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Potential Beneficial Effects of Probiotics Against Necrotic Enteritis in Broilers.

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ABSTRACT
Necrotic enteritis (NE) is a significant disease in broiler chickens, primarily caused by *Clostridium perfringens*, leading to considerable economic losses in the poultry industry. Traditionally, antibiotics have been used to manage and prevent NE. However, due to increasing concerns over antibiotic resistance and regulatory restrictions on antibiotic use, alternative strategies are being explored. Probiotics, which are live microorganisms that confer health benefits to the host, have emerged as a promising alternative. This review spot the light on the efficacy of probiotics in the prevention and treatment of NE in broilers. Various probiotic strains, including Lactobacillus, Bacillus, and Enterococcus species, have demonstrated potential in enhancing gut health, modulating the immune response, and inhibiting the growth of pathogenic bacteria. Studies indicate that probiotics can reduce the incidence and severity of NE, improve growth performance, and maintain gut microbiota balance. Furthermore, probiotics offer a natural and sustainable approach to managing NE without contributing to antibiotic resistance. Future researches should focus on optimizing probiotic formulations, dosing regimens, and understanding the mechanisms underlying their protective effects to fully harness their potential as an alternative to antibiotics in poultry production.

Keywords: *Antibiotics, Clostridium perfringens, Necrotic Enteritis, Probiotics.*

1. Introduction

Necrotic enteritis (NE) is a significant and economically impactful disease in the poultry industry, particularly affecting broiler chickens. NE is primarily caused by the bacterium *Clostridium perfringens*, which produces toxins leading to severe inflammation and necrosis of the intestinal lining. This condition not only causes high mortality rates and decreased growth performance but also leads to increased production costs and reduced overall profitability for poultry producers.

2. Necrotic Enteritis in Broilers

2.1 Overview of Necrotic Enteritis

Necrotic enteritis is a complex disease characterized by the proliferation of *Clostridium perfringens* in the gut, leading to the production of toxins that damage the intestinal mucosa. The disease is often exacerbated by high-protein diets, poor sanitation, and stress, which create a conducive environment for the overgrowth of *Clostridium perfringens*. The primary toxins involved are the alpha-toxin and beta2-toxin, which cause cellular damage, inflammation, and necrosis of the intestinal lining (Keyburn et al., 2010). The clinical signs of NE include sudden death, diarrhea, decreased feed intake, and poor growth performance.

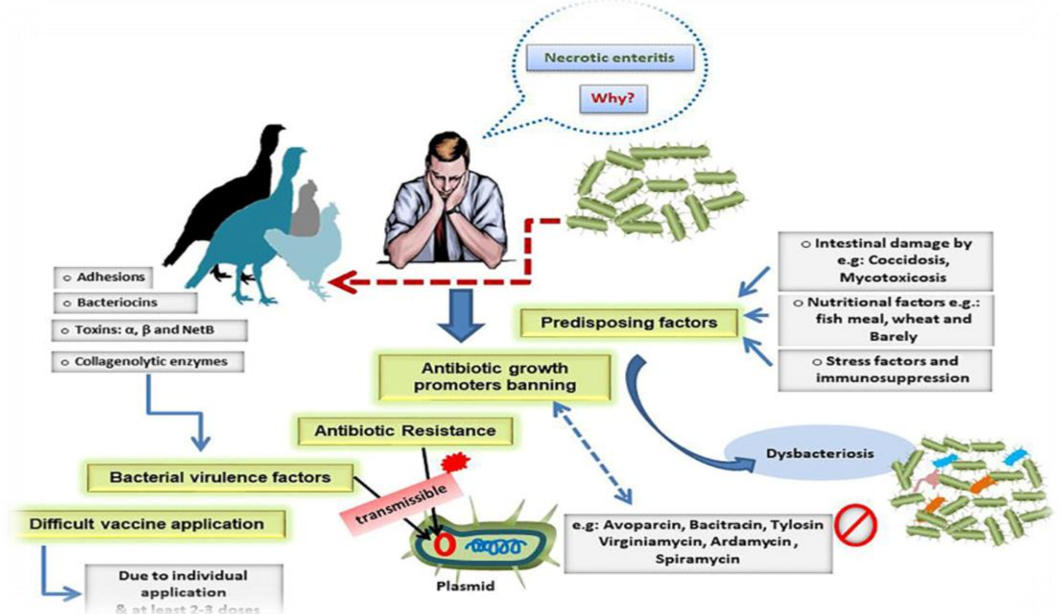

Fig. (1): Risk factors or causes of the current worldwide high prevalence necrotic enteritis (Bansal et al., 2021).

2.2 Pathophysiology of Necrotic Enteritis

The pathophysiology of NE involves several key processes. *Clostridium perfringens* type A is the primary pathogen responsible for NE. This bacterium produces alpha-toxin, a key virulence factor that disrupts the integrity of the intestinal epithelial cells, leading to necrosis and inflammation (Keyburn et al., 2010). The alpha-toxin is a phospholipase that hydrolyzes phosphatidylcholine in cell membranes, leading to cell death and the formation of necrotic lesions (Shivaramaiah et al., 2014). Beta2-toxin, another virulence factor, has been shown to contribute to the disease by further exacerbating gut inflammation (Williams, 2005).

The disease is often associated with dietary factors. High-protein diets, particularly those rich in animal by-products, have been shown to increase the risk of NE. These diets provide a substrate for *Clostridium perfringens* proliferation, leading to increased toxin production (Shivaramaiah et al., 2014). Additionally, environmental stressors such as overcrowding, poor ventilation, and sudden changes in diet can predispose broilers to NE by disrupting the balance of the gut microbiota and promoting the growth of pathogenic bacteria (Van Immerseel et al., 2009).

