200 µg TSOL45 + GST, at 4 weeks intervals; 3rd: 200 µg TSOL45 + MBP, 2 weeks later. Group 3: (control) 2 doses of 200 µg GST, at 4 weeks intervals. Group 4: (control) 3 doses. 1st and 2nd: 200 µg GST, at 4 weeks intervals; 3rd: 200 µg MBP.	(González et al., 2005)
Taenia solium	*T. solium* oncospheres + IFA	89	2-month-old pigs distributed in 4 groups, all received two doses at 20-day interval of: Group 1: 200 µg 45WB/X-GST + 16K-GST + 18K-GST of *T. ovis* + 1 mg QuilA® (IM.) Group 2: 200 µg GST + 1 mg QuilA® (IM). Group 3: 0.1 ml antigen (equivalent to 60 000 *T. solium* oncospheres) + IFA. Group 4: (control) 200 µL PBS/IFA (IM).	(Plancarte et al., 1999)
Taenia solium	TSOL16 TSOL45-1A TSOL45-1B + QuilA®	99.18 97.9 18.8	8-week piglets distributed in 4 groups. Group 1, 2 and 3: (3 doses) 1st and 2nd: 1 ml of 200 µg TSOL16, TSOL45-1A or TSOL45-1B, respectively, + 1 mg QuilA® + GST, at 4 weeks intervals; 3rd dose: TSOL16, TSOL45-1A or TSOL45-1B + MBP, two weeks later. Group 4: (control) 3 doses. 1st and 2nd: GST + 1 mg QuilA®; 3rd: MBP + 1mg QuilA®.	(Gauci et al., 2012)
Taenia solium	S3Pvac+ Saponina®	50	2-month-old piglets received 2 immunizations at 60 and 90 days of age: 250 µg S3Pvac + 100 µg Saponina® (SC). The control group received 100 µg Saponina® (SC).	(Díaz et al., 2003)
Ascaris suum	AsHb+ QuilA®	66.2	Pigs distributed in 6 groups. Group 1, 2 and 3: (controls) QuilA® + PBS. Group 4, 5 and 6: 3 doses of 100 µg AsHb + 500 µg of QuilA® + PBS, (IM at 2-week intervals).	(Vlaminck et al., 2011)

Authors
TSOL18. TSOL45. TSOL16: Antigens from Taenia solium oncosphere, 45WB/X-GST. 16K-GST. 18K-GST: Recombinant proteins from T. ovis, S3Pvac: Anti-cysticercus triple-peptide synthetic vaccine, GST: Glutathione S-transferase, IM: Intramuscular, SC: Subcutaneous, AsHb: Ascaris suum purified hemoglobin, Quil-A®: Adjuvant saponin, PBS: phosphate-buffered saline, MPB: maltose-binding protein, CFA: Complete Freund's adjuvant, IFA: Incomplete Freund's adjuvant.

Researchs to development effective vaccines against this disease have been taking place. Thus, several works were generated about the promising vaccine candidate: TSOL18 antigen. A research, using this recombinant antigen, detected high levels of antibodies in immunized pigs, possibly associated to the protection against *T. solium*, which evidenced a 94 % - 100 % reduction in the loads of meta-cestoids (Cai et al., 2007). Furthermore, an investigation found that the recombinant proteins TSOL18 and TSOL45-1A induced more than 97 % of protection (in independent vaccine trials) against an experimental infection with *T.*

solium eggs in pigs (Kyngdon et al., 2006). In summary, these three antigens (TSOL16, TSOL18 and TSOL45) induce high levels of protection into the immunized pigs; however, it has been demonstrated that TSOL18 antigen has been the most effective in field conditions (*in situ*) to stop the parasitic agent transmission (Garcia et al., 2016).

A synthetic S3Pvac vaccine, consisting of three peptides (GK1, KETc1 and KETc12), to prevent the transmission of T. solium was shown to be successful (De Aluja et al., 2005). This S3Pvac vaccine caused a 50 % reduction of the parasitic load and, in the case of cysticercus, a reduction of 98 % in immunized pigs (Sciutto et al., 2008). It has been demonstrated that immunization with S3Pvac is effective for preventing porcine cysticercosis; however, its effectiveness is still limited to reduce the prevalence of the cestode, besides its high manufacturing costs (Sciutto et al., 2013).

