Letters in Animal Biology

Journal homepage: www.liabjournal.com

Vaccination and non-antibiotic strategies for effective control of multidrug-resistant *Salmonella* bacteria of medical and veterinary importance

Ahmed Shandookh Hameed [1], Jannat Riaz [2], Ahmed Raheem Rayshan [3], Areej Salih Saihood Al-Kinani [4], Anwar Saleh Saihood Al-Kinani [5], Ammar Younas [6], Rawaa Najim Alkhamessi [7], Mustafa Jawad Kadham [8], Mirza Muhammad Haris [9], Ayesha Bintay Farooq [10], Silla Ambrose [11], Arslan Muhammad Ali Khan* [12]

[1] *Medical Lab Techniques, Nassiriya Technical Institute Organization, Southern Technical University, Iraq*
[2] *Department of Eastern Medicine, Faculty of Life Sciences, Government College University Faisalabad, Pakistan*
[3] *Department of Physiology, Pharmacology and Biochemistry, College of Veterinary Medicine, University of Al-Qadisiyah, Al-Diwaniyah, Iraq*
[4] *Department of Anatomy, College of Medicine, University of Al-Qadisiyah, Al-Diwaniyah, Iraq*
[5] *Department of Microbiology, College of Medicine, University of Al-Qadisiyah, Al-Diwaniyah, Iraq*
[6] *School of Humanities, University of Chinese Academy of Sciences, Beijing, China*
[7] *Department of Biology, College of Science, Mustansiriyah University, Baghdad, Iraq*
[8] *Forensic Evidence Department, College of Science, Al-Fahidi University, Baghdad, Iraq*
[9] *Faculty of Life Sciences, Institute of Microbiology, Government College University Faisalabad, Pakistan*
[10] *Department of Physiology, Life Sciences, Government College University Faisalabad, Pakistan*
[11] *Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan*
[12] *Department of Parasitology, University of Agriculture Faisalabad, 38040, Pakistan*

Article info

Received: 02 September 2025
Received in revised form: 04 October 2025
Accepted: 26 October 2025
Published online: 30 October 2025

Keywords

Salmonella
Vaccination
Probiotics
Bacteriophages
Organic acids
Essential oils

* *Corresponding author:*
Arslan Muhammad Ali Khan
Email: arslanrajpootkhan374@gmail.com

Reviewed by:

Consent to publish the name of first reviewer could not be obtained

Hasnain Idress

Gluck Equine Research Center Department of Veterinary Sciences University of Kentucky Lexington KY USA

Abstract

With conservatively estimated millions of illnesses and deaths each year, most of which are caused by food contamination, *Salmonella* is now a threat and economic cost to the world. Traditional control measures become challenging because of the extensive variety of serovars of the *Salmonella* bacterium, coupled with increased antimicrobial resistance. With special focus on animal reservoir immunization strategies and new antibiotic regimens, the review critically assesses current and potential future control measures against *Salmonella* infection. Live-attenuated, inactivated, subunit, and novel DNA/mRNA platforms are some of the vaccines that attenuate pathogen shedding and zoonotic transmission in animals to a considerable degree. Maintaining the integrity of the gut microbiome, or host immune system activation through adjunct mechanisms like probiotics, bacteriophages, organic acids, essential oils, phytobiotics, and immunomodulators, present non-antibiotic options. Successful control of *Salmonella* requires a combination of strong biosecurity, farm management, and "One Health" strategy together with intersectoral coordination and improved surveillance. To become more acceptable and contribute towards the long-term influence on public health, both legal obstacles and financial barriers will have to be overcome. This article presents these key points concerning the transmission of the infection and pathogenesis of *Salmonella*. The vaccine and alternative measures utilized for control of the transmission are also highlighted.

1. Introduction

Salmonella, with more than 2600 serotypes, is a zoonotic pathogen of complex makeup, which can survive in varied environments due to its complex biology and rod-like structure. Multi-dimensional virulence mechanisms of toxin production and production, often supplemented by drug resistance, are the primary reasons for its pathogenicity. High frequency, economic significance, and zoonotic transmission patterns of *Salmonella* persist to make it a pertinent international public health and veterinary concern (Naushad et al. 2023). The most common type of *Salmonella* is the non-typhoidal *Salmonella* (NTS), and it produces huge outbreaks on several continents and contributes to approximately 93.8 million human and animal cases and causes millions of animal deaths worldwide each year (Nazir et al. 2025). This far-reaching influence incurs massive economic losses by raising the cost of treatment and lowering productivity through sickness. The wide social and economic influence of the pathogen is also indicated by the financial loss to the food sector that arises from product recall and loss of public confidence (Teklemariam et al. 2023).

With more than 2,300 identified strains, *Salmonella* is a lethal foodborne disease that is mostly transmitted through contaminated foods, especially of animal origin. The bacterium is generally classified into two groups: typhoidal *Salmonella* and non-typhoidal *Salmonella* (NTS) (Kirti et al. 2024). The two groups are distinguished by different clinical syndromes and a range of illnesses. *Salmonella bongori* is a minor, distinct subgroup, but the majority of these diverse strains belong to *Salmonella enterica*, which contains roughly 2,400 serovars classified based on their O, H, and K antigenic determinants (Ayuti et al. 2024). *S. enterica* is responsible for infections in both humans and animals. In equines, *Salmonella* serovars have also been detected in an aborted mare fetus (Borovikov et al. 2023). Control measures are significantly hampered by the broad diversity of the serovars, including host-restricted strains as well as strains that can infect a very diverse group of hosts. The zoonotic nature of the disease is evident as while poultry, beef, and pigs are significant sources, fruits and vegetables can also be potential carriers due to fecal contamination during processing. Among the pressing challenges in controlling *Salmonella* infection is increasing drug resistance, hugely decreasing the available therapies, as well as increasing the demand for the development of new forms of control in addition to standard antibiotic treatment. This calls for ongoing research and diligence in monitoring food safety measures (Jajere 2019).

The *Salmonella* poisoning of this huge chunk of the population is, to a very large degree, a function of having a colossal reservoir of infection in animals. Cattle, pigs, and chickens are all culpable as a prime source of disease transmission amongst human beings (Kuria 2023). Chicken foods are implicated more commonly in foodborne disease outbreaks, though control is frustrated by the fact that disease can be horizontally transmitted from free-living animals and pets. Though direct contact with ill animals or their surroundings remains a significant risk, most human infection arises as a result of the consumption of contaminated animal food, including beef, poultry, and pork (Saleem et al. 2023). Water, land, and environmental pollution are also major drivers of the continued occurrence of *Salmonella*. The issue is further complicated by the persistence of drug-resistant bacteria and must be tackled with a multifaceted approach that includes not only improved sanitation and judicious antibiotic use, but also the establishment of effective immunization policies (Marus et al. 2019).

The new trend of antimicrobial resistance, the inherent limitations of the conventional antibiotic regimens, and the multi-dimensional epidemiology involving the entire farm-to-fork supply chain make *Salmonella* control difficult and a complex issue. Overuse of antibiotics for human and veterinary medicine on an enormous scale is a primary cause of the increased emergence of multidrug-resistant (MDR) *Salmonella*, particularly to the first-line drugs such as fluoroquinolones and beta-lactams (Lamichhane et al. 2024). Because new antimicrobial drug development lags behind the rapid evolution of microbial resistance, this overall resistance seriously incapacitates classical antibiotic therapy, making the research and use of alternative therapies unavoidable (Vt Nair et al. 2018). Control measures along the food chain are still further complicated by the newly acquired ability of the pathogen to infect a wide variety of hosts and survive in a wide variety of environments (Nazir et al. 2025). Poultry products serve as a critical reservoir, and farm environments require strict control measures right from the feed level to processing (Obe et al. 2023). Thus, in order to successfully combat *Salmonella*, double and multi-level measures are necessary, not only with enhanced sanitation and judicious application of antibiotics but also through the development of effective broad-spectrum vaccines, along with realistic measures such as feeding-based approaches, stringent biosecurity measures, and careful surveillance for antibiotic-resistance genes (Nazir et al. 2025). Finally, the successful management of the overwhelming complexity of *Salmonella* is a function of ongoing research, vaccine manufacture, upgrade of surveillance, strict biosecurity, and collective world effort to utilization of more judicious antibiotic stewardship (Raut et al. 2023).

This review presents a critical overview of the global health issue posed by *Salmonella*, according to an assessment of current and forthcoming vaccination methods in animal reservoirs and their capacity to repress pathogen shedding, colonization, and zoonotic transfer, particularly from common hosts like poultry, swine, and cattle (Siddique et al. 2024a). To promote global food safety, this review outlines the key knowledge gaps and suggests R&D avenues to facilitate the control of *Salmonella* including the development of new broad-spectrum vaccines, streamlining new interventions, and enhanced surveillance for antimicrobial resistance (Ruvalcaba-Gómez et al. 2022; Corti Isgro et al. 2024; Magnoli et al. 2024). It also clarifies how these combined measures can be applied synergistically to offer more stable and consistent solutions to the mitigation of *Salmonella's* detrimental impacts on humans, animals, and the economy throughout the food chain. In order to further global food safety, this program also identifies key knowledge gaps and makes research and development recommendations for facilitating the control of *Salmonella*. These include development of new broad-spectrum vaccines, optimization of delivery of new interventions, and establishment of surveillance against antimicrobial resistance.