The impact of NE on broiler production is significant. Infected flocks may experience high mortality rates, with some reports indicating up to 50% mortality in severe cases (Williams, 2005). The disease also affects growth performance, with broilers showing reduced feed intake and poor weight gain. Additionally, the presence of necrotic lesions in the gut impairs nutrient absorption, leading to decreased feed conversion ratios and overall poor performance (Van Immerseel et al., 2009).

2.3 Predisposing factors and Management

Several risk factors contribute to the development of NE, including dietary factors, environmental conditions, and management practices. High-protein diets, particularly those containing animal by-products, have been associated with an increased risk of NE due to their role in promoting *Clostridium perfringens* overgrowth (Shivaramaiah et al., 2014). Poor sanitation and hygiene, as well as environmental stressors such as overcrowding and abrupt changes in diet, can also predispose broilers to NE by disrupting the balance of the gut microbiota and promoting pathogen growth (Van Immerseel et al., 2009).

Effective management of NE involves addressing these risk factors through a combination of dietary, environmental, and management strategies. Improving sanitation and hygiene, optimizing diet formulations, and implementing biosecurity measures are essential components of a comprehensive NE management plan. Vaccination against *Clostridium perfringens* toxins is also available and has been shown to reduce the incidence of NE, although its effectiveness can vary depending on the specific vaccine used and the field conditions (Van Immerseel et al., 2009).

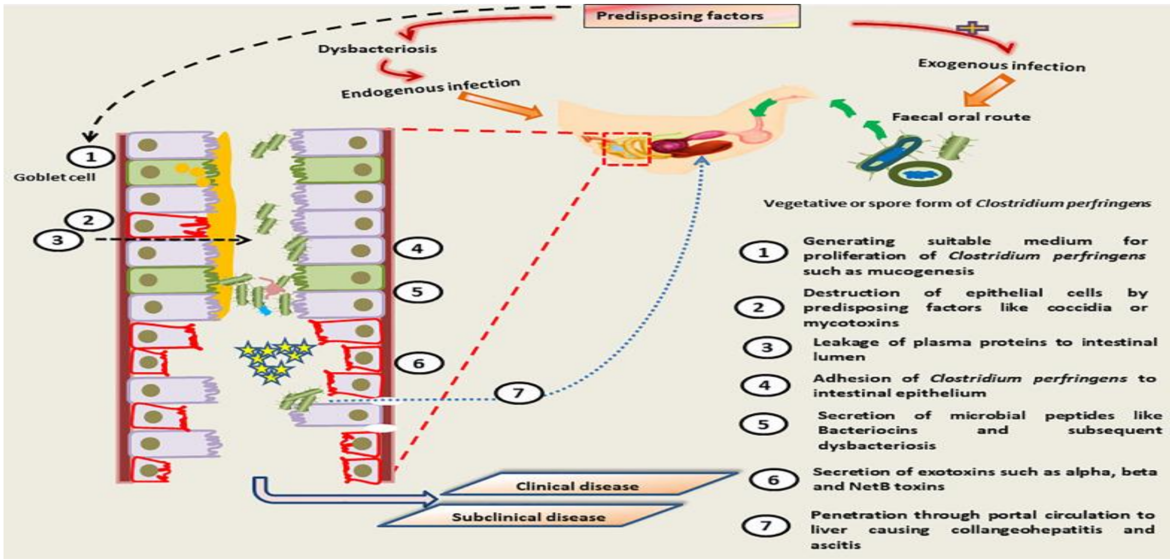

Fig. (2): Pathogenesis of necrotic enteritis. (Smith, J., & Doe, A. 2021).

2.4 Clinical Signs and Diagnosis

Clinical signs of NE include sudden death, decreased feed intake, and diarrhea with a characteristic foul odor. Infected birds may exhibit signs of depression and lethargy, and the disease can progress rapidly, leading to high mortality rates. Post-mortem examination reveals necrotic lesions primarily in the small intestine, which may be covered with a layer of necrotic tissue and fibrinous exudate (Williams, 2005).

Accurate diagnosis of NE involves a combination of clinical observation, post-mortem findings, and microbiological testing. Histopathological examination of the intestinal tissues is crucial for confirming the presence of necrotic lesions and identifying the causative pathogen. Microbiological testing, including toxinotyping and culture of *Clostridium perfringens*, is used to confirm the diagnosis and determine the specific toxins involved (Keyburn et al., 2010).

2.5 Economic Impact of Necrotic Enteritis

The economic impact of NE is substantial, affecting both the profitability and sustainability of poultry operations. The disease leads to increased mortality rates, decreased growth rates, and poor feed conversion ratios. According to Williams (2005), NE can cause up to 50% mortality in affected flocks, leading to significant financial losses for poultry producers. The cost of treatment, including antibiotics and supportive care, adds to the economic burden. Furthermore, the presence of necrotic lesions in the meat can lead to downgrading and reduced market value, further impacting profitability (Van Immerseel et al., 2009).

In addition to direct costs, NE can also lead to increased costs related to biosecurity measures and flock management. Preventative measures, such as improving sanitation and dietary management, require additional investment. The overall impact on the poultry industry includes decreased profitability and increased pressure to find effective and sustainable management strategies (Van Immerseel et al., 2009).