Another gastrointestinal parasite of great concern for pig production systems is *Ascaris suum* (*A. suum*), which is usually located in the small intestine of its host and migrates to different organs before its destination, causing significant tissue damage (Masure et al., 2013). Because of this migratory capacity, it is responsible for high rates of animal morbidity and considerable economic losses in pig productions; besides is a very relevant agent in zoonotic geohelminth infection (Tsuji et al., 2003). Several clinical studies of vaccine experimentation have been carried out to study immunoprophylaxis as a control strategy of this parasite in pigs. The inoculation of 10000 irradiated A. suum eggs resulted in a reduction of 88 % of *A. suum* larvae. The parasite was extracted post-mortem from the inoculated pigs (Urban & Tromba, 1982).

Gastrointestinal deworming vaccines currently commercialized in veterinary medicine

Over the years, vaccines containing different antigens and adjuvants have been developed, which help to reduce the damage generated by the presence of gastrointestinal parasites in animal production systems, and to animal and human health (Meeusen et al., 2007). This has provoked an extensive work by researchers, to generate effective vaccines that fulfill the needs of producers opportunely, and be economically viable (Redding & Weiner, 2009). Currently research on helminth vaccines has produced successful results, and has been characterized for using innovative technologies, but their commercialization is limited, leading to a reduction in the production (Hein & Harrison, 2005).

Since 2014, the first vaccine for gastrointestinal nematode control in ruminants is in the market. It is an antigenic subunit vaccine, based on hidden native intestinal membrane antigens obtained from adult *H. contortus* (Jacob et al., 2013). The vaccine compounds are the glycoproteins complex of aspartyl and metallo-proteases (H-gal-GP), and a family of leucine aminopeptidases (H11); associated to an adjuvant of saponin nature. The adjuvant commercial name is Quil-A®. This vaccine is commercialized for the control of *haemonchosis* in sheep (with some successful research studies in goats, alpacas, among other ruminants); its release was carried out in Australia, where the vaccine was named as Barbervax® (Wormvax, Australia Pty Ltd) (Preston et al., 2015; Matthews et al., 2016). Barbervax® is available in South Africa, where it is known as Wirevax®, and in the United Kingdom it is sold only under veterinarian's prescriptions (http://barbervax.com.au/). By 2018, its respective commercial registration was obtained in New Zealand and Europe.

The vaccine for controlling hydatidosis (*Echinococcus granulosus*) in its intermediate hosts (sheep, goats, cattle, pigs, and camelids) was the first commercial vaccine for the control of gastrointestinal cestodes (Claerebout & Geldhof, 2020). It is based in a recombinant antigen and is in the market since 2006 as Providean® Hydatil EG95 (Tecnovax, Buenos Aires, Argentina). This vaccine is based on the EG95 mature oncosphere antigen (cloned from the respective gene in a plasmid vector) expressed in *E. coli* K12BB4-pGex-3Ex, and then associated to an oil adjuvant: Montanide ISA 70® (Matthews et al., 2016). The benefit of this vaccine is that by controlling the infection in its intermediate hosts, its definitive host (dogs) hardly come in contact with the hydatid cysts generated by *E. granulosus*, interrupting its life cycle. Humans are accidental host of this parasite, and the mechanism of action of this vaccine highly diminishes the probability of contamination, exerting a beneficial effect on public health in an indirect way (Tecnovax, n.d.) (Jacob et al., 2013).