2. Pathogenesis and transmission of *Salmonella*

Because of their specific reservoir associations with other animal hosts and human disease syndromes that they invoke, *Salmonella* serovars, that is, *S. Enteritidis, S. Typhimurium, S. Newport,* and *S. Heidelberg*, are of public health significance (Wibisono et al. 2020). *S. Enteritidis* is a leading cause of human gastroenteritis and is most commonly associated with poultry, particularly eggs (Ayuti et al. 2024). Likewise, *S. Typhimurium,* which accounts for most cases of non-typhoidal salmonellosis, can infect a large host range including cattle and poultry (Arya et al. 2017). *S. Enteritidis* and *S. Typhimurium* are most often recovered from gastroenteritis, while S. Newport and S. Heidelberg serovars have caused more serious systemic disease, especially among immunocompromised individuals (Kuria 2023). Although often separated from gastroenteritis, especially from *S. Enteritidis* and *S. Typhimurium*, *S. Newport* and *S. Heidelberg* serovars have also been implicated to cause more systemic illness, especially in immunocompromised patients (Lynch and Tauxe 2009). New serovars *S. Drogana* and *S. Elisabethville* have since appeared, illustrating that *Salmonella* epidemiology is constantly changing and that surveillance and study must be ongoing to cope with the dynamic public health risk of these heterogeneous illnesses (Shekhar and Singh 2015).

Salmonella Pathogenicity Islands (SPIs) are horizontally acquired virulence-required genes for the bacterium (Kombade and Kaur 2021). SPI1 and SPI2 with varied Type III Secretion Systems (T3SS) belong to the most striking among the 17 SPIs identified (Lou et al. 2019). *Salmonella* is able to inject a wide variety of effector proteins into host cells through the existence of unique molecular syringes, which are important virulence determinants (Palmer and Slauch 2020). Whereas Although T3SS encoded by SPI2 plays an important role in host macrophage growth and survival and in disseminating systemic infection, the T3SS encoded by SPI1 initiates invasion into epithelial cells, which results in the acute inflammatory reaction and enteritis of *Salmonella* infection (Carneiro et al. 2024). *Salmonella* employs a range of host colonization mechanisms in addition to T3SS, including the production of adhesin and other effector proteins, which enhance survival in host tissue (Fàbrega and Vila 2013). These SPI-encoded virulence factors interact with host immune mechanisms in a highly interdependent manner, regulating host specificity and significantly influencing disease development and intensity (Wang et al. 2020). Having defined SPIs and T3SS functions, studies continue which will define the entire process by which they interact with host molecules and how this leads to disease virulence. Further knowledge on how these interactions are established is important in order to allow treatment and control strategies to be formulated more effectively against *Salmonella* infection.

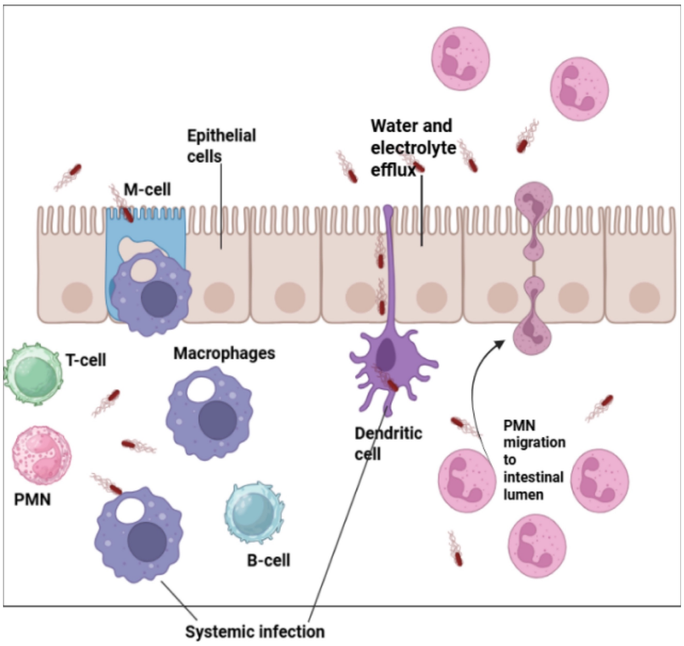

Fig. 1. *Entry of Salmonella into the host cells and the pathogenesis mechanism*

The complex cycle of *Salmonella* transmission in the food chain often originates from farm contamination, where bacteria gain access via an unclean environment, water, and feed (Nair and Kollanoor 2019). Seasonality trends and environmental conditions that affect shedding rates and bacterial proliferation, i.e., impact *Salmonella* dynamics. Broiler farms are also at risk of vertical transmission from breeder to chicks, with significant impacts on prevalence over cycles of production (Siddiqui et al. 2024b). Beyond the farm, processing and handling phases are high-risk for cross-contamination as *Salmonella* easily transfers from piece of equipment to piece of equipment and from surface to surface, and cleanliness measures are necessary (Kilonzo-Nthenge and Mukuna 2018). Since previous use of antibiotics had the effect of causing antimicrobial-resistant strains of *Salmonella*, which had made the treatment cumbersome and raised stakes for public health, Quantitative Microbiological Risk Assessment (QMRA) models assert the necessity of monitoring at these instances with caution (Rajan et al. 2017). Last but not least, incorrect handling of contaminated products continues to be a major driver of cross-contamination at retail and consumer levels, more so in home cooking environments (Sayed et al. 2024). The extensive prevalence of *Salmonella* along this entire food chain necessitates it absolutely to maintain improved sanitation at all times, enhance surveillance, and offer complete training on proper food handling procedures in order to minimize the likelihood of transmission and address the emerging problems caused by antibiotic resistance (Willis et al. 2023). Given its far-reaching transmission and complex pathogenesis, several effective interventions, particularly vaccination, have been instrumental in limiting the effect of *Salmonella*.

3. Vaccination strategies to control *Salmonella* infections in animals

3.1 Live attenuated vaccines

With special strengths such as the activation of intense systemic and mucosal immunity, precise for full protection and preventing invasion by pathogens at mucosal surfaces, live attenuated vaccines provide a valuable method for controlling salmonellosis in humans and animals (Shin et al. 2022). But these advantages are balanced against sharp disadvantages, such as the possibility that the attenuated strains will reassort into the virulent strain and cause harm to animal health (Gil et al. 2020). It is also worth noting that vaccinated animals shed the vaccine strain, which can infect the local environment and potentially cross-infect other animals (Cawthraw et al. 2024). That is why their administration has to be performed with the utmost care. However, live attenuated vaccines have been very effective in all other species of animals. For instance, vaccination of hens with live attenuated *Salmonella Typhimurium* has enhanced their immune response and significantly reduced shedding (McWhorter and Chousalkar 2018). These vaccines are still being researched to be optimized for broader application in livestock, although specific data on cattle and pigs are not as frequent. This is due to the fact that underlying immunological fundamentals have equal potential (Chagas et al. 2024). Therefore, as promising, the extensive application of live attenuated *Salmonella* vaccines hinges on continued research to assuage safety concerns and minimize shedding, thereby maximizing their protective benefits to animal health (Aehle and Curtiss Iii 2017).

3.2 Inactivated vaccines

Since inactivated (killed) vaccines are safe and stable in nature, they offer an effective means of *Salmonella* control in humans and animal populations. Since the vaccines do not include living organisms, they pose minimal risk for disease spread, and thus can be used broadly (Daniel Huberman et al. 2022). They remain stable for a longer duration without undergoing extreme loss of potency and hence become easy to distribute. Their ability to cause good immunity has been repeatedly shown in tests, and this has resulted in a significant reduction in pathogen shedding from the vaccinated animals (Cho et al. 2013). The failure of inactivated vaccines to induce good cell-mediated immunity, which is critical in fighting intracellular pathogens such as *Salmonella*, is their major limitation (Daniel Huberman et al. 2022). Such vaccines often require adjuvants to overcome this disadvantage and enhance humoral immune response, complicating formulation and delivery. Other models have been shown to be of high efficacy in lowering fecal shedding and colonization in chicken, such as a trivalent inactivated vaccine for *S. Enteritidis*, *Typhimurium*, and *Infantis* (Senevirathne et al. 2020). Besides, efficacy is route-dependent, but preliminary mouse trials gave 100% protection against lethal challenge. Although inactivated vaccines are certainly worth something due to their safety factor and simplicity of use, additional research must be done to address their shortcomings in inducing complete cell-mediated immunity and to increase overall efficacy against *Salmonella* infection (Won and Lee 2017).

3.3 Subunit vaccines

Subunit vaccines that target certain antigens, such as outer membrane proteins (OMPs) and flagellin, to induce certain immune responses without running into safety concerns involving live or inactivated vaccines are a possible way of controlling *Salmonella* in humans and animals (Dolatyabi et al. 2024). OMPs are good targets because research has established that OMP-based vaccines can significantly enhance the production of certain antibodies as well as cell-mediated immunity. As proven by enhanced delivery of flagellin-coated nanoparticles to chicken immune cells, flagellin, conversely, is a potent adjuvant that enhances the overall immunogenicity of subunit vaccines (Renu et al. 2018). The primary advantage of these vaccines is their better safety profile, i.e., they are less likely to induce adverse effects compared to live-attenuated counterparts, and their ability to induce very specific humoral and cellular immune responses, which are critical for protective *Salmonella* immunity (Liu et al. 2018). To ensure the optimal presentation of the vaccine to the immune system and a good response, there are still numerous challenges ahead in their production, particularly in exactly knowing the most protective antigens among the over 4,000 proteins that *Salmonella* carries and in designing effective delivery systems, such as polyanhydride nanoparticles (Liang et al. 2025). Despite their advantages in terms of safety and customized immunity, additional investigation is needed to overcome these challenges to antigen delivery and identification and achieve the full promise of subunit vaccines (Siddique et al. 2024a).