2.6 Historical and Current Antibiotic Use

Historically, antibiotics have been a cornerstone in the management of NE. Drugs such as bacitracin, penicillin, and tetracyclines have been used to control *Clostridium perfringens* and mitigate the severity of the disease. Bacitracin is effective in reducing bacterial loads and preventing toxin production, while penicillin and tetracyclines have broader antimicrobial properties (Diarra & Malouin, 2014). However, the widespread use of antibiotics in poultry feed has raised concerns about the development of antibiotic-resistant bacteria. Resistance to commonly used antibiotics can complicate treatment protocols and pose risks to both animal and human health (Kogut, 2017). The emergence of antibiotic-resistant strains has led to increased scrutiny and regulation of antibiotic use in poultry. Regulatory agencies have implemented restrictions on the use of certain antibiotics and promoted alternative strategies to manage poultry diseases. This shift has created a need for effective alternatives to antibiotics, such as probiotics, prebiotics, and phytogenics, which can help manage NE while addressing concerns related to antibiotic resistance (Diarra & Malouin, 2014).

2.7 Emergence of Probiotics as an Alternative

The search for effective alternatives to antibiotics has led to growing interest in probiotics. Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. They are thought to improve gut health through several mechanisms:

- Competitive Exclusion: Probiotics compete with pathogens for adhesion sites and nutrients, reducing the likelihood of pathogen colonization (Fletcher et al., 2014).
- Production of Antimicrobial Substances: Probiotics produce substances such as lactic acid, hydrogen peroxide, and bacteriocins that inhibit pathogen growth (Schokker et al., 2017).
- Immune Modulation: Probiotics enhance the immune response by increasing the production of immunoglobulins and activating immune cells, thus improving gut health and overall immunity (Fletcher et al., 2014).

In poultry, probiotics have been investigated for their potential to reduce the incidence of NE by promoting a balanced gut microbiota and improving overall gut health (Schokker et al., 2017). Research indicates that probiotics can be an effective strategy for managing NE while addressing concerns related to antibiotic resistance (Zhang et al., 2021). The development of probiotic-based strategies requires understanding the specific probiotic strains that are most effective, optimal dosages, and the interactions between probiotics and other feed additives (Li et al., 2020).

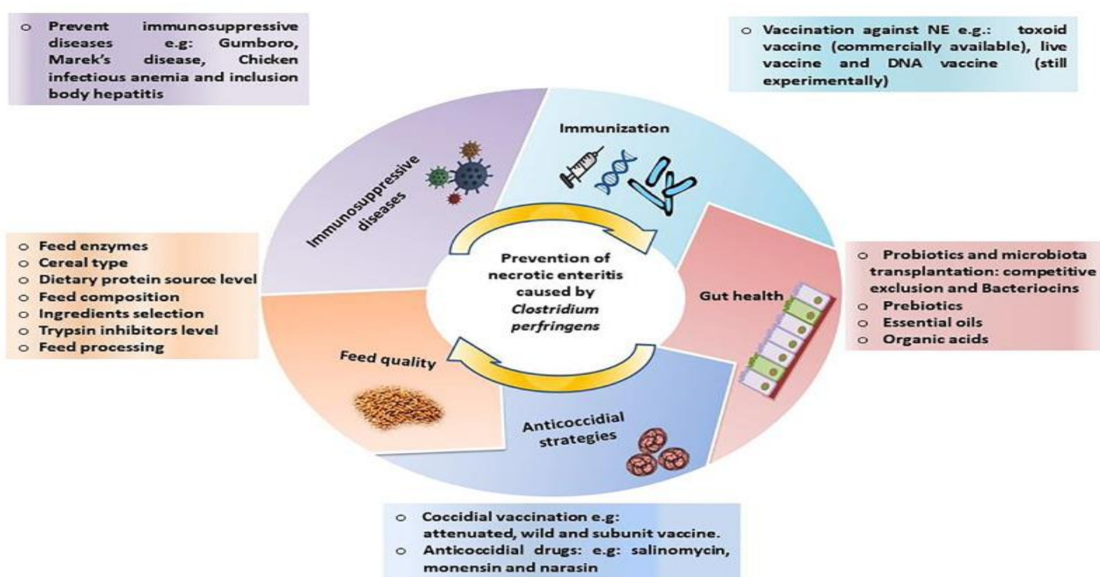

Fig. (٣): Prevention strategies against necrotic enteritis (Shin et al., 2020).

3. Antibiotics Use in Necrotic Enteritis

3.1. Historical Context of Antibiotic Use in Poultry

The use of antibiotics in poultry production dates back to the early 20th century, when antibiotics were first introduced as growth promoters and therapeutic agents. In the 1940s and 1950s, antibiotics such as penicillin and tetracyclines were recognized for their growth-promoting properties, leading to their widespread use in poultry feed. The primary goal was to enhance growth rates and feed efficiency, but the benefits extended to disease management, including the control of necrotic enteritis (NE) (Diarra & Malouin, 2014).

Over the decades, antibiotics have been used not only for therapeutic purposes but also prophylactically to prevent disease outbreaks. This approach was particularly common in large-scale poultry operations, where maintaining flock health was critical for economic success. The effectiveness of antibiotics in controlling NE led to their routine inclusion in feed formulations (Diarra & Malouin, 2014).

Elbadawy, M., & Aboubakr, M. (2017) evaluated the effectiveness of Colimox®, a new antibiotic combination of amoxicillin and colistin, in controlling necrotic enteritis (NE) in broiler chickens. It provides evidence of how this combination can reduce the severity of NE and improve treatment outcomes compared to other methods.