In 1999, Fort Dodge Laboratories (USA) launched a vaccine called GiardiaVax™, generated from chemically inactivated trophozoites of the protozoan G. lamblia (syn. *G. duodenalis* or *G. intestinalis*). This protozoon is the main causative agent of diarrhea in global children population, because its cysts are expelled to the environment through the feces of pets (and wild species of dogs and cats) and can reach humans through the oral route (Meeusen et al., 2007; Payne & Artzer, 2009; Molina, 2017). The vaccine contributed to the reduction and impact of cyst expulsion from the protozoan *G. lamblia* in canine feces, and prevented giardiasis (Meeusen et al., 2007). Ten years after its commercial release, Fort Dodge Laboratories stopped the production of GiardiaVax™ because of its low efficacy (Molina, 2017). Paradoxically, this same vaccine is commercialized still in some countries of the American continent, such as in the United States, Brazil, and Argentina, by other laboratory: Zoetis (Australia PTY LTD) for its use in dogs (Zoetis, 2013).

In 1951, the first commercial vaccine against avian coccidiosis was recognized and, until today, several series of vaccines have been commercialized for controlling this disease in different species of production birds (commercial laying hens, broilers, breeders, turkeys, among others) (Li et al., 2012). Thus, the first commercial vaccine for the control of *Eimeria* spp. (cause of avian coccidiosis) was the *live vaccine* named CocciVac®-D (Schering Plough Animal Health, USA) formulated with a series of low doses of oocysts from eight different *Eimeria* species (*E. tenella*, *E. maxima*, *E. mivati*, *E. acervulina*, *E. brunetti*, *E. hagani*, *E. necatrix* and *E. praecox*) to be administered in birds.

This same commercial line of vaccines (Merck Animal Health, n.d.), one year later was called CocciVac®-D2 (MSD, Kenilworth, NJ, USA). Is similar in its antigenic content to the previous one, but have been modified by reducing the oocyst doses of the eight Eimeria spp. that have not been transformed to modulate their pathogenicity (Peek and Landman, 2011). Furthermore, in the same vaccine production path, years later appeared CocciVac®-B (MSD, Kenilworth, NJ, USA), which is formulated for broilers, composed by four Eimeria species (*E. acervulina*, *E. maxima*, *E. mivati* and *E. tenella*) (Reid, 1990); and Coccivac®-B52 (Intervet Inc, through Merk animal health), which prevents infection by *E. mivati* and *E. tenella*, in addition to reducing injuries caused by *E. acervulina* and *E. maxima* in broilers (Merck Animal Health, n.d).

In 1985, Vetech Laboratories Inc. in Canada started to commercialize a vaccine for the control of Eimeria spp. called Immucox® (https://www.immucox.com/Range), developed in Ceva Animal Health (Cambridge, ON). It has been evolving year by year and, until today, it has developed three commercial vaccines under the precept of live sporulated oocysts (via oral administration) at low doses for this kind of birds: 1) for broilers: Immucox®3 (*E. acervulina*, *E. maxima* and *E. tenella*); 2) for broilers and laying hens: Immucox®5 (*E. acervulina*, *E. maxima*, *E. tenella*, *E. necatrix* and *E. brunetti*) and 3) for turkeys: ImmucoxT® (*E. adenoids* and *E. meleagrimitis*).

In addition, in 1989, the live attenuated vaccine Paracox® was launched by Schering Plough Animal Health in the United Kingdom. Later, in association with Intervet UK Ltd-MSD animal health (MSD Animal Health, n.d), generated two new commercial vaccines under the same technological precept: 1) Paracox®8, which is formulated with different low doses of oocysts from seven different *Eimeria* species (*E. acervulina*, *E. brunetti*, *E. maxima*, *E. mitis*, *E. necatrix*, *E. praecox* and *E. tenella*), it is indicated for broilers, laying hens and reproducers. 2) Paracox®5, which is formulated with four different *Eimeria* spp. (*E. acervulina*, *E. maxima*, *E. mitis* and *E. tenella*). These vaccines are called "8" and "5" respectively, even having only 7 and 4 *Eimeria* spp., since the attenuated field strain of *E. maxima* has two types ("attenuated line" (CP) and "mixed field strain precocious" (MFP)).