3.4 Vector vaccines

Salmonella-based vector vaccines have potential in veterinary science as a method of immunization of animals against various infections. To present foreign antigens of nonhomologous viruses and bacteria to the immune system, these vaccines use attenuated forms of *Salmonella*, such as *Salmonella typhi*, as live-attenuated vectors (Lloren and Lee 2023). Recombinant live-attenuated *Salmonella* vaccines (RASVs) produce long-lasting immunity and stability and can also be engineered to produce protective antigens of a wide range of pathogens (Bansal et al. 2024). Multivalency vaccinal protection, which is available against a number of pathogens at the same time and useful for many diseases. Multivalent *Salmonella* vaccines have elicited potent immune responses with preclinical models in preparation for their extensive application in veterinary medicine (Lauer et al. 2017). Heartening as this is, sustainment of long-term immunogenicity in clinical trials is a primary concern for which a delicate balance needs to be struck between the ability of the vaccine to confer immunity and attenuation (Sears et al. 2021).

3.5 Novel vaccine approaches

New vaccine platforms to prevent animal *Salmonella* are under development at a fast pace, employing novel technologies to improve vaccine effectiveness and fight multidrug-resistant bacteria. To elicit a robust immune response, DNA and mRNA vaccines introduce genetic material into host cells, and the cells translate to develop antigens (Aehle and Curtiss Iii 2017). DNA vaccines, for example, have been demonstrated to offer considerable promise against *Salmonella* in a number of animal models. Twenty-two top-scoring proteins of *Salmonella Pullorum* were identified successfully through the use of reverse vaccinology and immunoinformatics based on genetic data to identify lead antigen candidates. Some of these proteins highly protected chick embryos. In addition, CRISPR-Cas9 gene editing is being researched to create recombinant vaccines with increased immunogenicity and safety. This approach holds the promise of multivalent vaccinations against several pathogens at once (Yero et al. 2020). While these newer methods show tremendous potential, traditional methods of vaccination are still required in veterinary practice, indicating that using both old and new techniques would be optimal for giving the best protection against *Salmonella* infection in animals (Khalid and Poh 2023). The most robust mucosal and systemic immunity is provided by live attenuated vaccines, but potentially virulence and shedding may recur. While inactivated vaccines are safer and more stable, they cannot elicit strong cell-mediated immunity (Bansal et al. 2024). Subunit and vector vaccines yield safe, targeted replacements; more research is required to optimize antigen delivery and achieve broad efficacy. The ideal solution finds a compromise between the strength and totality of the immune response and safety and stability.

4. Impact of vaccination on zoonotic transmission

Through the reduction of shedding, colonization, and environmental contamination in food animals, vaccination plays a crucial role in restricting the zoonotic transmission of *Salmonella* to improve public health and food safety (Daniel Huberman et al. 2022). Live and inactivated vaccines both significantly mitigate *Salmonella* infection and subsequent shedding in poultry, which is central to preventing egg and meat contamination (Kogut and Santin 2019). The studies repeatedly show that vaccination has a great impact on diminishing fecal excretion and gastrointestinal colonization of *Salmonella* in animals, as seen from the effectiveness of the DIVA vaccine against *S. Typhimurium* in swine (Bearson et al. 2017). Given that *Salmonella* causes more than 95 million cases every year across the world, ensuring that vaccination efforts are put in place to lower the prevalence of the bacterium in animals and protect humans from contamination is crucial (Nazir et al. 2025). Furthermore, mass vaccination reduces the need for antibiotics, something which is vital in the worldwide struggle against antibiotic resistance. In spite of its obvious advantages, there are problems that still exist, including the fact that universal vaccinations of broad serovar coverage must be developed and the cost factors of large-scale immunization campaigns (Ayuti et al. 2024).

5. Non-antibiotic control strategies

Other than antibiotics and vaccines, *Salmonella* can also be managed with alternative strategies, including probiotics, prebiotics, organic acids, essential oils, and immunomodulators (Rabetafika et al. 2023; Fayyaz et al. 2025). These alternatives can be given to humans and animals through diet, and they improve gut health and decrease *Salmonella* invasion. Other than this, phage therapy (bacteriophage) has also been used in modern research to control *Salmonella* infections (Kinanti et al. 2024). The major advantage of these therapies is that they are less toxic and eco-friendly as compared to antibiotic treatment. Some of the important non-antibiotic therapies are discussed below and are shown in Fig. 2.

5.1 Use of probiotics and prebiotics

Probiotics and prebiotics, whose well-characterized mechanisms of action include stimulating host defense and inhibiting the pathogen growth directly, are promising alternatives to antibiotics for preventing *Salmonella* infection in humans and animals (Ayalp et al. 2025). Competitive exclusion is an important process wherein beneficial

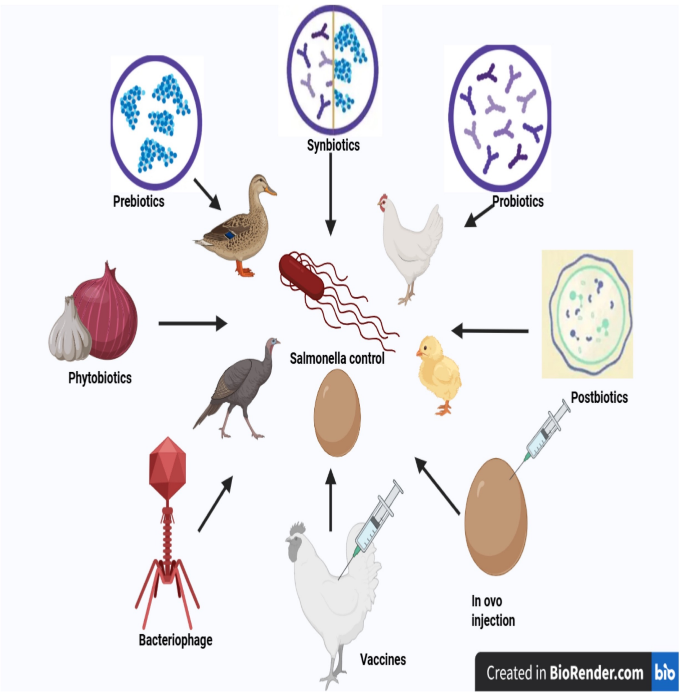

***Fig. 2.** Strategies to control Salmonella infection*

bacteria come in and occupy the good space in the gut so that *Salmonella* would not colonize and attach (Rabetafika et al. 2023). In addition, as shown by increased blood markers of TNF-α and Pig-MAP in treated animals, probiotics engage actively with immunomodulation to enhance the host's innate and adaptive immunity and exhibit a heightened immunological response to infection. In addition, some probiotic strains contribute to the production of antimicrobial compounds (Coniglio et al. 2023) by producing compounds such as organic acids and bacteriocins that inhibit *Salmonella* from proliferating (Solfaine et al. 2024). These therapies' efficacy is often strain-dependent, with differing positive effects for different animal species. In weaned pigs, for instance, *Lactobacillus rhamnosus* HN001 has exhibited effective *Salmonella* clearance, and in broilers, *Lactiplantibacillus plantarum* exhibited strong inhibitory effects against *Salmonella* Heidelberg (Kowalska et al. 2020). Similarly, it has been established that *Bifidobacterium longum* enhances immunological functions and significantly reduces *Salmonella* colonization in pigs (Cameron and McAllister 2019).

Probiotics and prebiotics hold great promise but do encounter a couple of challenges in the future. Choosing the most favorable probiotic strains for target animal species and *Salmonella* serovars is necessary to maximize gains, so selection of the strain is a crucial step. Because clearance of new probiotic products takes time and is complicated, regulatory obstacles can be a considerable challenge. Furthermore, observed variation in probiotic function can represent a confounding factor determined by a broad variety of environmental factors, host physiological characteristics, and the particular *Salmonella* challenge (Sachdeva et al. 2025). Thus, while probiotics and prebiotics present a strong argument in favor of *Salmonella* control, further work is needed to maximize their composition, application, and selection to achieve widespread and uniform efficacy in clinical and agricultural contexts (Hosseini et al. 2018).

5.2 Phage therapy (Bacteriophages)

During the time when antibiotic resistance is on the rise, bacteriophages, or phages, are a very promising option to standard medication in the fight against *Salmonella* infections in animals and humans (Kinanti et al. 2024). They are an attractive therapeutic option because of their inherent advantages (Khan and Rahman 2022). First, unlike broad-spectrum antibiotics that can disrupt the gut microbiota, phages exhibit high specificity, killing *Salmonella* bacteria while largely leaving the healthy commensal microbiota intact (Hu et al. 2018). Second, phages possess the unique characteristic of being able to propagate and multiply, where they cause infection provided their host bacteria are present. This would increase the effectiveness of the treatment and minimize the need for frequent high dosing (Kutter et al. 2005). Thirdly, unlike most drug treatments, phages are generally low in toxicity for non-target species, including humans and animals, with minimal side effects and a good safety profile (Hibstu et al. 2022).

Phage therapy's plasticity permits the promise of having an overwhelmingly large number of applications in the food supply. Phages can be intentionally targeted to deliver to pigs and poultry in feed or water during pre-harvest conditions (Thanki et al. 2021). This lowers *Salmonella* colonization within the animals prior to reaching the food supply. By being proactive in this step, the bacterial burden is significantly diminished at the source (Pelyuntha et al. 2022). Phages can be sprayed directly onto food surfaces, such as carcasses and processed foods in post-harvest use to actively decrease *Salmonella* contamination. This enhances food safety and reduces the likelihood of acquiring a foodborne illness (De Veg et al. 2019).