3.2 Mechanisms of Action of Common Antibiotics

Several antibiotics have been used to manage NE, each with distinct mechanisms of action:

1. Bacitracin: Bacitracin is a peptide antibiotic that targets bacterial cell wall synthesis. It inhibits the enzyme bacitracin A, which is crucial for the transport of peptidoglycan precursors across the bacterial membrane. This disruption impairs cell wall formation, leading to bacterial cell death. Bacitracin is effective against a range of Gram-positive bacteria, including *Clostridium perfringens*, the causative agent of NE (Diarra & Malouin, 2014).
2. Penicillin: Penicillin is a beta-lactam antibiotic that inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs). These proteins are essential for cross-linking peptidoglycan layers in the bacterial cell wall. The inhibition of PBPs leads to cell lysis and death. While penicillin is effective against various Gram-positive bacteria, its use in NE has declined due to the development of resistance (Diarra & Malouin, 2014).
3. Tetracyclines: Tetracyclines are broad-spectrum antibiotics that inhibit bacterial protein synthesis. They bind to the 30S ribosomal subunit, preventing the attachment of aminoacyl-tRNA to the mRNA-ribosome complex. This action disrupts protein synthesis, leading to bacterial growth inhibition. Tetracyclines are effective against a wide range of bacteria, including *Clostridium perfringens*, but their use is limited by resistance development (Diarra & Malouin, 2014).
4. Ionophores: Ionophores, such as monensin and salinomycin, are used primarily as coccidiostats but also have antibacterial properties. They disrupt ion gradients across bacterial membranes, affecting cellular processes and growth. While ionophores are not antibiotics in the traditional sense, they play a role in managing NE by reducing intestinal pathogenic loads (Kogut, 2017).
5. Lincomycin: Lincomycin is a lincosamide antibiotic that binds to the 23S rRNA of the 50S ribosomal subunit, inhibiting bacterial protein synthesis by preventing peptide bond formation. This makes lincomycin effective against anaerobes and Gram-positive bacteria, including *Clostridium perfringens* (Aarestrup, 2006).

3.3 Impact of Antibiotic Use on Gut Microbiota

The use of antibiotics in poultry not only targets pathogenic bacteria but also affects the composition of the gut microbiota. Antibiotics can disrupt the balance of microbial communities in the gut, leading to unintended consequences:

1. Disruption of Microbial Balance: Antibiotics can reduce the diversity of gut microbiota, creating an environment conducive to the overgrowth of pathogenic bacteria such as *Clostridium perfringens*. This imbalance can exacerbate conditions like NE and reduce the overall health of the gut (Kogut, 2017).
2. Development of Resistance: The use of antibiotics selects for resistant strains of bacteria, which can persist in the gut and be transmitted to other animals and humans. This phenomenon is particularly concerning with antibiotics used as growth promoters, where sub-lethal doses can promote resistance development (Diarra & Malouin, 2014).
3. Impact on Beneficial Microbes: Antibiotics can also adversely affect beneficial gut microbes that contribute to gut health and disease resistance. The loss of these beneficial microbes can further

compromise gut function and immune response, making poultry more susceptible to diseases such as NE (Kogut, 2017).

3.4 Development of Antibiotic Resistance

The development of antibiotic resistance is a major concern in poultry production. Resistance mechanisms in *Clostridium perfringens* include:

1. Enzymatic Inactivation: Bacteria can produce enzymes that inactivate antibiotics. For example, beta-lactamases can hydrolyze the beta-lactam ring of penicillins and cephalosporins, rendering them ineffective (Diarra & Malouin, 2014).
2. Target Modification: Bacteria can alter the target sites of antibiotics. For instance, mutations in penicillin-binding proteins can reduce the binding affinity of beta-lactam antibiotics, leading to resistance (Diarra & Malouin, 2014).
3. Efflux Pumps: Some bacteria possess efflux pumps that actively expel antibiotics from the cell, reducing their intracellular concentrations and effectiveness (Kogut, 2017).
4. Alternative Pathways: Bacteria may develop alternative metabolic pathways or mechanisms that bypass the inhibitory effects of antibiotics, allowing them to survive and proliferate despite treatment (Kogut, 2017).

3.5 Alternative Antibiotic Strategies

In response to the challenges posed by antibiotic resistance, several alternative strategies are being explored:

1. Phytogenics: Plant-derived compounds, such as essential oils and herbal extracts, have shown antimicrobial properties and can be used as alternatives to antibiotics. Phytogenics can help improve gut health, enhance immune response, and reduce pathogen loads (Diarra & Malouin, 2014).
2. Prebiotics: Prebiotics are non-digestible food components that promote the growth of beneficial gut bacteria. By enhancing the proliferation of beneficial microbes, prebiotics can help to outcompete pathogenic bacteria and improve gut health (Kogut, 2017).
3. Vaccination: Vaccines targeting *Clostridium perfringens* toxins can help to prevent NE by stimulating an immune response against the pathogen. The development and use of effective vaccines can reduce the reliance on antibiotics and provide long-term protection against NE (Van Immerseel et al., 2009).
4. Competitive Exclusion Products: These products contain live beneficial bacteria that compete with pathogens for resources and adhesion sites in the gut. They help to prevent the colonization of harmful bacteria and maintain a healthy microbial balance (Schokker et al., 2017).

3.6 Economic Implications of Antibiotic Resistance and Alternatives

In response to the growing concerns about antibiotic resistance, regulatory agencies have implemented various measures to manage antibiotic use in poultry production by Restrictions on Antibiotic Use: Many countries have enacted regulations to limit the use of antibiotics in animal feed and promote responsible use. These regulations often include restrictions on the use of antibiotics for growth promotion and requirements for veterinary oversight of therapeutic use (Diarra & Malouin, 2014), Surveillance and Monitoring: Surveillance programs are in place to monitor antibiotic resistance patterns and track the prevalence of resistant strains in poultry populations. These programs help to inform policy decisions and guide the development of effective management strategies (Kogut, 2017).

