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The Current Status of Vaccines Against Parasitic Diseases of Livestock

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Abstract: Parasitic diseases are the major problems that can cause mortality and reduce production and reproduction performance of animals worldwide. Parasites are successful in evading host immune responses and vaccination can prove to be an effective way to control them. However, currently very few vaccines are available in the market against parasitic infection. Important limitations in the emergence and commercialization of effective parasitic vaccines are lack of knowledge on the immune mechanisms of parasitic infection, its variable antigen, complex developmental stages and the lack of precise information regarding host-pathogen interactions. Precise identification of parasite genes and the role of their products in parasite biology may assist in the identification of useful antigens, which could then be produced in recombinant systems. Many recombinant parasitic antigens have been successfully used in livestock and new vaccines are under trail. Numerous vaccine antigens are defined to target a wide range of parasite species. Thus vaccines offer a green solution to control disease that is why vaccination is environmental friendly. Vaccines have multiple beneficial effects such as improvement of animal health and welfare by controlling animal infestations and infections; diminishing resistance to anthelmintics, acaricides and antibiotics to improving public health status by controlling food borne pathogens and zoonoses aspect related to animals for keeping animals and the environment free of chemical residues and maintaining biodiversity. However, the availability of parasitic vaccine in the market is limited due to various reasons and it is not commonly applied but few trails may present in Ethiopia. This review is to indicate the nature of the disease problem and the opportunities and challenges of parasitic vaccines and their use to counter the adverse effects of infection in livestock.

Key words: Control · Immune Response · Livestock · Parasites · Vaccines

INTRODUCTION

Parasitic diseases are a major problem on the health and production of livestock globally. Both endoparasites that live inside the body (like helmenths and protozoans) and ectoparasites that live on the body (like ticks, mites, lice, fleas and flies) attack the body surface of animals are responsible for decline population and production losses. After repeated exposure to nematode infection cattle and sheep gradually become resistant to reinfection due to the development of immunity against nematode infection especially when they become adult animals. This fact is the base to believe and explore for vaccines against parasitic diseases. However, there are many factors to be considered for the development of immunity against parasites including genetic makeup of individuals, age, physiological status and several characteristics of co-infecting nematode species. In addition, good management such as provision of clean pasture and adequate nutrition can greatly influences the development of immune response against parasite infection. Vaccine development against parasites faces several fundamental challenges like the isolation of native antigens from none blood feeders which elicit protective immunity if delivered to the immune system in an appropriate manner [1].

Helminth parasites had a great impact on animal health and productivity from the time that animals were first reared. There is various control approach for the

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effect of parasites. Among the control methods chemical methods (like chemotherapy) and non-chemical methods (like biological control, good management and selection of genetic resistant breed) are commonly employed. From the control methods, antiparasitic drug will not continue in the foreseeable future due to its high selection pressure of parasite that leads to drug resistance. Anthelminthic, anti-protozoans and pescticides drugs are a serious problem on the effect of parasite. This is due to insurgence of resistance against the drugs by the parasites of animals, high cost of drugs, less availability and food safety issues concerning drug residues and environmental contamination. These challenges of antiparasitic drugs as seen in different regions of the world provide an insight of opportunity for the development and use of vaccine [2].

Vaccines have an effect on a parasite by coated its virulent epitope or to interrupt the life cycle of certain helminth parasites to reduce its antigenicity. Vaccination could be applied either to protect the most susceptible animals in a flock/ herd or to minimize the buildup of larvae on pasture and so reduce the rate of infection in susceptible animals. However, vaccines have not been widely used at field level to control the widely distributed parasitic infections globally [2].

The development of a protective vaccine, which can prevent the consequences of acute infection, is therefore, desirable alternative. Although live attenuated vaccine has been available for veterinary use for several years, it is expensive, causes side effects, has a short self-life and provides protection for not more than 3 years [3]. The advancement of molecular techniques is also considered as a favorable condition for development of new vaccines against parasites in the near future [4]. Therefore, the objective of this paper is to review the current status of vaccines parasitic vaccine and their use in livestock.