While these are key advantages, there are a variety of barriers to the general application of phage therapy. Host range is one of the primary limitations of phages; certain phages may be effective against very few *Salmonella* strains, so phage cocktails or the development of new phages must be done to obtain coverage of a range of serovars (Molina et al. 2024). Similar to antibiotic resistance, phages can also be resisted by bacteria, making long-term treatment plans difficult and necessitating ongoing research on new isolates of phages. Lastly, the regulatory factor is a significant barrier; in most countries, there is no well-documented and standardized protocol for phage therapy approval and administration, effectively limiting its application in veterinary as well as human medicine (Khan and Rahman 2022). In spite of these difficulties, phage therapy offers much potential as a long-term, specific treatment for *Salmonella* infection. This is particularly so in light of the increasing problem of antibiotic resistance and the need for urgent research and the development of robust legal frameworks to allow its safe and effective use (Alsayed and Permana 2024).

5.3 Use of organic acids and essential oils

Essential oils (EOs) and organic acids are gaining prominence for their powerful antibacterial action against human and animal *Salmonella* infections as new antimicrobials for replacing traditional antibiotics (Bagheri et al. 2024). They exert action by inhibiting the metabolism and integrity of bacteria through complex mechanisms (Al-Harrasi et al. 2022; Rashid et al. 2024). The most potent of these is the cell membrane disruption, where bioactive compounds such as carvacrol and thymol in essential oils lyse the bacterial cell membrane through a mechanism of increased permeability, leading to loss of the cellular contents and finally death of the cells. Additionally, EOs are also able to induce metabolic inhibition of *Salmonella* by targeting the key biochemical pathways for pathogen growth and survival (Gómez-García et al. 2020; Iqbal et al. 2024). These products have been used practically in animal production, especially when supplemented to water and feed. Addition of EO and blends of organic acids to feed has shown outstanding in broiler hens, which effectively controlled *Salmonella* loads, boosted growth, and improved gut health (Hu et al. 2023). In the same way, organic acid treatment of water is also needed in an attempt to eliminate *Salmonella* contamination of animal environments and provide a safer environment for animal keeping. Likewise, organic acid water treatment is important in an attempt to limit *Salmonella* invasion of animal environments and provide a safer environment to animals (Hu et al. 2023).

Aside from their direct antibacterial effect, essential oils and organic acids also exhibit positive effect on the intestinal microbiota of the host. By stimulating the growth of the beneficial bacteria such as the butyric acid-producing bacteria, they can modulate the gut microbiota and establish a normal gut environment by competing with *Salmonella* (Nhara et al. 2024). This change, therefore, yields lower amounts of *Salmonella* colonization in the infected animal's intestines, which lower the shedding of the pathogen and retard its spread (Qiao et al. 2022). Although the utilization of organic acids and essential oils as a control measure of *Salmonella* is a long-lasting, potent, and antibiotic-free method, there exist certain disadvantages. Host animal overall health status, intended *Salmonella* serovar, and environment are all contributory factors and may have a main role in their potency (Stingelin et al. 2023). Additionally, for optimal consumption and best possible outcome, potential impacts on feed palatability and nutrient formulation concerns need to be addressed with care. To develop their application further and formulate significant protocols for their effective and large-scale use in agricultural settings, additional research must be performed (Dhakal and Aldrich 2023).

5.4 Phytobiotics and immunomodulators

The central function of phytobiotics and immunomodulators in supporting host defense against *Salmonella* infection in animal and human hosts is progressively well understood. These endogenous compounds are strong substitutes for traditional antibiotics because they contain intrinsic antibacterial activity as well as immune system stimulation (Noor et al. 2023). Innate and adaptive immunity are completely enhanced as part of their mechanism of action. For instance, immunomodulators trigger major immune cells such as dendritic cells and macrophages, which consequently lead to the secretion of major cytokines such as IL-12 and IL-18. These cytokines, working in tandem, are purported to enhance the host's immunity against *Salmonella*. Similarly, phytobiotics have shown potential to improve humoral as well as cellular immunity in poultry, particularly after vaccination. These plant materials show direct antibacterial activity along with their immune-stimulating effect (Abd El-Ghany 2020). Recombinant human β-defensins derived from plants (hBD-1 and hBD-2) have shown great promise, inhibiting in vitro *Salmonella* growth by up to 96%. Phytochemicals also actively act against antibiotic resistance determinants of *Salmonella* by effectively inhibiting efflux pumps and biofilm formation, making them potential antimicrobial agents (Patro et al. 2015). Despite such promising developments, there are still obstacles to overcome, namely relating to standardizing these natural compounds and negotiating the hurdles of securing regulatory approval to utilize them more extensively in veterinary and human medicine (Orimaye et al. 2024). Compared to traditional antibiotics, the non-antibiotic *Salmonella* treatments are less harmful and ecologically friendly. Through mechanisms such as chemical synthesis of antimicrobial compounds, they inhibit the growth of pathogens in a direct action, facilitate gut wellness, and cause competitive exclusion. High specificity treatments such as phage therapy also maintain the healthy gut flora.

6. Farm management practices and biosecurity

Farms need to apply a multi-pronged approach based on optimal biosecurity and farm management practices to manage *Salmonella* infections. Strict hygiene within the farm in the form of regular cleansing and decontamination of facilities and separation of sick animals are key strategies (Raut et al. 2023). Pest control is also essential, such as the use of bait boxes and traps for rodents and insects and the exclusion of wildlife to avoid cross-contamination. To prevent cross contamination between groups, all-in/all-out batch management systems need to be employed and water quality monitored and treated (Poudel and Adhikari 2024). Environmental contamination can be prevented by effective disposal of waste, such as effective manure management. Lastly, regular feed testing and treatment widely reduces the risk of infection by feed safety and decontamination (Youssef et al. 2021). Farms must implement a multi-layered approach based on good biosecurity and farm management practice in order to combat infection of *Salmonella*. Sanitizing the farm is of basic importance, from the regular maintenance of cleaning and disinfection of buildings through to segregation of infected animals (Pedersen et al. 2023). Pest control, such as the employment of rodent and insect control in the form of reutenent stations and traps and wildlife encroachment prevention to prevent cross-contamination, is also as important. All-in/all-out batch control systems and water quality in the form of treatment and monitoring must be employed to prevent cross-contamination between batches (Smith et al. 2023). Environmental pollution can be avoided with proper waste disposal, such as safe manure handling. Lastly, frequent testing and treatment of feed greatly lowers the risk of infection from feed safety and disinfection (Zamora-Sanabria and Alvarado 2017). A summary of the control strategies for *Salmonella* is given in Table 1.

7. One Health approach to control *Salmonella*

Because human, animal, and environmental health are all highly interdependent, the One Health approach provides an integrated and unified framework for addressing *Salmonella* infections. To address foodborne outbreaks effectively and inhibit the spread of infections like *Salmonella*, this multifaceted approach promotes preventive, intersectoral action by a variety of sectors (Feng et al. 2023). Intersectoral coordination, through fostering good partnerships between environmental, animal, and human health agencies, is at the heart of the One Health approach. As has been demonstrated by simulation exercises such as those conducted in Portugal, which placed high priority on the inherent need for harmonization and safe data exchange in a quest to improve readiness for subsequent epidemics, this multidisciplinary approach acknowledges that the control of disease is not plausibly attainable unilaterally. These exercises underpin the need for cooperation by highlighting communication and coordination breakdowns. The effectiveness of One Health planning depends on successful surveillance and information exchange. To provide information gathering and analysis on zoonotic disease on a required basis, capable surveillance systems such as the United States' National Notifiable Disease Surveillance System are needed. Systematic data collection facilitates targeted, timely action through early outbreak

Table 1. Summarized table for control strategies for *Salmonella*

Control strategy	Type	Advantage	Limitation	Key findings	Future directions	References
Vaccination	Live attenuated vaccines	Good systemic and mucosal immunity	Shedding of vaccination strain pathogenicity regain	Reduced shedding in chickens that were vaccinated with *Salmonella Typhimurium*	Ongoing research to mitigate shedding and assuage safety concerns	(Raccoursier et al. 2024)
	In-activated vaccines	Long shelf life Stability less disease transmission and safety	Require adjuvants Cannot develop good cell-mediated immunity	Reduced fecal shedding in chickens against *S. Enteritidis, Typhimurium,* and *Infantis*	Studies to enhance overall effectiveness and cell-mediated immunity	(Walker and Bourgeois 2023)
	Sub-unit vaccines	Better safety profile induce specific cellular and humoral immune responses	The challenges of identifying the best protective antigens Develop effective delivery systems	OMP-based immunizations induce cell-mediated immunity and antibody production	Additional studies are needed to identify and deliver antigens.	(Marasini and Kaminskas 2019)
	Vector vaccines	Can deliver multivalent protection Immunity is constant and durable.	Challenging to achieve consistent immunogenicity	Robust immune reactions were demonstrated in preclinical models.	Vaccine attenuation and immunity potential equilibrium	(Roland et al. 2020)
	Novel vaccine approaches (DNA/mRNA/ CRISPR Cas-9)	Induce robust immune reactions Hold promise against MDR bacteria	Still under development	In animal models, DNA vaccines hold promise; CRISPR-Cas9 for recombinant immunizations	Ongoing R&D complemented with traditional methods	(Zahedipour et al. 2024)
Alternative control strategies	Prebiotics/ probiotics	Immunomodulation, pathogen growth inhibition competitive exclusion stimulation of host defense	Strain dependence, activity Unpredictability and regulatory restriction.	For the elimination of *Salmonella* from pigs, use *Lactobacillus rhamnosus* HN001.	Strain selection, application, and composition optimization	(Kosuri et al. 2025)
	Phage therapy (Bacteriophages)	*Salmonella* specificity, site of infection amplification low toxicity	Limited host range, phage-resistant organisms regulatory issues	It may be applied onto food surfaces post-harvest or in feed and water prior to harvest.	Enforcing robust legislative structures and prompt research are vital for safe and effective utilization.	(Palma and Qi 2024)
	Organic acids and essential oils	Enhance gut health promote good bacteria disrupt bacterial metabolism and integrity.	Environment, host, and serovar influence all efficacy; palatability issues	Reduce *Salmonella* loads in broiler hens by the use of feed additives	Further research for use and credible practice in agriculture	(Hu et al. 2023)
	Phytobiotics & immunomodula tors	Innate and adaptive immune system stimulation Inherent antibacterial activity	Regulatory approval standardization issues	Enhance chicken humoral and cellular immunity; prevent *Salmonella* growth in vitro	Overcoming legal barriers to facilitate wider use	(Abd El-Ghany 2020)
	Farm management & biosecurity	Feed testing waste management, all-in/ all-out systems pest control, and strict hygiene	Needs regular monitoring	Eliminates the likelihood of infection and prevents cross-contamination.	Continual improvement and adherence to best methodologies	(Smith et al. 2023)

warning (Mehmood et al. 2023). Also, application of most of the modern technologies, such as Geographic Information Systems, is a big help towards the powerful representation of disease patterns. GIS allows tracking of the transmission channels in spatial analysis and data mapping so that it can be possible to target resources and interventions more effectively.