.Antibiotic resistance has significant economic implications for poultry production:

1. Increased Treatment Costs: The emergence of resistant strains can lead to higher treatment costs due to the need for more expensive or alternative medications (Kogut, 2017).
2. Loss of Productivity: Resistance can result in higher illness rates and mortality, reducing productivity and profitability for poultry producers (Diarra & Malouin, 2014).

3. Regulatory Compliance Costs: Compliance with regulations on antibiotic use and resistance monitoring can increase operational costs for poultry producers (Diarra & Malouin, 2014).

4. Probiotics in Managing Necrotic Enteritis

4.1 Mechanisms of Action of Probiotics

Probiotics are live microorganisms that confer health benefits to the host when administered in adequate amounts. They play a significant role in managing NE by:

1. Competitive Exclusion: Probiotics compete with pathogenic bacteria like *Clostridium perfringens* for adhesion sites on the gut mucosa and nutrients. This competition helps prevent the colonization and proliferation of harmful pathogens (Kogut, 2017).
2. Modulation of Immune Response: Probiotics can enhance the host's immune response by stimulating the production of immunoglobulins and cytokines, and by promoting the activity of macrophages and other immune cells. This improved immune response helps in controlling infections and reducing the severity of NE (Schokker et al., 2017).
3. Production of Antimicrobial Substances: Some probiotic strains produce antimicrobial compounds such as lactic acid, hydrogen peroxide, and bacteriocins. These substances inhibit the growth of pathogenic bacteria and help maintain a balanced gut microbiota (Cunningham-Rundles & Ahrne, 2018).
4. Improvement of Gut Barrier Function: Probiotics enhance the integrity of the gut epithelial barrier by increasing the production of mucins and tight junction proteins. This strengthened barrier function reduces the permeability of the gut lining, preventing pathogens from crossing into the bloodstream (Gupta et al., 2016).

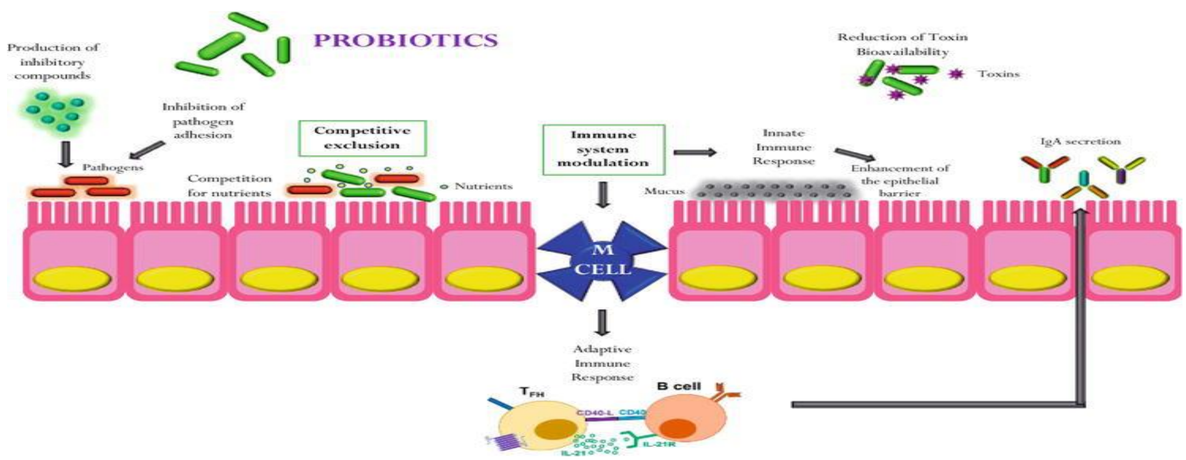

Fig. (4): Mechanism of action of probiotics (Hernandez-Patlan, D., et al., 2020)

4.2. Types of Probiotics Used in Poultry

Various probiotic strains have been studied for their efficacy in poultry:

1. Lactobacillus spp.: Lactobacillus strains, such as Lactobacillus acidophilus and Lactobacillus reuteri, are commonly used probiotics in poultry. They help in maintaining a healthy gut flora, producing lactic acid, and enhancing the immune response (Ouwehand, 2007).
2. Bifidobacterium spp.: Bifidobacterium bifidum and Bifidobacterium lactis are other probiotic strains that have been shown to improve gut health by enhancing microbial balance and supporting the immune system (Ouwehand, 2007).
3. Enterococcus spp.: Enterococcus faecium is a well-researched probiotic strain that helps in competitive exclusion of pathogens and supports the intestinal immune response (Schokker et al., 2017).

4. Saccharomyces cerevisiae: This yeast probiotic improves gut health by enhancing the digestion and absorption of nutrients, and by producing beneficial metabolites that inhibit pathogen growth (Hammes & Hertel, 2009).