General Overview

Importance of Parasites: Parasitic diseases of animals have been known to cause population decline and huge production losses. It also affects the health of humans. Both endoparasite and ectoparasite can affect the health of livestock and its production through death, weight loss, prolong the period of breeding and it has also zoonotic importance. Many parasitic diseases are zoonoses with disease arising from both helimenthes and protozoan agents. Hydatid disease, due to infection with tapeworms of the *Echinococcus* genera, is a public health problem in many parts of the world. Disease caused by the digenetic trematode is a major zoonosis in South East Asia affecting over 250 million people and causing a quarter of a million deaths annually in sub-Saharan Africa alone [5]. Fascioliosis is caused by infection with the liver fluke, *Fasciola hepatica*. Widespread infestation is common in sheep and bovines and it can also occur in humans. Infection in humans arises from ingestion of uncooked, unwashed aquatic vegetables contaminated with encysted larvae. While animals can carry large worm burdens without developing serious disease, *Fasciola spp*. can cause severe, even fatal disease in humans [5, 6].

Some parasites such as *Heamonchus contortus, Anclyostoma species* and other bloodsucking parasites cause clinical aneamia. Their hematophagous nature causes degeneration of epithelial cells of gastrointestinal tract that can cause greater morbidity and mortality of animals. Blood loss as a result of *Heamonchus*, *Fasciola*, other intestinal helminthes and protozoa species have been known to cause degeneration of gastrointestinal tract. Some parasites like Fasciola, Schistosoma, lungworm, Ascarid, Flaroids, etc. have also been known to cause organ damage due to their migration. This will cause severe morbid processes and reduction in productive and reproductive performances [4].

Ticks are known to cause skin damage which result in deterioration of the market value of skin, tick paralysis, anemia which leads to death and serve as a vector for various tick born disease (TBD). Mites, fleas and lice cause skin damage due to delayed type hypersensitivity reactions; myasis producing insects cause annoyance and death [6].

Control of Parasites

Chemotherapy: Chemotherapy has one of the most controlling methods of parasites that have been practiced throughout the world. Yet this method has its own drawback as it induces drug resistance, residues on animal by products, environmental degradation and also it can induce teratogenic effect to their hosts. The degree of discrimination is sometimes small, sometimes considerable, but never perfect, so that application of parasiticides always hazard to the host. In fact it is deleterious effects that parasiticides quite frequently exert on the host. For instance, organophosphates and carbamates block cholinesterase neurotransmitter causing accumulation of acetylcholine and blockage of the respiratory muscles followed by death [7].

Nowadays, Chemotherapy and Chemoprophylaxis are not promising. This is due to development and escalating issue of drug resistance, food safety concern arising from

residues and environmental issues. Drug resistance can be defined as the loss of the initial sensitivity of parasites to the effect of substances to which they were previously sensitive. For example, there are several reports on resistance of ivermectin including resistance in *Cooperia* species in several countries in the southern hemisphere [8].

Integrated Control: Integrated pest control approach is very important for the control of parasitic infestation. Rational use of a combination of biological, bio-technological and chemical control measures in all farming practices or breeding strategies is crucial in order to reduce the use of chemical control agents to an absolute minimum. A classic example of this approach is the combination of grazing management and anthelmintic treatment. The relevance of an integrated approach has grown for several reasons. A single antiparasitic treatment of animals in an infected environment proved to have a very transitory effect as it becomes reinfected shortly after treatment. The sparing use of parasiticides has been advocated due to increasing problems with chemical resistance. A combination of two or more effective methods may substantially reduce infection levels and give appropriate control. Lastly, under some conditions control programs of very high efficacy for example use of sustained release devices may be unwanted as it may compromise the development of immunity. For these reasons an integrated approach combining different methods is likely to achieve the best control [8, 9].