To combat successfully the complex challenges posed by zoonotic diseases, One Health actually needs to be addressed by concerted efforts from all the involved sectors. Case-control research has the tendency to provide the foundation for tailored interventions to reduce transmission through systematic recognition of outbreak origins (Qureshi et al. 2024). Organizational and political will at a large scale must, however, come into play for successful implementations of such concerted policies. Strong leadership and continued support of committed agencies and organizations would be prevented from effectively and efficiently controlling *Salmonella* and other zoonotic risks by fragmented action and unnecessary consumption of resources. There are however barriers to implementation despite the obvious advantages of the One Health strategy. These are broken systems of data that conventionally work in silos within multiple sectors and hence make it difficult to achieve integrated analysis and scarce resources that potentially constrain building and sustaining effective surveillance programs and intervention schemes. Unlocking the true potential of the One Health approach for the protection of public and animal health, these are challenges that must be overcome by commitment to enhance intersectoral collaboration and build surveillance capacity.

8. Challenges and limitations

There are certain obstacles to effective *Salmonella* control in the poultry supply chain that affect ease and effectiveness of interventions. One considerable such obstacle is cost-effectiveness of treatment, particularly due to the fact that producers, especially from the developing world, may have severe financial limitations when implementing extensive measures such as improved biosecurity, vaccine programs, and aggressive feed hygiene (Rabie et al. 2023). Probiotics and bacteriophages are other possible alternative technologies just starting to make waves, but requiring gigantic amounts of research and development funding to demonstrate their safety and effectiveness before they can be applied to masses (Susalam et al. 2024). Current control measures and treatments are magnified by the emergence of antibiotic-resistant pathogens such as *Salmonella* Infantis, which is typically multidrug-resistant. This necessitates sharp vigilance and stern management practices that can fight against the evolving nature of *Salmonella* along with resistance (Rabie et al. 2023). In addition to ongoing research funding into other treatments and health education for the public, resolving these interlinked issues is a collective effort by industry stakeholders, regulators, and consumers (Mahmoud et al. 2023). Continuous investment in research and development of possible non-antibiotic treatments such as probiotics and bacteriophages to determine their safety and large-scale use is one of means to end the danger of *Salmonella*. Industry, regulators, consumers, and all have to work together to aggressively combat antibiotic-resistant strains and support public health education.

9. Conclusions

Salmonella bacteria, because of their multiple strains, exhibit antimicrobial resistance to traditional antibiotic medicines and resulting in massive economic losses worldwide. Vaccination is among the more effective strategies that have yielded remarkable results, but vaccines against non-typhoidal *Salmonella*, particularly in poultry, continue to develop but are restrained by the variable efficacy of serovars and production systems. Other therapeutic interventions like prebiotics, probiotics, organic acids, plant extracts, essential oils, bacteriophages, and immunomodulators provide effective outcomes to inhibit bacterial colonization, shedding, and transmission. These treatments can be used with optimal benefits if they are administered with stringent biosecurity protocols. In addition, regimens of One Health genomic surveillance will be necessary to minimize the global burden of salmonellosis and maintain human and animal health.

Declarations

Funding: Not applicable

Conflict of interest: Authors declare no conflicts of interest

Acknowledgements: None

References

Abd El-Ghany WA. (2020). Phytobiotics in poultry industry as growth promoters, antimicrobials and immunomodulators–A review. Journal of World's Poultry Research 10(4): 571-579. https://dx.doi.org/10.36380/jwpr.2020.65

Aehle S, Curtiss Iii R. (2017). Current and future perspectives on development of *Salmonella* vaccine technologies. In: Ricke SC, Gast RK, editors, Producing Safe Eggs: Microbial Ecology of *Salmonella*. Academic Press, Elesvier. Pp. 281-299. https://doi.org/10.1016/B978-0-12-802582-6.00014-8

Al-Harrasi A, Bhatia S, Behl T, Kaushik D, Ahmed MM, Anwer K. (2022). Antibacterial mechanism of action of essential oils. In: Al-Harrasi A, Bhatia S, Behl T, Kaushik D, Anwer K, Ahmed MM, Babu P, Sharma A, Kabir MT, Mittal V, editors, Role of Essential Oils in the Management of COVID-19. CRC Press, Boca Raton. Pp. 227-237

Alsayed AR, Permana AD. (2024). Bacteriophages therapy: exploring their promising role in microbiome modulation and combatting antibiotic resistance. OBM Genetics 8(2): 1-8. https://doi.org/10.21926/obm.genet.2402237

Arya G, Holtslander R, Robertson J, Yoshida C, Harris J, Parmley J, Nichani A, Johnson R, Poppe C. (2017). Epidemiology, pathogenesis, genoserotyping, antimicrobial resistance, and prevention and control of non-typhoidal *Salmonella* serovars. Current Clinical Microbiology Reports 4(1): 43-53. https://doi.org/10.1007/s40588-017-0057-7

Ayalp G, Borum AE, Akyol ET. (2025). The use of probiotic footbaths for the treatment of ovine interdigital dermatitis. Kafkas Universitesi Veteriner Fakultesi Dergisi 31(2): 197-205. https://doi.org/10.9775/kvfd.2024.33091

Ayuti SR, Khairullah AR, Al-Arif MA, Lamid M, Warsito SH, Moses IB, Hermawan IP, Silaen OSM, Lokapirnasari WP, Aryaloka S. (2024). Tackling salmonellosis: A comprehensive exploration of risks factors, impacts, and solutions. Open Veterinary Journal 14(6): 1313-1329. https://doi.org/10.5455/OVJ.2024.v14.i6.1

Bagheri E, Shori AB, Peng CW, Baba AS, Alzahrani AJ. (2024). Phytochemical analysis and medicinal properties of some selected traditional medicinal plants. International Journal of Agriculture and Biosciences 13(4): 689-700. https://doi.org/10.47278/journal.ijab/2024.177

Bansal G, Ghanem M, Sears KT, Galen JE, Tennant SM. (2024). Genetic engineering of *Salmonella spp*. for novel vaccine strategies and therapeutics. EcoSal Plus 12(1): eesp-0004. https://doi.org/10.1128/ecosalplus.esp-0004-2023

Bearson BL, Bearson SMD, Brunelle BW, Bayles DO, Lee IS, Kich JD. (2017). *Salmonella* DIVA vaccine reduces disease, colonization and shedding due to virulent *S. Typhimurium* infection in swine. Journal of Medical Microbiology 66(5): 651-661. https://doi.org/10.1099/jmm.0.000482

Borovikov S, Kuibagarov M, Akibekov O, Muranets A. (2024). Clinical case of Salmonella detected in an aborted mare fetus and its characteristics. International Journal of Veterinary Science 13(3): 357-361. https://doi.org/10.47278/journal.ijvs/2023.103

Cameron A, McAllister TA. (2019). Could probiotics be the panacea alternative to the use of antimicrobials in livestock diets? Beneficial Microbes 10(7): 773-800. https://doi.org/10.3920/BM2019.0059

Carneiro DG, Vidigal PMP, Morgan T, Vanetti MCD. (2024). Genome sequencing and analysis of *Salmonella* enterica subsp. enterica serotype Enteritidis PT4 578: insights into pathogenicity and virulence. Access Microbiology 6(11): 000828-v000823. https://doi.org/10.1099/acmi.0.000828.v3

Cawthraw SA, Goddard A, Huby T, Ring I, Chiverton L, Mueller-Doblies D. (2024). Early vaccination of laying hens with the live bivalent *Salmonella* vaccine AviPro™ *Salmonella* DUO results in successful vaccine uptake and increased gut colonization. Frontiers in Microbiology 14: 1327739. https://doi.org/10.3389/fmicb.2023.1327739

Chagas DB, Santos FDS, de Oliveira NR, Bohn TLO, Dellagostin OA. (2024). Recombinant live-attenuated *Salmonella* vaccine for veterinary use. Vaccines 12(12): 1319. https://doi.org/10.3390/vaccines12121319

Cho Y, Kang Z.-W, Kang KS, Jeong S, Yoon HJ, Suh S, Hahn TW. (2013). Efficacy and clinical trials of Salenvac-T, bivalent killed vaccine containing *Salmonella* Enteritidis and *Salmonella* Typhimurium. Korean Journal of Veterinary Research 53(1): 43-48. https://doi.org/10.14405/kjvr.2013.53.1.043

