



Pathogenic Bacteria and Ticks: A Bad Combination for Sustainable Livestock Farming

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Pathogenic Bacteria and Ticks: A Bad Combination for Sustainable Livestock Farming

Bacterias patógenas y garrapatas: una mala combinación para la ganadería sustentable

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RESUMEN

En esta revisión, bajo el enfoque de la visión "Una Salud", se propone el desarrollo de vacunas como estrategia que promueve la salud animal y contribuye a mantener el equilibrio ecológico para un manejo sostenible de los recursos naturales. En este sentido, los factores incontrolables como las enfermedades animales, requieren investigación científica para identificar soluciones y desarrollar vacunas o medicamentos de producción nacional que favorezcan la salud del ganado. Las propuestas actuales se basan en la vacunología reversa para el diseño de vacunas multiepitopo tales como las desarrolladas contra *Brucella melitensis* y *Mycoplasma hyopneumoniae* y evaluadas en animales modelo. Por lo que, este tipo de vacunas son una estrategia novedosa con potencial para controlar enfermedades en el sector veterinario.

PALABRAS CLAVE: manejo de ganado, sustentabilidad, anaplasmosis, *Rhipicephalus microplus*, recursos naturales.

ABSTRACT

This review, framed within the One Health approach, proposes vaccine development as a strategy to promote animal health and to help maintain ecological balance for the sustainable management of

natural resources. In this context, uncontrollable factors such as animal diseases require scientific research to identify solutions and develop domestically produced vaccines or medications that promote livestock health. Current proposals are based on reverse vaccinology for the design of multi-epitope vaccines, such as those developed against *Brucella melitensis* and *Mycoplasma hyopneumoniae* and evaluated in animal models. Therefore, these types of vaccines represent a novel strategy with the potential to control diseases in the veterinary sector.

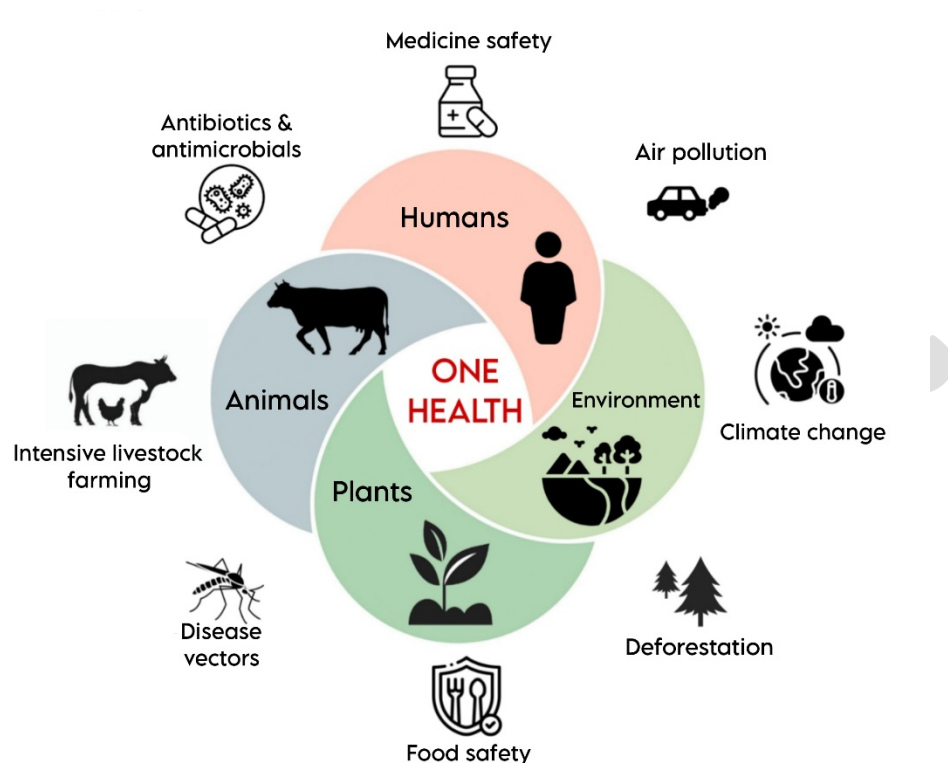
KEYWORDS: cattle management, sustainability, anaplasmosis, *Rhipicephalus microplus*, natural resources.