Biological Control: Biological control may be defined as the use of one living organism introduced into the environment to obtain control of a target parasite and thereby reducing the population growth of the latter below a threshold where it causes minimal clinical problems and /or economic losses. For instance, nematophagous fungi were shown to reduce populations of preparasitic stages of nematodes significantly. These fungi are relatively easy to culture and use for the control of helminth parasite at preparasitic stage to colonize the helminth egg and larvae. The fungus *Duddingtoniaflagransis* is very efficient in controlling most of the economically important gastrointestinal nematodes of grazing livestock by reducing pasture infectivity [9, 10].

Immunoprophylaxis: Immunization is the most desirable and powerful controlling mechanism of combating infectious agents. The fact that vaccines are potentially safer, cheaper and more efficacious as prophylactics than drugs is based mainly on our experience to date with antimicrobial vaccines. Except the vaccine used against bovine lung worm infection that is prepared from irradiated larvae of *Dictyocaulus viviparous,* there are no commercially available vaccines for the control of most of the parasitic infections of animal diseases caused by nematode parasites. Vaccine for babesiosis and arthropods are also limited on the market due to antigenic complexity and level of antibody production on the host to attack arthropod infection [9].

Criteria for Vaccine Development Against Parasites: Few vaccines against parasites have been developed and reached the market. Although some of the arguments that explain market failure are correct in their own right there are many more factors that affect commercial success [11]. Some of the most important factors for the development of vaccine are summarized below:

Quality: A vaccine should be safe at production and during application. The quality assurance system comprises the microbiological status of these animals and preferably specific pathogen free animals must be used. Additionally a validated final product test on sterility or purity is required [10].

Safety: A product must be safe to the target animal but it must also be assured not to pose a danger to other animals or man that may come into contact with the product or to the environment. In addition, the safety of an overdose or Repeated doses of the vaccine must be shown. A special requirement is that live vaccine strains must be stable that means should not revert to virulence during consecutive passages. In general, a vaccine has to be produced with a limited number of passages from the master seed stock which is usually limited to five passages. The safety of the parasite vaccines at the lowest and highest passages should be shown in animal studies using the most sensitive target animal species. This is a mandatory prerequisite before marketing the product [12].

Efficacy: A product must be able to do what is claimed. For instance, limit parasite multiplication or the development of clinical signs. This need to be shown in large number of target hosts under various geographical locations and different animal farming systems [13].

Potency: The vaccine must provide data that guarantees the efficacy of a product over the entire shelf life. This is a major hurdle in vaccine development. The discovery of

the protective effect of specific immunogenic parasite strain or partially purified parasite fraction is usually done or further established by vaccination challenge experiments. Such experiments are preferably not used as potency tests as they involve animals for experimentation and take long time in case of some live vaccines this is a serious problem. An alternative test must be developed and potency test carried out at the time of batch release which has predictive value as to the efficacy of that particular batch at the end of shelf life. Hence, the dynamics of the signal of the potency test must be studied over the period of the shelf life and correlate with the level of efficacy (real time stability data). If the protective mechanism of immunity against a specific parasite is not known it may take years before an accurate potency test is developed. This has been one of the standing problems in commercializing parasitic vaccines [14].

Immunity Against Parasite Antigens

Immunity to Protozoa: Protozoan parasites are considered one of the major constraints causing extensive morbidity and mortality in animals. Among these many of the protozoan parasites are zoonotic in nature that also increases their economic importance [14, 15]. At present, vaccine for human protozoal disease is available commercially; similarly, several veterinary vaccines are marketed with varying efficacy. Among vaccines available against protozoan diseases of livestock, many are based on live organisms, but recently there is progress in development and commercialization of killed subunit vaccines [15].

Protozoans are fully antigenic but due to their antigenic variation and soluble blocking antigen it is difficult to produce vaccine against protozoa. Like other antigenic particles parasitic protozoa can stimulate both humoral and cell mediated immune responses [14].

Immunity to Helminths: There are few helminth parasite have a vaccine. Immunoglobulins like the IgM, IgG and IgA isotypes are produced in response to helminth antigens; an increasing body of evidence suggests that the most significant immunoglobulin isotope involved in resistance to helminth is IgE. As a result, the development of a worm burden provokes a local acute type I hypersensitivity reaction in the parasitized regions of the body. The combination of helminth antigens with mast cell bound IgE leads to mast cell degranulation and release of vasoactive amines. These compounds stimulate smooth muscle contraction and increase vascular permeability which results in dislodgement and expulsion of worms [7, 16].