Coniglio MV, Luna MJ, Provensal P, Watson S, Ortiz ME, Ludueña HR, Cavaglieri L, Magnoli AP. (2023). Use of the probiotic Saccharomyces cerevisiae var. boulardii RC009 in the rearing stage of calves. International Journal of Agriculture and Biosciences 12(3): 188-192. https://doi.org/10.47278/journal.ijab/2023.063

Corti Isgro M, Magnoli A, Poloni V, Rosales L, Luna MJ, Carranza A, Cavaglieri L, Parada J. (2024). Enhancing sow and piglet performance: evaluation of a probiotic additive of Saccharomyces boulardii RC009 from late gestation through lactation. International Journal of Agriculture and Biosciences 13(4): 836-841. https://doi.org/10.47278/journal.ijab/2025.016

Daniel Huberman Y, Caballero-Garcia M, Rojas R, Ascanio S, Hipolito Olmos L, Malena, R, Lomonaco J, Nievas P, Chero P, Levano-Gracia J. (2022). The efficacy of a trivalent inactivated *Salmonella* vaccine combined with the live *S. Gallinarum* 9R vaccine in young layers after experimental infections with *S. Enteritidis*, *S. Typhimurium*, and *S. Infantis*. Vaccines 10(7): 1113. https://doi.org/10.3390/vaccines10071113

De Veg B, Sirdesai S, Peterson R, Pinheiro M, Nuboer W, Kan A, Van Mierlo J. (2019). Efficiency of phage intervention against *Salmonella* in meat and poultry processing. Meat and Muscle Biology 3(2): 142. https://doi.org/10.22175/mmb.10823

Dhakal J, Aldrich CG. (2023). Application of acidulants to control *Salmonella* spp. in rendered animal fats and oils with different levels of unsaturation. Animals 13(8): 1304. https://doi.org/10.3390/ani13081304

Dolatyabi S, Renu S, Schrock J, Renukaradhya GJ. (2024). Chitosan-nanoparticle-based oral *Salmonella enteritidis* subunit vaccine elicits cross-protection against *Salmonella typhimurium* in broilers. Poultry Science 103(5): 103569. https://doi.org/10.1016/j.psj.2024.103569

Fàbrega A, Vila J. (2013). *Salmonella enterica* serovar *Typhimurium* skills to succeed in the host: virulence and regulation. Clinical Microbiology Reviews 26(2): 308-341. https://doi.org/10.1128/cmr.00066-12

Fayyaz A, Fatima J, Mahmood S, Khurram Y, Naz G, Aslam RS, Sarwar A, Sarwar F, Israr Y, Israr A, Ahmad A, Rafay A, Shehzad T. (2025). Role of probiotics in the control of Salmonella infections in animals and humans. Letters in Animal Biology 5(2): 06-16. https://doi.org/10.62310/liab.v5i2.202

Feng Z, Hag ME, Wang N, Qin T, Chen S, Peng D. (2023). Negative regulation of RpoS-mediated stm1703 in biofilm formation of *Salmonella Pullorum*. Pakistan Veterinary Journal 43(1): 25-32. https://doi.org/10.29261/pakvetj/2022.086

Gil C, Latasa C, García-Ona E, Lázaro I, Labairu J, Echeverz M, Burgui S, García B, Lasa I, Solano C. (2020). A DIVA vaccine strain lacking RpoS and the secondary messenger c-di-GMP for protection against salmonellosis in pigs. Veterinary Research 51(1): 3. https://doi.org/10.1186/s13567-019-0730-3

Gómez-García M, Argüello H, Puente H, Mencía-Ares Ó, González S, Miranda R, Rubio P, Carvajal A. (2020). In-depth in vitro evaluation of the activity and mechanisms of action of organic acids and essential oils against swine enteropathogenic bacteria. Frontiers in Veterinary Science 7: 572947. https://doi.org/10.3389/fvets.2020.572947

Hibstu Z, Belew H, Akelew Y, Mengist HM. (2022). Phage therapy: A different approach to fight bacterial infections. Biologics: Targets and Therapy 16: 173-186. https://doi.org/10.2147/BTT.S381237

Hosseini NG, Modarressi MH, Mousavi SN, Ebrahimi MT. (2018). Evaluation of novel probiotic Bacillus strains based on enzyme production and protective activity against salmonellosis. Journal of the Hellenic Veterinary Medical Society 69(4): 1205-1212. https://doi.org/10.12681/jhvms.16089

Hu Yoo, Hugerth LW, Bengtsson C, Alisjahbana A, Seifert M, Kamal A, Sjöling Å, Midtvedt T, Norin E, Du J. (2018). Bacteriophages synergize with the gut microbial community to combat *Salmonella*. mSystems 3(5) 10-1128. https://doi.org/10.1128/msystems.00119-18

Hu Z, Liu L, Guo F, Huang J, Qiao J, Bi R, Huang J, Zhang K, Guo Y, Wang Z. (2023). Dietary supplemental coated essential oils and organic acids mixture improves growth performance and gut health along with reduces *Salmonella* load of broiler chickens infected with *Salmonella* Enteritidis. Journal of Animal Science and Biotechnology 14(1): 95. https://doi.org/10.1186/s40104-023-00889-2

Iqbal T, Altaf S, Fatima M, Rasheed R, Laraib K, Azam M, Karamat M, Salma U, Usman S. (2024). A narrative review on effective use of medicinal plants for the treatment of parasitic foodborne diseases. Agrobiological Records 16: 79-92. https://doi.org/10.47278/journal.abr/2024.016

Jajere SM. (2019). A review of *Salmonella* enterica with particular focus on the pathogenicity and virulence factors, host specificity and antimicrobial resistance including multidrug resistance. Veterinary World 12(4): 504-521. https://doi.org/10.14202/vetworld.2019.504-521

Khalid K, Poh CL. (2023). The promising potential of reverse vaccinology-based next-generation vaccine development over conventional vaccines against antibiotic-resistant bacteria. Vaccines 11(7): 1264. https://doi.org/10.3390/vaccines11071264

Khan MAS, Rahman SR. (2022). Use of phages to treat antimicrobial-resistant *Salmonella* infections in poultry. Veterinary Sciences 9(8): 438. https://doi.org/10.3390/vetsci9080438

Kilonzo-Nthenge A, Mukuna W. (2018). *Salmonella* and antimicrobial resistance in fresh produce. In: Mascellino MT, editor, *Salmonella* - A Re-emerging Pathogen. IntechOpen, London, UK. https://doi.org/10.5772/intechopen.72894

Kinanti AS, Prihanto AA, Jatmiko YD, Kobun R, Felicia WXL. (2024). Harnessing bacteriophages: a promising approach to combat foodborne pathogen biofilms. International Journal of Agriculture and Biosciences 13(4): 656-668. https://doi.org/10.47278/journal.ijab/2024.172

Kirti N, Krishna SS, Shukla D. (2024). *Salmonella* infections: an update, detection and control strategies. In: Huang C, editor, *Salmonella*-Current Trends and Perspectives in Detection and Control. IntechOpen, London, UK. https://doi.org/10.5772/intechopen.1004835

Kogut MH, Santin E. (2019). Advances in vaccines for controlling foodborne *Salmonella* spp. in poultry. In: Venkitanarayanan K, Thakur S, Ricke S, editors, Food Safety in Poultry Meat Production. Springer, Cham. Pp. 161-189. https://doi.org/10.1007/978-3-030-05011-5_8

Kombade S, Kaur N. (2021). Pathogenicity island in *Salmonella*. In: Lamas A, Regal P, Franco CM, editors, *Salmonella spp.*-A Global Challenge. IntechOpen, London, UK. https://doi.org/10.5772/intechopen.96443

Kosuri P, Muttathukonam SH, Reddyvari R, Gao M, Ren Y, Amalaradjou MA. (2025). Probiotic application reduces Salmonella Enteritidis contamination in layer hatching eggs and embryos. Poultry Science 104(9): 105389. https://doi.org/10.1016/j.psj.2025.105389

Kowalska JD, Nowak A, Śliżewska K, Stańczyk M, Łukasiak M, Dastych J. (2020). Anti-*Salmonella* potential of new *Lactobacillus* strains with the application in the poultry industry. Polish Journal of Microbiology 69(1): 5-18. https://doi.org/10.33073/pjm-2020-001

Kuria JKN. (2023). Salmonellosis in food and companion animals and its public health importance. In: Huang H, Naushad S, editors, *Salmonella*-Perspectives for Low-Cost Prevention, Control and Treatment. IntechOpen, London, UK. https://doi.org/10.5772/intechopen.109324

Kutter E, Kuhl S, Alavidze Z, Blasdel B. (2005). Phage therapy: bacteriophages as natural, self-limiting antibiotics. In: Pizzorno JE, Murray MT, editors, Textbook of Natural Medicine. Elsevier, Churchill Livingstone. Pp. 945-956. https://doi.org/10.13140/2.1.1100.3840

Lamichhane B, Mawad AMM, Saleh M, Kelley WG, Harrington PJ, Lovestad CW, Amezcua J, Sarhan MM, El Zowalaty ME, Ramadan H. (2024). Salmonellosis: an overview of epidemiology, pathogenesis, and innovative approaches to mitigate the antimicrobial resistant infections. Antibiotics 13(1): 76. https://doi.org/10.3390/antibiotics13010076

Lauer KB, Borrow R, Blanchard TJ. (2017). Multivalent and multipathogen viral vector vaccines. Clinical and Vaccine Immunology 24(1): e00298-00216. https://doi.org/10.1128/CVI.00298-16