In 1992, the avian industry worldwide had a new possibility to control avian coccidiosis, based on the same trend of developing vaccines for the gastrointestinal pathogen *Eimeria* spp. Thus, BioPharm of the Czech Republic (https://www.bri.cz/en) released a new line of attenuated live vaccines called Livacox®, which offers two vaccines based on attenuated sporulated oocytes: Livacox®T (*E. acervulina*, *E. máxima* and *E. tenella*) and Livacox®Q (*E. acervulina*, *E. máxima*, *E. necatrxi* and *E. tenella*). The vaccines are indicated for broilers and reproducers laying hens, respectively.

Following the vaccines' purpose of controlling avian coccidiosis (but using innovation and technology for its synthesis) it was promulgated in 2002 (by ABIC Biological Laboratories Teva Ltd in Israel (www.abic-vet.com)) the CoxAbic® vaccine (Novartis, AH). This vaccine has three subunits of antigenic proteins inactivated: 230kDa, 82 kDa, 56 kDa (also called gam230, gam82 and gam56, respectively), known as Affinity Purified Gametocyte Antigen (APGA). The proteins were isolated from the sexual-stage gametocytes of the protozoan *E. maxima* (these protein fractions are located around the wall-forming bodies -WFBs- of the macrogametocytes) (Li et al., 2012).

In the pig industry is important to stand out the efforts focused on controlling *T. solium*, a cestode of great zoonotic impact associated with cysticercosis disease in humans (Lightowlers & Donadeu, 2017). In 2016, the vaccine known as Cysvax™ was developed and launched by Indian Immunological Limited with the collaboration of various economic and technical sources, including the Global Alliance for Livestock Veterinary Medicines -GALVmed- (https://www.galvmed.org/). It is the first and only vaccine against cysticercosis based on TSOL18, which is a recombinant antigen from the oncosphere of the parasite, expressed in Pichia pastoris, and an oily adjuvant (Sciutto et al., 2013). This vaccine provides 100 % effectiveness and contributes to a significant decrease in the parasitic load of this cestode in pigs (Sepúlveda et al., 2020).

Finally, not just a positive effect on animal health, welfare and production, has been generated by veterinary vaccines; also on human health, confirming that the continuous exchange of knowledge between health researchers of these two matters, considering environmental interactions (One Health principle), is essential to address the always-present threat of problematic emerging diseases (Meeusen et al., 2007). Figure 3 shows the main commercial vaccines for controlling gastrointestinal parasites examined in this review, as well as their global distribution.

FIGURE 3

Vaccines marketed for the control of parasites in animals, according to their country of distribution. (A): countries where Providean® Hidatil EG95 is marketed, (A1): countries where Barbervax® is marketed, (A2): countries where Cysvax™ is marketed, (A3): countries where GiardiaVax™ is marketed and (A4): countries where Coccivax®, Immucox®, Livacox® and Paracox® are marketed.

Authors

4. CONCLUSIONS

The control of parasitic diseases played by vaccines is transcendental, particularly in animal production for human consumption. Like all other remedies, they must be endorsed by the competent entities (Heldens et al., 2008). However, the high costs of certain vaccines reduce the possibilities of commercialization, as ultimately users seek saving money, rather than quality (Schetters, 1995). Despite progress in experimental vaccine research, very few vaccines are promising to finally become commercialized (Schetters, 1995). In the future, changes in legislation are expected to provide subsidies for the manufacturing and marketing of commercial deworming vaccines (Schetters & Gravendyck, 2006), and it is expected to have available a range of immunoprophylactic and immunotherapeutic biologics importance for the control or even eradication of gastrointestinal parasites.

Vaccination is an effective alternative to prevent many diseases that affect animals species of veterinary interest. This has increased the levels of confidence in public health globally (Unnikrishnan et al., 2012) and has provided welfare to various animal species. Even so, and despite the scientific advances in the world, gastrointestinal parasitic infections persist; therefore, vaccination is recognized as one of the most viable and

effective option for controlling these diseases. However, the development of preventive vaccines against these parasites has proven to be enormously difficult for scientific and economic reasons (Versteeg et al., 2019).

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Notes

[1] All works which had not the data mentioned in the inclusion criteria were excluded (e.g., preclinical trials preclinical of vaccine candidates for these same parasites and others).

Alternative link

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