There has been evidence that suggest sensitized T-lymphocytes in the intestinal mucosa is involved in resistance against helminths such as *Trichinella spiralis* and *Trichostrongylus colubriformis* infections. Sensitized T-lymphocytes depress the activities of helminths by two mechanisms [17]. First, the developments of an inflammatory response of the delayed hypersensitivity type tend to attract mononuclear cells to the site of larval invasion and render the local environment unsuitable for growth or migration (Figure.1). Second, cytotoxic lymphocytes may be capable of causing larval destruction [18].

Immunity to Arthropods: Ectoparasitic arthropods would seem to be the ultimate challenge in vaccine development, as they not only are large and complex but also spend most of their life outside or on the surface of the host. The vaccine is effective when host antibidies gain access throgh the vector during feeding. Ticks have a potential to induce an immune response when their saliva deposit to the host. Other salivary antigens may bind and induce cutaneous basophil hypersensitivity reaction associated with IgG antibodies and a basophil infiltration [6].

In general, for all classes of parasites protozoa, helminths and arthropods the mechanism of natural immunity has been understood. The knowledge of immunity to natural infection forms a benchmark for development and production of efficacious vaccines to induce protective immunity. Hence, a number of vaccines have so far been developed and tested [19].

Vaccination Against Parasitic Infection: Vaccination against protozoan infections of domestic animals is currently limited to Babesiosis, Toxoplasmosis and Theileriosis even though they are not available in the market (Table 1). Animals that recover from acute Babesiosis are resistant to further clinical disease and this immunity has been considered to be a form of premunity. It is possible to infect young calves deliberately so that they will acquire infection while they are still relatively insusceptible to disease and later become resistant to re-infection [15].

Vaccines against helminths or their extracts have been uniformly unsuccessful in conferring protection because of this studies have tended to concentrate on the use of irradiated larvae. Experimentally it has been shown

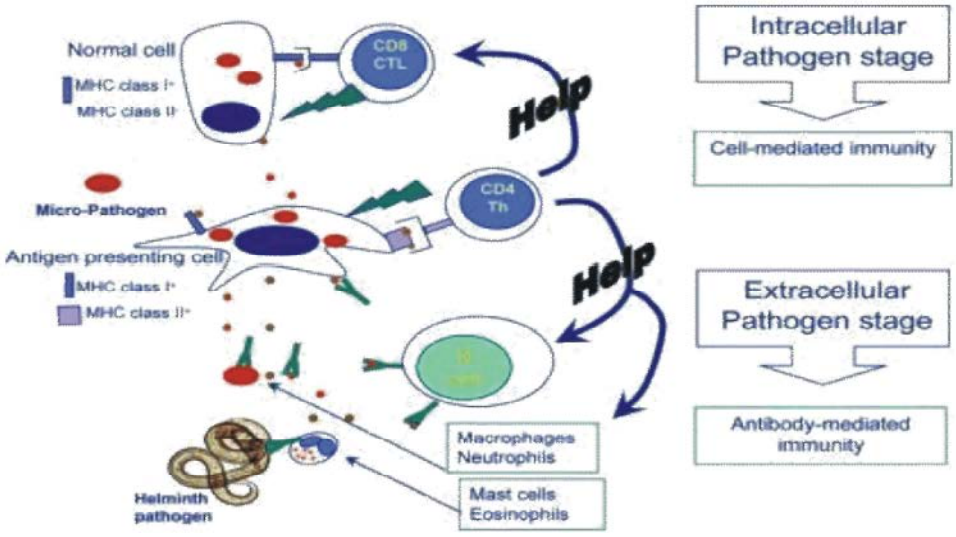

Fig. 1: Schematic representation of immune system mechanisms; adopted from Foster and Elsheikha [17].