Liang J, Yao L, Liu Z, Chen Y, Lin Y, Tian T. (2025). Nanoparticles in subunit vaccines: immunological foundations, categories, and applications. Small 21(1): 2407649. https://doi.org/10.1002/smll.202407649

Liu B, Wu Z, Liu T, Qian R, Wu T, Liu Q, Shen,A. (2018). Polymeric nanoparticles engineered as a vaccine adjuvant-delivery system. In: Immunization-Vaccine Adjuvant Delivery System and Strategies. IntechOpen, London, UK. http://dx.doi.org/10.5772/intechopen.81084

Lloren KKS, Lee JH. (2023). Live-attenuated *Salmonella*-based oral vaccine candidates expressing PCV2d Cap and Rep by Novel expression plasmids as a vaccination strategy for mucosal and systemic Immune responses against PCV2d. Vaccines 11(12): 1777. https://doi.org/10.3390/vaccines11121777

Lou L, Zhang P, Piao R, Wang Y. (2019). *Salmonella* pathogenicity island 1 (SPI-1) and its complex regulatory network. Frontiers in Cellular and Infection Microbiology 9: 270. https://doi.org/10.3389/fcimb.2019.00270

Lynch MF, Tauxe RV. (2009). Salmonellosis: nontyphoidal. In: Brachman P,Abrutyn E, editors, Bacterial Infections of Humans: Epidemiology and Control. Springer, Boston, MA. Pp. 677-698. https://doi.org/10.1007/978-0-387-09843-2_32

Magnoli AP, Parada J, Luna MarÃa J, Corti M, Escobar FM, FernÃ¡ndez C, Coniglio MV, Ortiz ME, Wittouck P, Watson S, Cristofolini LA, Cavaglieri L. (2024). Impact of probiotic Saccharomyces cerevisiae var. boulardii RC009 alone and in combination with a phytase in broiler chickens fed with antibiotic-free diets. Agrobiological Records 16: 1-10. https://doi.org/

10.47278/journal.abr/2024.006

Mahmoud DH, Ali AAA, Khalil AM, Amin YA, Ali AO. (2023). Low temperature-survivability behavior of *Salmonella enterica* subsp. *Enterica* serovar *Typhimurium* and *Salmonella enterica* subsp. *enterica* serovar *Enteritidis* in a minced beef meat model as an evaluation of the cold chain's preserving-effectiveness. International Journal of Veterinary Science 12(6): 853-859. https://doi.org/10.47278/journal.ijvs/2023.052

Marasini, N., Kaminskas, L. M. (2019). Subunit-based mucosal vaccine delivery systems for pulmonary delivery-Are they feasible? Drug Development and Industrial Pharmacy 45(6): 882-894. https://doi.org/10.1080/03639045.2019.1583758

Marus JR, Magee MJ, Manikonda K, Nichols MC. (2019). Outbreaks of *Salmonella* enterica infections linked to animal contact: Demographic and outbreak characteristics and comparison to foodborne outbreaks—United States, 2009–2014. Zoonoses and Public Health. 66(4): 370-376. https://doi.org/10.1111/zph.12569

McWhorter AR, Chousalkar KK. (2018). A long-term efficacy trial of a live, attenuated *Salmonella Typhimurium* vaccine in layer hens. Frontiers in Microbiology 9: 1380. https://doi.org/10.3389/fmicb.2018.01380

Mehmood A, Nawaz M, Rabbani M, Mushtaq MH. (2023). Probiotic effect of *limosilactobacillus fermentum* on growth performance and competitive exclusion of *Salmonella gallinarum* in poultry. Pakistan Veterinary Journal 43(4): 659-664. http://dx.doi.org/10.29261/pakvetj/2023.103

Molina WPC, Riofrio MDP, Espinosa PMJ, Jurado MAS. (2024). Phage therapy against multiresistant bacteria. Interamerican Journal of Health Sciences 4: 91-91. https://doi.org/10.59471/ijhsc202491

Nair DVT, Kollanoor Johny A. (2019). *Salmonella* in poultry meat production. In: Venkitanarayanan K, Thakur S, Ricke S, editors, Food Safety in Poultry Meat Production. Springer, Cham. Pp. 1-24. https://doi.org/10.1007/978-3-030-05011-5_1

Naushad S, Ogunremi D, Huang H. (2023). *Salmonella*: A brief review. In: Huang H, Naushad S, editors, *Salmonella*—Perspectives for Low-Cost Prevention, Control and Treatment. IntechOpen, London, UK. Pp. 1-22. http://dx.doi.org/10.5772/intechopen.112948

Nazir J, Manzoor T, Saleem A, Gani U, Bhat SS, Khan S, Haq Z, Jha P, Ahmad SM. (2025). Combatting *Salmonella*: a focus on antimicrobial resistance and the need for effective vaccination. BMC infectious diseases 25(1): 84. https://doi.org/10.1186/s12879-025-10478-5

Nhara RB, Marume U, Nantapo CWT. (2024). Potential of organic acids, essential oils and their blends in pig diets as alternatives to antibiotic growth promoters. Animals 14(5): 762. https://doi.org/10.3390/ani14050762

Noor G, Badruddeen, Akhtar J, Singh B, Ahmad M, Khan MI. (2023). An outlook on the target-based molecular mechanism of phytoconstituents as immunomodulators. Phytotherapy Research 37(11): 5058-5079. https://doi.org/10.1002/ptr.7969

Obe T, Boltz T, Kogut M, Ricke SC, Brooks LA, Macklin K, Peterson A. (2023). Controlling *Salmonella*: strategies for feed, the farm, and the processing plant. Poultry Science 102(12): 103086. https://doi.org/10.1016/j.psj.2023.103086

Orimaye OE, Ekunseitan DA, Omaliko PC, Fasina YO. (2024). Mitigation potential of herbal extracts and constituent bioactive compounds on *Salmonella* in meat-type poultry. Animals 14(7): 1087. https://doi.org/10.3390/ani14071087

Palma M, Qi B. (2024). Advancing phage therapy: a comprehensive review of the safety, efficacy, and future prospects for the targeted treatment of bacterial infections. Infectious Disease Reports 16(6): 1127-1181. https://doi.org/10.3390/idr16060092

Palmer AD, Slauch JM. (2020). Envelope stress and regulation of the *Salmonella* pathogenicity Island 1 type III secretion system. Journal of Bacteriology 202(17): 10-1128. https://doi.org/10.1128/jb.00272-20

Patro S, Maiti S, Panda SK, Dey N. (2015). Utilization of plant-derived recombinant human β-defensins (hBD-1 and hBD-2) for averting salmonellosis. Transgenic Research 24(2): 353-364. https://doi.org/10.1007/s11248-014-9847-3

Pedersen L, Houe H, Rattenborg E, Nielsen LR. (2023). Semi-quantitative biosecurity assessment framework targeting prevention of the introduction and establishment of *Salmonella* Dublin in dairy cattle herds. Animals 13(16): 2649. https://doi.org/10.3390/ani13162649

Pelyuntha W, Yafa A, Ngasaman R, Yingkajorn M, Chukiatsiri K, Champoochana N, Vongkamjan K. (2022). Oral administration of a phage cocktail to reduce *Salmonella* colonization in broiler gastrointestinal tract—a pilot study. Animals 12(22): 3087. https://doi.org/10.3390/ani12223087

Poudel I, Adhikari PA. (2024). Combating the persistence of *Salmonella* infections in laying hens: nutritional, managemental and vaccination strategies. World's Poultry Science Journal 80(2): 423-452. https://doi.org/10.1080/00439339.2023.2298513

Qiao J, Shang Z, Liu X, Wang K, Wu Z, Wei Q, Li H. (2022). Regulatory effects of combined dietary supplementation with essential oils and organic acids on microbial communities of Cobb broilers. Frontiers in Microbiology 12: 814626. https://doi.org/10.3389/fmicb.2021.814626

Qureshi MHF, Azam F, Shafique M, Aslam B, Farooq M, Rafique MK, Meraj MT, Ahmed I. (2024). A one health perspective of pet birds bacterial zoonosis and prevention. Pakistan Veterinary Journal 44(1): 1-8. http://dx.doi.org/10.29261/pakvetj/2024.147

Rabetafika HN, Razafindralambo A, Ebenso B, Razafindralambo HL. (2023). Probiotics as antibiotic alternatives for human and animal applications. Encyclopedia 3(2): 561-581. https://doi.org/10.3390/encyclopedia3020040

Rabie NS, Fedawy HS, Sedeek DM, Bosila MA, Abdelbaki MM, Ghetas AM, Elbayoumi KM, Hassan ER, Girh ZMSA, Mekky HM. (2023). Isolation and serological identification of current *Salmonella* species recovered from broiler chickens in Egypt. International Journal of Veterinary Science 12(2): 230-235. https://doi.org/10.47278/journal.ijvs/2022.169

Raccoursier M, Siceloff AT, Shariat NW. (2024). In silico and PCR screening for a live attenuated *Salmonella Typhimurium* vaccine strain. Avian Diseases 68(1): 18-24. https://doi.org/10.1637/aviandiseases-D-23-00051

Rajan K, Shi Z, Ricke SC. (2017). Current aspects of *Salmonella* contamination in the US poultry production chain and the potential application of risk strategies in understanding emerging hazards. Critical Reviews in Microbiology 43(3): 370-392. https://doi.org/10.1080/1040841X.2016.1223600

Rashid MHU, Mehwish, Wahab H, Ahmad S, Ali L, Ahmad N, Ali M, Fazal H. (2024). Unraveling the combinational approach for the antibacterial efficacy against infectious pathogens using the herbal extracts of the leaves of Dodonaea viscosa and fruits of Rubus fruticosus. Agrobiological Records 16: 57-66. https://doi.org/10.47278/journal.abr/2024.012