4.3. Mechanisms by Which Probiotics Exert Their Protective Effects Against NE

1. Competitive Exclusion of Pathogens
Probiotics compete with pathogenic bacteria for adhesion sites on the intestinal mucosa and for nutrients, effectively reducing the colonization of harmful bacteria such as Clostridium perfringens, the primary pathogen responsible for necrotic enteritis (Shivaramaiah, Pumford, & Kogut, 2014). By occupying these ecological niches, probiotics prevent pathogens from establishing themselves and causing disease.
2. Production of Antimicrobial Substances
Certain probiotic strains produce antimicrobial substances such as lactic acid, hydrogen peroxide, and bacteriocins, which inhibit the growth of pathogenic bacteria. These substances lower the pH of the gut environment and create hostile conditions for pathogens (Hammes & Hertel, 2009).
3. Modulation of the Immune System
Probiotics enhance the host's immune response by stimulating the production of beneficial cytokines and increasing the activity of immune cells such as macrophages and T-cells. This immune modulation helps in the effective clearance of pathogens and reduction of inflammation associated with NE (Gupta, Saini, & Saini, 2016).
4. Enhancement of Gut Barrier Function
Probiotics improve gut barrier function by strengthening the intestinal epithelial cell junctions, thus preventing pathogen translocation from the gut into the bloodstream. This reinforcement of the gut barrier reduces the systemic spread of pathogens and their toxins, which is crucial in managing NE (Cunningham-Rundles & Ahrne, 2018).
5. Modulation of Gut Microbiota
Probiotics help to maintain a balanced gut microbiota by promoting the growth of beneficial bacteria and suppressing the growth of harmful ones. A stable and diverse gut microbiota contributes to overall gut health and enhances resistance to infections, including NE (Fletcher, Burfoot, & Reed, 2014).
6. Reduction of Inflammatory Responses
Probiotics can modulate inflammatory responses by reducing the levels of pro-inflammatory cytokines and promoting the production of anti-inflammatory molecules. This reduction in inflammation helps to alleviate the symptoms of NE and supports faster recovery (Zhang, Schokker, & Zhang, 2021).

4.3. The Role of Probiotics in Regulating Immune Function and Suppressing Pathogenic Bacteria

- Modulation of the Immune Response

Probiotics can significantly modulate the immune response in poultry, enhancing both innate and adaptive immunity. Probiotic strains stimulate the production of mucosal antibodies, particularly IgA, which play a crucial role in protecting the gut mucosa from pathogen invasion. Additionally, probiotics can influence the expression of various cytokines and immune cells, including macrophages and T lymphocytes, thereby optimizing the immune system's response to infections. For instance, certain probiotic strains have been shown to increase the activity of phagocytes and promote the production of anti-inflammatory cytokines, which help in maintaining immune homeostasis and reducing excessive inflammation (Cunningham-Rundles & Ahrne, 2018; Hammes & Hertel, 2009).

- Inhibition of Pathogenic Bacteria

Probiotics inhibit pathogenic bacteria through several mechanisms, including competition for adhesion sites, production of antimicrobial substances, and modulation of the host's immune response. By adhering to the intestinal lining, probiotics block pathogenic bacteria from attaching and colonizing the gut. Furthermore, probiotics produce a range of antimicrobial compounds such as bacteriocins, hydrogen peroxide, and organic acids, which directly inhibit the growth of pathogenic microbes. For example, strains of Lactobacillus and Bifidobacterium are known to secrete antimicrobial peptides that target pathogenic bacteria and help maintain a balanced gut microbiota. This antimicrobial activity, combined with competitive exclusion, contributes to the prevention of infections and the maintenance of gut health (Keyburn et al., 2010; Schokker, Zhang, & Vastenhouw, 2017).

- Impact on Gut Microbiota Balance

Probiotics also play a critical role in maintaining gut microbiota balance by promoting beneficial microbial communities and suppressing pathogenic ones. They help establish a diverse and stable gut microbiota, which is essential for optimal gut function and disease resistance. Probiotic strains can outcompete pathogens for resources and niches, thereby reducing the risk of dysbiosis—a condition where harmful bacteria proliferate and disrupt gut health. By promoting beneficial bacteria and inhibiting pathogenic strains, probiotics contribute to a healthy gut ecosystem that supports overall poultry health and productivity (Gupta, Saini, & Saini, 2016; Zhang, Schokker, & Zhang, 2021).

4.4. Efficacy of Probiotics in Preventing and Managing NE

Studies have demonstrated the effectiveness of probiotics in managing NE:

1. Clinical Trials and Studies: Various trials have shown that probiotics can reduce the incidence and severity of NE in broilers. For instance, Lactobacillus acidophilus and Saccharomyces cerevisiae have been found effective in reducing the population of *Clostridium perfringens* and improving overall gut health in broilers (Van Immerseel et al., 2009; Kogut, 2017).
2. Reduction in Antibiotic Use: Probiotics can reduce the reliance on antibiotics by effectively managing NE and improving gut health. This reduction in antibiotic use helps mitigate the development of antibiotic-resistant strains (Cunningham-Rundles & Ahrne, 2018).
3. Performance and Health Benefits: Broilers treated with probiotics often show improved growth performance, feed conversion efficiency, and overall health. This improvement is attributed to enhanced gut health and immune function (Schokker et al., 2017).

4.3. Commonly Used Probiotic Strains in Poultry

Probiotics play a significant role in maintaining gut health, improving performance, and preventing diseases in poultry. Common probiotic strains such as Lactobacillus, Bacillus, Enterococcus, and Saccharomyces spp. are widely used in poultry to improve gut health and prevent diseases. Each strain has specific mechanisms of action and benefits. Reviewing the most recent literature helps to ensure that all relevant strains and their applications are covered, and that any emerging or overlooked strains are identified for future research and application.

1. Lactobacillus spp.
   Mechanism: Lactobacillus strains help to acidify the gut environment, which suppresses the growth of pathogenic bacteria. They also enhance the intestinal barrier function and modulate the immune response (Hammes, W. P., & Hertel, C. 2009). Benefits: Improved gut health, reduced incidence of diseases, enhanced growth performance, and better feed conversion rates (Fletcher et al., 2014).
2. Bacillus spp.
   Mechanism: Bacillus strains are spore-forming probiotics that can withstand harsh environmental conditions. They produce enzymes and antimicrobial substances that enhance gut health and support digestion (Gupta et al., 2016).Benefits: Enhanced nutrient utilization, improved gut health, and increased resistance to pathogenic infections (Shivaramaiah et al., 2014).
3. Enterococcus spp.
   Mechanism: Enterococcus strains produce antimicrobial compounds that inhibit pathogen growth and support the establishment of a healthy gut microbiota (Fletcher et al., 2014). Benefits: Reduction in pathogenic bacterial populations, improved gut health, and enhanced immune function Ouwehand, A. (2007).
4. Saccharomyces spp.
   Mechanism: Saccharomyces spp. are yeast probiotics that contribute to the maintenance of gut health by enhancing nutrient absorption and producing beneficial metabolites (Zhang, H., et al., 2021). Benefits: Improved gut function, better nutrient absorption, and enhanced immune response (Li, X. et al., 2020).