Table 1: List of some important commercialized anti-parasitic vaccine; adapted from Coyne and Brake [22].

A nti-protozoal Parasite vaccine	Recipient	Registered Name		Company		*Antigen type*
Babesia bovis	*Cattle*	*Numereous*		*Local*		Live attenuated
Theileria annulata	Cattle	RakshavaacT,		Indian		Live attenuated
Theileria parva	Cattle	Muguga cocktail		Africa		Live virulent
Trichomonas foetus	Cattle	TrichGuard		BoehringerIngelheim		Inactivated
Toxoplasma gondii	Sheep	Toxovax		Intervet/ Mycofarm		Live attenuated
Anti-helminth Parasite vaccine	Recipient	Registered Name		Company		Antigen type
Dictylcaulus viviparus	Cattle	Bovilis®		Intervet (now MSD		Live attenuated
Echinococcus granulosus	Cattle	ProvideanHydatil		Tecnovax		Recombinant
Cysticercus cellulosae	Pigs	Cysvax		Indian		Recombinant
Haemonchus contortus	Sheep,	Barbervax		Morendun	Research	Purified native
Dictyocaulus filaria	Sheep,	Difil	(now)	Indian	Veterinary gamma-	
Anti-tick Parasite	Recipient	Registered		Company	Antigen type	
Vaccine		Name				
Rhipicephalus	Cattle	Gavac Plus/		Heber Biotec	Recombinant	
Boophilus microplus		VacunaHebert		S.A.	subunit (Bm86)	
R.(B. microplus)	Cattle	Go-Tick /		Limor de	Recombinant	

Table 2: Vaccination agents of parasites; adapted from Sumbria and Singla [21].

Parasite	Vaccination agent	Reference
Trichinella spiralis	Excretory–secretory, Ts87 and gp43 recombinated	[21]
Strongyloides ratti	HSP60 in alum	[21]
Strongyloides stercoralis	Ss-IR	[21]
Brugia malayi	Irradiated infective mosquito-borne L_3 larvae, ALT-	[21]
Litomosoides sigmodontis	Plasmids encoding *L. sigmodontis* antigens	[21]
Dictyocaulus viviparous	Radiation-attenuated larval vaccines (Dictol,	[21]
Dictyocaulus filari	X-irradiated larvae vaccine (Difill)	[21]
T. circumcincta	Tci-MIF; apyrase, Tci-APY-1; TGFb homolog, Tci-	[21]
Strongylus vulgaris	Irradiated larval vaccines	[21]
Ascaris suum	Recombinant protein vaccines As 14, As 16, As 24	[21]
Toxocaracanis	Excretory–Secretory	[21]
Onchocerca volvulus	Irradiated L_3 larvae, tropomyosin, CPI-2, FAR1	[21]

that irradiated metacercariae can reduce burden in calves. However, very few of these preparations have been commercially produced with success (Table 1 and 2). Perhaps the most important of those vaccines that have been produced to protect livestock is the vaccine against verminous pneumonia caused by the lungworm *Dictyocaulus viviparous* [20].

The arthropod antigen is present on the saliva of parasites. Although vaccination against salivary antigens is unlikely to be very effective in conferring effective immunity against blood feeding arthropods because the host antibody may not gain access to sufficient amount to the parasite, there is an alternative approach. Since many of the arthropods of veterinary importance take the blood of their host into their digestive tract it follows that they will also take up immunoglobulin's complement, [6].This suggests that if an animal were immunized with internal antigens from the parasite this could lead to local damage. The internal antigens have been called hidden or concealed antigens since under normal circumstances the host would not encounter those. Vaccines made against antigens from the intestine of the tick *Boophilus microplus* was shown to inhibit tick production. Recombination tick vaccine based on such antigens Bm86 is available in Australia [21].

On the other hand vaccines containing salivary antigens may be more effective in reducing tick feeding and thus the transmission of pathogens. The antibodies produced inhibit endocytosis by gut endothelial cells and prevent the tick from engorging fully. In addition, tick feeding on vaccinated animal produce significantly fewer eggs than normal. The larvae of the warble flies *Hypoderma bovis* and *Hypoderma lincatum* migrate through body tissues. Vaccination with cloned hypoderma proteins has effectively protected animals against subsequent infections [22].