INTRODUCTION

Livestock farming is a crucial factor in achieving sustainable development in the agricultural sector. It contributes to food security, nutrition, poverty alleviation, and global economic growth (FAO-UN, 2024). In this regard, sustainable livestock farming represents a strategy for improving both the production and quality of derived products while reducing the impact on natural resources. Since animal health is crucial for feeding the population, pathogen surveillance and control are necessary. These measures help minimize disease risks, optimize productivity, and ensure food security (Kocan et al., 2000). However, certain diseases, such as bovine anaplasmosis, have a significant impact on livestock health. Anaplasmosis can cause signs in cattle such as anemia, weight loss, jaundice, abortion, and, in some cases, death. In Mexico, economic losses from this disease are estimated to be approximately \$100 million per year, primarily due to damage and the high cost of treatment (OIE, 2015). Additionally, in Mexico, there is no effective vaccine to protect or reduce the symptoms of infected livestock (Quiroz Castañeda et al., 2016). In response to this situation and the increase in diseases in livestock, the World Health Organization has coined the term "One Health." This represents a comprehensive and unifying vision aimed at sustainably balancing and optimizing the health of animals, humans, and related ecosystems (WHO, 2020) (Figure 1). Given this scenario, research advancements aim to contribute to maintaining the health of cattle. This is achieved not only by incorporating the One Health vision but also by generating solutions and by providing new vaccines or drugs that differ from those typically used (based on chemical compounds). Thus, approaches based on immunoinformatics tools are presented as a promising alternative, since they help identify potential and novel targets for developing

vaccines and drugs that control pathogens, thereby minimizing the risk of infection in cattle.

Figure 1
The One Health approach



The One Health concept encompasses a collaborative, transdisciplinary, and integrated approach that considers the interconnection between human, animal, and environmental health. Therefore, it aims to help prevent and control the spread of zoonotic diseases, address the issue of antimicrobial resistance by promoting the correct use of antibiotics, and provide strategies to address global health threats (pandemics and emerging diseases). Image created by E.L. Castillo-Díaz. Source: Lebov et al., 2017; WHO, 2020.

1. IMPORTANCE OF LIVESTOCK AS A NATURAL RESOURCE

According to the Convention on Biological Diversity, genetic resources are all material of plant, animal, or microbial origin that contains heritable units of actual or potential value (Deplazes-Zemp, 2018). Lands designated for grazing are home to more than one-third of the world's ruminants. Livestock farming can thus contribute to conserving genetic resources and biodiversity, thereby supporting significant ecosystem functions. Nevertheless, excessive and irrational use of antibiotics and other chemical compounds to control pathogenic bacteria, including acaricides and insecticides to control their vectors, has led to the elimination of microorganisms and arthropod species essential to the ecosystem. In contrast, the accumulation of resistant microorganisms can be toxic to the ecological niche, as it can

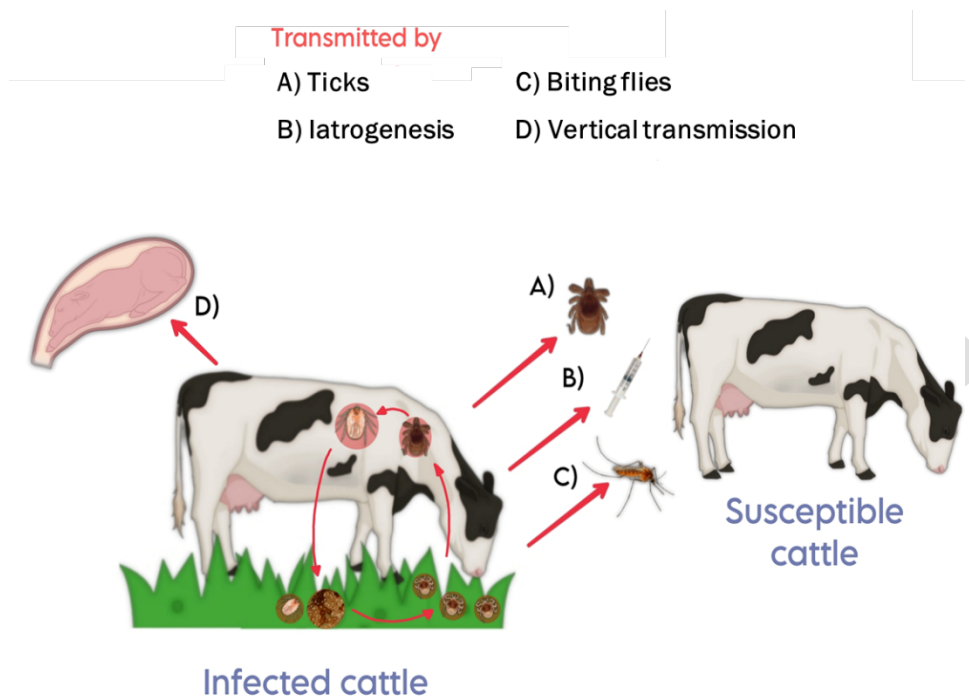
reduce microbial biodiversity. Socially, in rural communities, sick animals are more susceptible to other infections. This generates higher treatment costs, which economically impacts the people who depend on livestock farming. Likewise, the loss of animals can decrease meat and milk production, directly or indirectly impacting the region's food security. An alternative to addressing this situation is to conduct constant research to develop vaccination programs and control the vectors that transmit these diseases. Currently, these practices are starting to change for sustainable livestock production, where the goal is to minimize the negative environmental impacts associated with raising animals. These sustainable practices promote the long-term availability of natural resources, protect the environment, increase productivity, reduce production costs, and contribute to economic growth and rural development (FAO-UN, 2024).