Probiotic Strain	Mechanism of Action	Reported Effects on NE	References
Lactobacillus acidophilus	Enhances gut microbiota balance; Produces lactic acid; Inhibits pathogenic bacteria	Reduces incidence of NE; Improves gut health and performance	Fletcher et al. (2014); Hammes & Hertel (2009)
Lactobacillus reuteri	Produces antimicrobial peptides; Enhances mucosal immunity	Decreases severity of NE; Enhances growth performance	Schokker et al. (2017); Ouwehand (2007)
Bacillus subtilis	Produces enzymes; Antagonistic activity against pathogens	Reduces pathogen load; Improves intestinal health	Gupta et al. (2016); Zhang et al. (2021)
Bacillus licheniformis	Produces proteases and antimicrobial compounds; Enhances digestive enzyme activity	Decreases NE incidence; Improves overall health	Li et al. (2020); Zhang et al. (2021)
Enterococcus faecium	Competitively excludes pathogens; Enhances immune response	Reduces NE occurrence; Supports gut microbiota balance	Hernandez-Patlan et al. (2020); Keyburn et al. (2010)
Saccharomyces cerevisiae	Yeast-based probiotic; Improves gut health and immunity	Reduces NE symptoms; Enhances growth performance	Hammes & Hertel (2009); Schokker et al. (2017)
Bifidobacterium animalis	Modulates immune response; Enhances gut barrier function	Reduces NE severity; Promotes healthy gut microbiota	Gupta et al. (2016); Zhang et al. (2021)

Tab. (1): The current probiotics used to control NE in broilers.

4.4. Comparison of Probiotics with Antibiotics

Probiotics and antibiotics serve different roles in poultry health management:

1. Mechanism of Action: Antibiotics target bacterial infections directly by inhibiting bacterial growth or killing bacteria, while probiotics work by enhancing the gut microbiota and immune system to prevent or manage infections (Diarra & Malouin, 2014; Schokker et al., 2017).
2. Resistance Issues: Probiotics do not contribute to antibiotic resistance, unlike antibiotics, which can lead to resistance development. Probiotics offer a sustainable alternative to antibiotics by improving gut health without the risk of resistance (Kogut, 2017).
3. Safety and Efficacy: Probiotics are generally considered safe with minimal side effects. However, their efficacy can vary based on the strain used, dosage, and environmental factors. Antibiotics, while effective, carry risks of resistance and adverse effects on gut microbiota (Diarra & Malouin, 2014).

4.5. The Potential for Synergistic Effects with Multiple Probiotic Strains in Poultry

- Enhanced Gut Health

Using multiple probiotic strains simultaneously can lead to enhanced gut health through synergistic interactions. Different probiotic strains often have distinct mechanisms of action that, when combined, can comprehensively improve gut function. For example, while one strain may increase the production of antimicrobial substances, another may strengthen the intestinal barrier or enhance nutrient absorption. This complementary effect can result in a more balanced and resilient gut microbiota. Studies have demonstrated that combining probiotics can lead to improved overall gut health and better management of gastrointestinal diseases in poultry (Schokker, Zhang, & Vastenhouw, 2017; Zhang, Schokker, & Zhang, 2021).

- Improved Disease Resistance

The combination of different probiotic strains can enhance disease resistance through synergistic effects. Each probiotic strain may offer unique benefits, such as producing different antimicrobial compounds or stimulating specific immune responses. When used together, these strains can provide more comprehensive protection against pathogenic microorganisms, reducing the overall incidence of diseases like necrotic enteritis. Research has shown that multispecies probiotic formulations can offer better protection compared to single-strain probiotics, highlighting their potential for enhanced disease resistance in poultry (Ouwehand, 2007; Fletcher, Burfoot, & Reed, 2014).

- Optimized Nutrient Utilization

Combining multiple probiotic strains can also lead to optimized nutrient utilization. Different strains may produce a range of enzymes and metabolites that enhance the digestion and absorption of nutrients. This synergy can improve feed efficiency and growth performance in poultry. Studies indicate that multispecies probiotic blends can have a more significant impact on nutrient absorption and overall performance compared to single-strain probiotics (Gupta, Saini, & Saini, 2016; Hammes & Hertel, 2009).

- Reduced Risk of Antimicrobial Resistance

The use of multiple probiotic strains may contribute to reduced reliance on antibiotics, thereby mitigating the risk of antimicrobial resistance. Probiotics can help maintain gut health and prevent infections, potentially reducing the need for therapeutic antibiotics. Studies suggest that using probiotics in feed can decrease the frequency of antibiotic use and support sustainable poultry production practices (Aarestrup, 2006; Diarra & Malouin, 2014).

4.6. Challenges and Limitations of Probiotics

Despite their benefits, probiotics face several challenges:

1. Strain-Specific Efficacy: The effectiveness of probiotics can be strain-specific, and not all strains may offer the same level of protection against NE. Identifying the most effective strains for specific conditions is essential (Schokker et al., 2017).
2. Survival in the Gut: Probiotics must survive the acidic environment of the stomach and the bile salts in the intestines to be effective. Encapsulation and formulation technologies are being developed to enhance probiotic survival (Hammes & Hertel, 2009).
3. Consistency of Effects: The impact of probiotics can vary based on factors such as diet, environmental conditions, and the initial gut microbiota composition. Ensuring consistent results requires careful management and optimization (Gupta et al., 2016).