Types of Parasitic Vaccine: Most of the veterinary vaccines evaluated in livestock against parasites belong to one of the following categories: live attenuated vaccines, killed vaccines and recombinant subunit vaccines.

Live Vaccines: Live-attenuated vaccines induce a strong humoral and cellular immune response, but their safety is questionable due to the risk of virulence reversion [23]. In this respect one can distinguish two groups of live vaccines those that induce self-limiting infections and those that result in chronic infections. Vaccines that cause self-limiting infections have been based on the use of parasite strains that cause infections which does not usually present. They have no risk to the environment since the life cycle of the parasite is not perpetuated. Requirements are restricted to providing evidence that the biological characteristics of the vaccine strains do not change upon consecutive passage. This is referred to as reversion to virulence even in cases that a wild type strain is used for vaccination. Examples of the simplest form of such vaccines are the live vaccines against coccidiosis in chickens [24].

The pathogenesity of parasite strains derived from a single isolate can be variable. For example, using *Babesia bovis* isolates passage through splenectomised animals can select for strains of reduced virulence. Such parasite strains are being used to vaccinate cattle in Africa and Australia. The infection develops less virulently and the animals develop immunity against subsequent challenge infection [24].

Most parasite species have complex life cycles characterized by distinct stages of development sometimes involving more than one host. It may need environmental and host stage of development so that it is difficult to extract the target antigen for the production of vaccine. A major advantage is that spreading of the vaccine strain in the environmental does not occur. An example is the *Toxoplasma gondii* S48 that is used in a vaccine against abortion in sheep due to primary *Toxoplasma gondii* infection during pregnancy. This strain has the capacity to develop from the tachyzoite into bradyzoite stage but does not form tissue cysts [6].

Irradiation of parasites has also been used as a mechanism to truncate the life cycle. The live vaccine against lungworm infection in cattle contains L3 larvae of *Dictyocaulus viviparus* that do not develop further than the L4 stage. Vaccinated cattle are immune to challenge infections with L3 larvae. Live vaccines can be also being developed from parasites that cause chronic infections. In this case the parasites show a tendency to survive in the host for longer periods of time in which case chemotherapeutics cure of the infection is required [25].

Killed Vaccines: Inactivated vaccines are safer and more stable than attenuated ones, but they are less potent and confer a weaker humoral immunity [26]. Killed vaccines by themselves usually do not induce protective immunity and an appropriate adjuvant and formulation must be developed (Figure 2). Aluminum salts water in oil and oil in water and saponins are commonly used as adjutants. Killed vaccines are more stable and have longer shelf life due to the boosting activity of adjuvants.

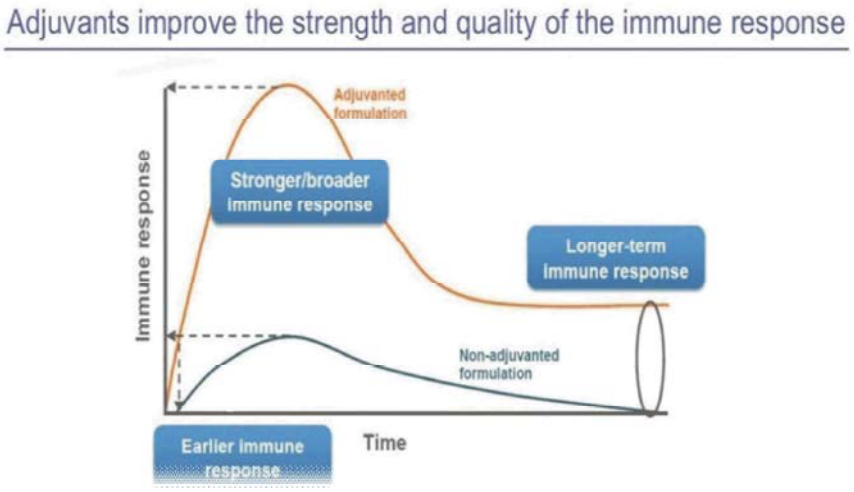

Fig. 2: The role of adjuvant in immune response; adopted from Pulendran and Ahmed [26].