2. BOVINE ANAPLASMOSIS

Anaplasmosis is a disease caused by the bacterium *A. marginale*. It is transmitted by diverse tick species, with *Rhipicephalus microplus* (the cattle tick) being the most important vector in Mexico (Kocan et al., 2010). However, mechanical transmission has also been demonstrated through contaminated surgical materials or specific species of *Tabanidae* flies (horseflies) and mosquitoes of the genus *Psorophora*, although this is less frequent (Hornok et al., 2008). The bacteria enter the bloodstream through the tick bite and infect erythrocytes. There, they multiply and cause severe anemia, jaundice, fever, and sometimes death of the animal (Tembo et al., 2018) (Figure 2). Later, the multiplied bacteria move to the tick's salivary glands and are transmitted to a new, uninfected host. Although anaplasmosis is directly associated with the vector, which is found in tropical and subtropical areas worldwide, global climate change has led to the vector's presence being identified in temperate environments, which is alarming. Additionally, abiotic factors are crucial in pathogens' survival, reproduction, and distribution, clearly influencing tick-borne diseases (Gray et al., 2009). For centuries, traditional farming systems have relied on grazing and foraging, which were considered the basis of early agricultural societies. Currently, these practices are evolving to promote sustainable livestock production and reduce the negative environmental impacts of animal agriculture. From a research perspective, and to protect animal health, several vaccine candidates against animal pathogens have been developed and tested, but they have produced limited results so far. This underscores the need to apply

innovative strategies and techniques to identify an effective vaccine candidate.

Figure 2
Bovine Anaplasmosis transmission



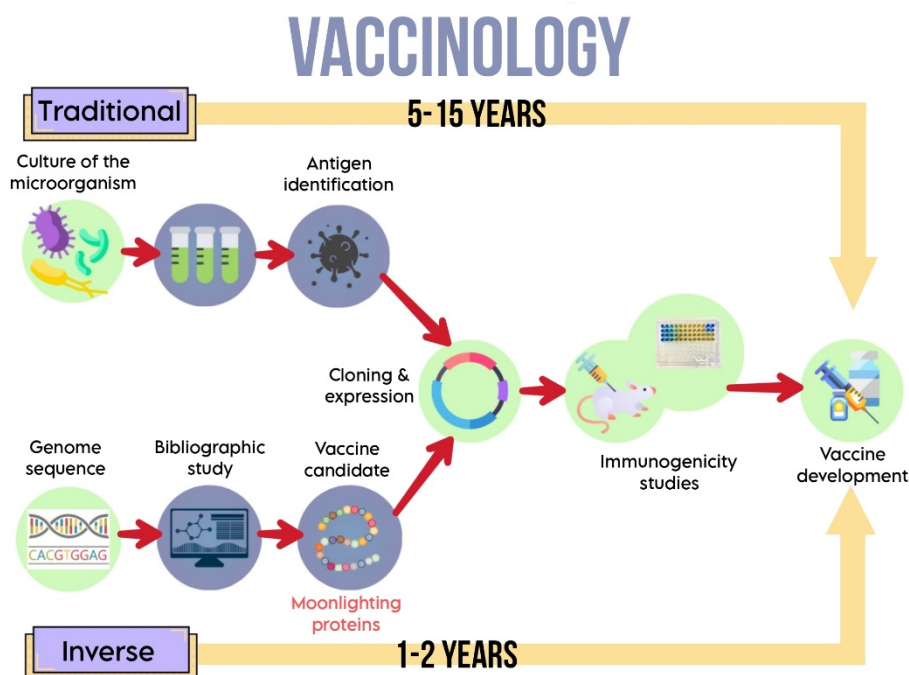
Transmission of Anaplasmosis may occur through biological vectors (ticks, *R. microplus*, *Dermacentor* sp.) that inhabit grasses, or by mechanical means, including veterinary surgical materials (iatrogenesis), horseflies, and mosquitoes. Vertical transmission may also occurs from pregnant female cows to the progeny. Image created by E.L. Castillo-Díaz. Source: Kocan et al., 2010.