Raut R, Maharjan P, Fouladkhah AC. (2023). Practical preventive considerations for reducing the public health burden of poultry-related salmonellosis. International Journal of Environmental Research and Public Health 20(17): 6654. https://doi.org/10.3390/ijerph20176654

Renu S, Markazi AD, Dhakal S, Lakshmanappa YS, Gourapura SR, Shanmugasundaram R, Senapati S, Narasimhan B, Selvaraj RK, Renukaradhya GJ. (2018). Surface engineered polyanhydride-based oral *Salmonella* subunit nanovaccine for poultry. International Journal of Nanomedicine 13: 8195-8215. https://doi.org/10.2147/IJN.S185588

Roland KL, Kong Q, Jiang Y. (2020). Attenuated *Salmonella* for oral immunization. In: Kiyono H, Pascual DW, editors, Mucosal Vaccines. Academic Press, Elsevier. Pp. 383-399 https://doi.org/10.1016/B978-0-12-811924-2.00022-5

Ruvalcaba-Gómez JM, Villagrán Z, Valdez-Alarcón JJ, Martínez-Núñez M, Gomez-Godínez LJ, Ruesga-Gutiérrez E, Anaya-Esparza LM, Arteaga-Garibay RI, Villarruel-López A. (2022). Non-antibiotics strategies to control *Salmonella* infection in poultry. Animals 12(1): 102. https://doi.org/10.3390/ani12010102

Sachdeva A, Tomar T, Malik T, Bains A, Karnwal A. (2025). Exploring probiotics as a sustainable alternative to antimicrobial growth promoters: mechanisms and benefits in animal health. Frontiers in Sustainable Food Systems 8: 1523678. https://doi.org/10.3389/fsufs.2024.1523678

Saleem M, Rahman HU, Abbas J. (2023). Rapid recovery of *Salmonella* from chicken meat and poultry fecal samples by selective pre-enrichment. Continental Veterinary Journal 3(1): 49-53. http://dx.doi.org/10.71081/cvj/2023.007

Sayed F, Kaur R, Jha V, Quraishi UA. (2024). Prevalence, Antibiotic Resistance, and Implications for Public Health Due to *Salmonella* Contamination in Food Products. South Asian Journal of Research in Microbiology 18(5): 18-29. https://doi.org/10.9734/sajrm/2024/v18i5359

Sears KT, Galen JE, Tennant SM. (2021). Advances in the development of *Salmonella*-based vaccine strategies for protection against Salmonellosis in humans. Journal of Applied Microbiology 131(6): 2640-2658. https://doi.org/10.1111/jam.15055

Senevirathne A, Hewawaduge C, Park S, Park JY, Kirthika P, Lee JH. (2020). O-antigen-deficient, live, attenuated *Salmonella* typhimurium confers efficient uptake, reduced cytotoxicity, and rapid clearance in chicken macrophages and lymphoid organs and induces significantly high protective immune responses that protect chickens against *Salmonella* infection. Developmental & Comparative Immunology 111: 103745. https://doi.org/10.1016/j.dci.2020.103745

Shekhar C, Singh SP. (2015). Molecular characterization of *Salmonella* serovars of zoonotic importance. The Indian Journal of Animal Sciences 85(2): 113-116. https://doi.org/10.56093/ijans.v85i2.46559

Shin H, La TM, Lee HJ, Kim T, Song SU, Park E, Park GH, Choi IS, Park SY, Lee JB. (2022). Evaluation of immune responses and protective efficacy of a novel live attenuated *Salmonella* enteritidis vaccine candidate in chickens. Vaccines 10(9): 1405. https://doi.org/10.3390/vaccines10091405

Siddique A, Wang Z, Zhou H, Huang L, Jia C, Wang B, Ed-Dra A, Teng L, Li Y, Yue M. (2024a). The evolution of vaccines development across *Salmonella* serovars among animal hosts: A systematic review. Vaccines 12(9): 1067. https://doi.org/10.3390/vaccines12091067

Siddiqui AA, Abbas A, Zaman H, Rehman A, Kashif M, Ahmad T, Nadeem M. (2024b). Continental Veterinary Journal. 4(2): 146-151. http://dx.doi.org/10.71081/cvj/2024.028

Smith RP, May HE, Burow E, Meester M, Tobias TJ , Sassu EL, Pavoni E, Di Bartolo I Prigge C, Wasyl D. (2023). Assessing pig farm biosecurity measures for the control of *Salmonella* on European farms. Epidemiology and Infection 151: e130. https://doi.org/10.1017/S0950268823001115

Solfaine R, Purnama MTE, Maslamama ST, Fikri F, Hamid IS. (2024). Bdellovibrio bacteriovorus: a boost for hematological and gut health in Salmonella enteritidis-infected mice. International Journal of Veterinary Science 13(6): 776-781. https://doi.org/10.47278/journal.ijvs/2024.165

Stingelin GM, Scherer RS, Machado AC, Piva A, Grilli E, Penha Filho RC. (2023). The use of thymol, carvacrol and sorbic acid in microencapsules to control *Salmonella* Heidelberg, S. Minnesota and S. Typhimurium in broilers. Frontiers in Veterinary Science 9: 1046395. https://doi.org/10.3389/fvets.2022.1046395

Susalam MK, Harnentis H, Marlida Y, Jamsari J, Ardani LR. (2024). The effect of probiotics consortium isolated from fermented fish (Budu) on broiler performances and meat quality. International Journal of Veterinary Science 13(1): 100-107. https://doi.org/10.47278/journal.ijvs/2023.066

Teklemariam AD, Al-Hindi RR, Albiheyri RS, Alharbi MG, Alghamdi MA, Filimban AAR, Al Mutiri AS, Al-Alyani AM, Alseghayer MS, Almaneea AM. (2023). Human salmonellosis: a continuous global threat in the farm-to-fork food safety continuum. Foods 12(9): 1756. https://doi.org/10.3390/foods12091756

Thanki AM, Hooton S, Gigante AM, Atterbury RJ, Clokie MRJ. (2021). Potential roles for bacteriophages in reducing *Salmonella* from poultry and swine. In: Lamas A, Regal P, Franco CM, editors, *Salmonella* spp.-A Global Challenge. IntechOpen, London, UK. https://doi.org/10.5772/intechopen.96984

Vt Nair D, Venkitanarayanan K, Kollanoor Johny A. (2018). Antibiotic-resistant *Salmonella* in the food supply and the potential role of antibiotic alternatives for control. Foods 7(10): 167. https://doi.org/10.3390/foods7100167

Walker RI, Bourgeois AL. (2023). Oral inactivated whole cell vaccine for mucosal immunization: ETVAX case study. Frontiers in Immunology 14: 1125102. https://doi.org/10.3389/fimmu.2023.1125102

Wang M, Qazi IH, Wang L, Zhou G, Han H. (2020). *Salmonella* virulence and immune escape. Microorganisms 8(3): 407. https://doi.org/10.3390/microorganisms8030407

Wibisono FM, Wibison FJ, Effendi MH, Plumeriastuti H, Hidayatullah AR, Hartadi EB, Sofiana ED. (2020). A review of salmonellosis on poultry farms: Public health importance. Systematic Reviews in Pharmacy 11(9): 481-486. http://repository.unair.ac.id/id/eprint/127145

Willis C, Jørgensen F, Cawthraw S, Aird H, Lai S, Kesby M, Chattaway M, Lock I, Quill E, Raykova G. (2023). A survey of *Salmonella*, *Escherichia coli*, and antimicrobial resistance in frozen, part-cooked, breaded, or battered chicken products on retail sale in the UK. Journal of Applied Microbiology 134(5): lxad093. https://doi.org/10.1093/jambio/lxad093

Won G, Lee JH. (2017). *Salmonella* Typhimurium, the major causative agent of foodborne illness inactivated by a phage lysis system provides effective protection against lethal challenge by induction of robust cell-mediated immune responses and activation of dendritic cells. Veterinary Research 48(1): 66. https://doi.org/10.1186/s13567-017-0474-x

Yero D, Conchillo-Solé O, Daura X. (2020). Antigen discovery in bacterial panproteomes. In: Pfeifer BA, Hill A, editors, Vaccine Delivery Technology: Methods and Protocols. Humana, New York. Pp. 43-62. https://doi.org/10.1007/978-1-0716-0795-4_5

Youssef DM, Wieland B, Knight GM, Lines J, Naylor NR. (2021). The effectiveness of biosecurity interventions in reducing the transmission of bacteria from livestock to humans at the farm level: A systematic literature review. Zoonoses and Public Health 68(6): 549-562. https://doi.org/10.1111/zph.12807

Zahedipour F, Zahedipour F, Zamani P, Jaafari MR, Sahebkar A. (2024). Harnessing CRISPR technology for viral therapeutics and vaccines: from preclinical studies to clinical applications. Virus Research 341: 199314. https://doi.org/10.1016/j.virusres.2024.199314

Zamora-Sanabria R, Alvarado AM. (2017). Preharvest *Salmonella* risk contamination and the control strategies. In: Mares M, editor, Current Topics in Salmonella and Salmonellosis IntecOpen, London, UK. http://dx.doi.org/10.5772/67399

Citation

Hameed AS, Riaz J, Rayshan AR, Al-Kinani ASS, Al-Kinani ASS, Younas A, Alkhamessi RN, Kadham MJ, Haris MM, Farooq AB, Ambrose S, Khan AMA. (2025). Vaccination and non-antibiotic strategies for effective control of multidrug-resistant *Salmonella* bacteria of medical and veterinary importance. Letters in Animal Biology 05(1): 89 – 99. *https://doi.org/10.62310/liab.v5i1.255*