Killed vaccines could be prepared from whole organisms or from their parts or products. If there is no chance for use of live vaccine strains one may want to inactivate the parasites before to the formulation of a vaccine. Examples of such vaccines are the vaccine against abortion in cattle due to *Neospora caninum* infection and a vaccine against giardiasis in dogs [27]. Irradiated vaccine against lungworm can be used by inactivating the virulence epitope. Similar vaccines would be effective against the *Trichostrongyle* species responsible for gastrointestinal infections in cattle and sheep [28].

Recombinant Subunit Vaccines: Recombinant subunit vaccines are easy to store, free of contaminants and proteolytic enzymes since they are chemically produced and they are able to induce a protective immunity without toxic side effects or cross-linked immune reactions caused by other components present in the pathogenic organism [29]. In addition, large scale production and purification of a well-defined product can be achieved [30]. However, there are several limitations for vaccines based on the use of recombinant proteins, such as the proper choice of antigen/s, deficient immunogenicity and poor cellular immune response [31- 35]. In addition, subunit vaccines do not have enough capacity to activate the innate immune response; therefore, they require the incorporation of some adjuvant into the vaccine formulation. Tick species and *Tania* species have this type of vaccine [33, 34].

Success of Vaccines Against Parasites: Successful vaccines have been developed infrequently and have been characterized by use of widely contrasting technologies. A crude and simple vaccine employi effectively used for the control of lungworms in cattle called *Dictyocaulus viviparous* [35].A similar approach has been proved effective for controlling infection with the sheep lungworm called *Dictyocaulus filaria* and the canine hookworm *Ancylostoma caninum* [21]. A rewarding advance occurred towards the end of the last century when a vaccine employing a recombinant antigen that conferred protection against a metazoan parasite *Taenia ovis* was developed. Similar strategies were then employed to develop recombinant vaccines against other cestodes parasites *Taenia saginata* and *Echinococcus granulosus* [21]. The most recent recombinant or sub fraction lungworm vaccines have not achieved levels of efficacy in any way comparable to the crude whole organism vaccine [21].

Subunit vaccines have also been tried against some parasites. This was based on more detailed analysis of the immune response acquired after natural infection or vaccine induced immunity that led to the discovery of critical antigenic components of an organism that can be used in a vaccine. An adjuvant is required for the induction of protective immunity. The best example is the vaccine against *Taenia ovis* in sheep which is based recombinant parasite antigens that induce antibodies that block the attachment of oncospheres to the gut epithelium [9].

Recombinant vaccine produced from gut wall antigens of the cattle tick *Boophilus microplus* up on vaccination of cattle high levels of antibodies are produced against to the gut wall of ticks. During feeding of the tick on the vaccinated animal these antibodies are ingested and destroy the gut epithelium of the tick thus

killing the parasite. Some protein antigens such as the H11 protein from *Heamonchus contortus* are highly effective in native form but seemingly lose a critical structural feature which accounts for immunogenicity when produced in recombinant form Hotez *et al.* [36].

Dictol was prepared 1000 X-ray irradiated (40krds) *Dictyocaulus viviparous* larvae. The vaccine has short shelf-life of around 6 weeks. Nowadays, drugs are more effective in treatment of clinical cases especially in older cattle. Thus in recent time, there is decline in production and sales in UK and Western Europe. Larvae in dictol are supposed to stay in mesenteric lymph node without further migration to stimulate the lymph node and immunize the animals [14]. Another vaccine of India origin, Difil was prepared for the control of *Dictyocaulus filarial* infection in sheep of Northern India. It consists of γ-irradiated L1 larvae. The shelf life of vaccine was only around 2 weeks. Vaccination with irradiated L3 larvae of the other economically important gastrointestinal nematodes has been attempted but was not successful due mainly to their lack of efficacy in inducing immunity in young animals [14].