3. IDENTIFICATION OF MOLECULAR TARGETS FOR THE CONTROL OF TICK-BORNE DISEASES

In recent years, the search for targets to control bovine anaplasmosis has focused on *A. marginale* polypeptide sequences. These often come from major surface proteins (MSPs), outer membrane proteins (OMPs), and type IV secretion system proteins (T4SS) (Brayton et al., 2005; Cangussu et al., 2018; Lockwood et al., 2011). Researchers believed these polypeptides could be recognized by the bovine immune system, triggering a protective response and preventing the disease. Unfortunately, these approaches have not been successful. As a result, priority has shifted to identifying new proteins as therapeutic targets that can induce an immune response against the bacteria. Recent studies have proposed multifunctional proteins (moonlighting proteins) as potential targets for vaccine development. These proteins participate in various biological and metabolic processes within

the bacteria (Pagani et al., 2019; Xue et al., 2021). In *A. marginale*, for example, the multifunctional protein enolase has been proposed as a promising molecular therapeutic target due to its potential role in bacterial adhesion, internalization into erythrocytes, and anchoring within the host cell (Quiroz-Castañeda et al., 2024). Several studies suggest that enolase is involved in cellular recognition of the bacteria within the host (Ghosh & Jacobs-Lorena, 2011; Vanegas et al., 2007). Additionally, in the swine pathogen *Mycoplasma suis*, enolase has been reported to induce an immune response in experimental animals. This highlights its antigenic and immunogenic properties, making it a potential vaccine candidate (Xue et al., 2021). Moreover, several studies have focused on the tick *R. microplus* (the transmission vector), since steroid hormone receptors from the bovine host have been identified in the tick and could serve as effective molecular targets for control (Aguilar-Díaz et al., 2018, 2023). Researchers believe that targeting specific antagonists of these receptors could block vital processes associated with tick reproduction and even decrease the arthropod's vectorial capacity to transmit pathogens to cattle. In the global context, these alternatives, based on inverse vaccinology, have great potential. They could serve as the basis for developing control methods that balance environmental, animal, and human health (Figure 3). In this regard, reverse vaccinology has been recently applied for vaccine development based on immunoinformatics in the veterinary field. For instance, the multiepitope vaccine designed against *Brucella melitensis* (a pathogen that infects goats and sheep and is the causal agent of human brucellosis) demonstrated that it can elicit both humoral and cellular immune responses in animal models (M. Li et al., 2022). In addition, the immunization of mice and piglets with a multiepitope vaccine for the swine pathogen *Mycoplasma hyopneumoniae* revealed the induction of both humoral and cellular responses (G. Li et al., 2022).

Figure 3
Reverse vaccinology approach



Traditional vaccinology was the basic strategy for developing many vaccines in recent years. It involved the culture of microorganisms and antigen identification, a process that can take up to 15 years to develop vaccines. However, with next-generation sequencing techniques and the high-quality data generated, the opportunity to develop vaccines has considerably shortened production to 1-2 years by employing an inverse vaccinology approach. In our investigation, moonlighting proteins are potential candidates for achieving a successful vaccine. Image created by E.L. Castillo-Díaz. Source: Bahrami et al., 2019; Jorge & Dellagostin, 2017.

4. RESEARCH CHALLENGES

To date, there is no vaccine against anaplasmosis or ticks in our country. Bioinformatics and immunoinformatics tools are essential for providing insights into molecules with better prognoses from Mexican isolates and strains, thereby facilitating the development of an effective strategy. A comprehensive view is needed to address this problem. It involves not only searching for and identifying molecules with vaccine potential, but also focusing on animal health, well-being, the environment, and human health (One Health). Within this integrative approach, actions should focus primarily on pathogens while also minimizing environmental exposure to chemical components. Investing in research is also crucial because expanding knowledge about animal health increases productivity and competitiveness. Mexican livestock farming faces the challenge of incorporating scientific research, technological development, and sustainable practices to strengthen the well-being

of rural communities and the country's economy.

PROSPECTIVE

Currently, it is undeniable that a country's food security must be guaranteed, as must the strategies to achieve it. To ensure this, comprehensive approaches that include key sectors, such as production and scientific research, are needed to achieve the common good. Generating novel knowledge with the potential to develop technology for Mexican livestock is a priority. There is no time to wait for technology developed elsewhere to solve our problems. This approach has only created technological dependence in recent decades. It is time to invest in generating knowledge and contributing to new technological developments that align with the environment, animal, and human health. Currently, our research focuses on identifying vaccine candidates through rigorous and thorough immunoinformatics analysis that supports their potential and can be verified through experimental validation. This effort will bring us closer to proposing an effective solution to the country's livestock health problems.

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