Failure of Vaccines Against Parasites: Due to complex life cycle having differential expression of genes and characters, large number of developmental stages, immune evasion strategies of parasites, latent or subclinical infection, unexplored reservoir host in the wild, poor market attention, farmer mindset for rapid action of drugs, multicellularity generating large antigenic variation unlike bacteria or viruses, co infection or multiple parasitic infection, lack of knowledge of complete genome and precise understanding of host pathogen interaction hinders the path of development followed by commercialization of parasitic vaccine in the market may affect the success of vaccine. Besides, among all pathogens, maximum antigenic diversity is recorded in parasites [37].

Similarly vaccine failure occurs when the normal immune response is suppressed. For example, stress like pregnancy, extremes of cold and heat, fatigue and malnourishment and heavily parasitized may reduce a normal immune response of animals probably because of increased steroid production. This is usually caused by the presence of passively derived maternal immunity in young animals. Many of the failures in vaccine efficacy may be attributable to an inability to conform to one or more of the following requirements. Firstly, antigen presenting cells must be stimulated so that they process antigen efficiently and release appropriate interleukins.

Secondly, both T and B cells must be stimulated so that they generate large numbers of memory cells. Thirdly, helper and effector T cells must be generated to several epitopes in the vaccines so that variations in major histocompatibility complex (MHC) class II polymorphism and epitopes properties are overcome and finally the antigen must persist [38]. There have been a large number of unsuccessful attempts to develop vaccines for helminths. Following early experiments where sheep were immunized systemically with ground up worm vaccine many research groups around the world have tested a wide variety of worm. Most of these attempts were ineffective in terms of inducing strong protective immunity and some even exacerbated worm infections [20].

Status of Parasitic Vaccine Production and Utilization in Ethiopia: Parasitic vaccine has a great potential for livestock protection against parasites globally. Although deworming is a widely used animal health intervention in Ethiopia, its impact on growth, drug resistance, environmental contamination and reproduction and survival is also significant. Immunization coverage against parasitic infection is not practice in Ethiopia due to insufficient availability and its short period of immunization. No parasitic vaccine is available anywhere in the country due to low attention and awareness of the government. Though it is not successful, decades a go there was an attempt to produce vaccine from irradiated larvae of *Dictyocaulus* at the Pathobiology Institute, Addis Ababa University. In Ethiopia, parasites are mainly controlled by strategic deworming with anthelmintics and other integrated approach to reduce helminths burdens [39]. However, no work has been reported from Ethiopia and very few from elsewhere in the tropics on the cost effectiveness of helminthes controls through deworming.

CONCLUSION AND RECOMMENDATIONS

Parasitic diseases caused by helminthes, protozoa and arthropods can reduce the agricultural economy through decline of livestock population, reduce production and productivity throughout the world. In addition in many cases they also affect human health. To alleviate these problems many control strategies are practiced. Among those control strategies of parasitic diseases chemotherapy and chemoprophylaxis are applied all over the world. However, this method of control is hindered by the development of drug resistance, high price of drugs, unavailability and growing concern about

drug residues and environmental pollution. Due to these reason there was an attempt to develop commercial vaccines against economically important parasites by identifying their target antigens. In the near future the use of vaccination against parasitic diseases of animals in veterinary health services is expected to contribute significantly in promoting livestock productivity. Various articles showed that several efficacious vaccines have been produced, but their availability in the market is limited. This is due to various regulatory and pharmacological vigilances which are often the first requirement by the regulatory and licensing authority. As a result it is hoped that in the future vaccination against parasitic diseases will be used as one of the best alternatives in the control of parasitic infections. Based on the above concluding remarks the following recommendation points are suggested:

- Thorough understanding of immune mechanism and pathogenesis stimulated by parasite is must for long term success of vaccines.
- Vaccination is the best option to maximize the level of immunity and reduce drug resistance
- The government anticipated to harmonize legislation that will facilitate the production and marketing of commercial products that should be realized in the future.

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