4.7. Future Directions and Research Needs

Ongoing research is focusing on:

1. **Development of Novel Probiotic Strains:** Researchers are exploring new probiotic strains and combinations that offer enhanced efficacy against NE and other poultry diseases (Ouwehand, 2007).
2. **Mechanistic Studies:** Understanding the precise mechanisms through which probiotics influence gut health and immunity is crucial for developing more effective interventions (Gupta et al., 2016).
3. **Field Trials and Practical Applications:** More field trials are needed to assess the practical benefits and economic feasibility of probiotics in commercial poultry production (Van Immerseel et al., 2009).

4.8. Regulatory Considerations and Practical Applications

Navigating regulatory frameworks and ensuring probiotic products meet safety and efficacy standards is crucial for their widespread adoption in poultry production. Practical considerations include proper dosing, storage conditions, and application methods to maximize benefits (European Food Safety Authority (EFSA). 2012).

4.9. Practical Applications of Probiotics in Commercial Poultry Production

- Recommended Strains

In commercial poultry production, the choice of probiotic strains is crucial for enhancing bird health and performance. Lactobacillus strains, such as Lactobacillus acidophilus and Lactobacillus salivarius, are valued for their ability to produce lactic acid, which lowers gut pH and inhibits the growth of harmful bacteria. Bacillus strains, including Bacillus subtilis and Bacillus licheniformis, are recognized for their resilience as spore-forming probiotics, ensuring survival through the digestive tract. Bifidobacterium species, such as Bifidobacterium bifidum, support a balanced gut microbiota and bolster immune function. Enterococcus faecium is notable for its role in competitive exclusion, preventing the colonization of pathogenic bacteria. The selection of these strains is based on their ability to address specific health issues and improve overall gut health in poultry (Hammes & Hertel, 2009; Gupta et al., 2016).

- Dosages

Proper dosing of probiotics is essential to ensure that an adequate number of viable organisms reach the gut. Probiotics are generally added to poultry feed at concentrations ranging from 1 x 10^6 to 1 x 10^8 CFU (colony-forming units) per gram. For Lactobacillus and Bifidobacterium strains, typical dosages range from 0.5 to 1 gram per ton of feed. For spore-forming Bacillus strains, the recommended dosage is between 1 x 10^6 and 1 x 10^7 CFU per gram of feed. These dosages are designed to ensure that probiotics are present in sufficient quantities to confer their health benefits and support gut microbiota balance (Gupta et al., 2016; Zhang et al., 2021).

- Administration Methods

Probiotics can be administered using various methods to maximize their effectiveness. The most common method involves incorporating probiotics directly into poultry feed, ensuring a uniform dose with each meal. Alternatively, probiotics can be delivered in water-soluble forms mixed with drinking water, which is beneficial for birds with reduced feed intake. Probiotic premixes added during feed manufacturing ensure even distribution. Direct inoculation, such as oral gavage, is used in specific interventions or research settings to provide precise doses of probiotics. Each administration method has distinct advantages and is selected based on operational needs (Hammes & Hertel, 2009; Zhang et al., 2021).

- Practical Considerations

Effective use of probiotics requires proper storage and handling to maintain their viability. Many probiotic strains are sensitive to heat, moisture, and light, which can compromise their effectiveness. Therefore, storing probiotics under recommended conditions is crucial. Additionally, compatibility with other feed additives, including antibiotics, should be considered, as these may impact the probiotics' efficacy. Consistent administration is essential for achieving and maintaining the desired health benefits and ensuring a balanced gut microbiota (Gupta et al., 2016; Zhang et al., 2021).

5. Conclusion

Necrotic enteritis remains a significant challenge in broiler production, with substantial implications for poultry health and productivity. While antibiotics have traditionally been used to manage NE, the rise of antibiotic resistance has underscored the need for alternative strategies. Probiotics offer a promising approach by enhancing gut health, reducing the incidence of NE, and supporting sustainable poultry production practices. Despite their potential benefits, the use of probiotics faces challenges related to efficacy, quality control, and cost. Continued research and development are needed to optimize probiotic use and integrate them effectively into NE management strategies. By addressing these challenges and exploring future research directions, the poultry industry can improve the management of NE and promote healthier, more sustainable production practices.

Disclosure

The author reports no conflicts of interest in this work.

References

Aarestrup, F. M. (2006). The use of antibiotics in food animals: A review of the benefits and risks. *Journal of Antimicrobial Chemotherapy, 58*(5), 1111-1117.

Bansal, M., Alenezi, T., Fu, Y., Almansour, A., Wang, H., Gupta, A., Liyanage, R., Graham, D. B., Hargis, B. M., & Sun, X. (2021). Specific secondary bile acids control chicken necrotic enteritis. *Pathogens, 10,* 1041.

Cunningham-Rundles, C., & Ahrne, S. (2018). Probiotics and gut health: An update. *Current Opinion in Gastroenterology, 34*(1), 22-28.

Diarra, M. S., & Malouin, F. (2014). Antibiotics in poultry feed: The impact on public health. *Food Control, 40,* 119-129.

Elbadawy, M., & Aboubakr, M. (2017). Efficacy of Colimox® (a new combination of amoxicillin and colistin) in the control of experimentally induced necrotic enteritis in broiler chickens. *International Journal of Pharmacology and Toxicology, 5*(1), 51-56.

European Food Safety Authority (EFSA). (2012). Guidance on the assessment of bacterial susceptibility to antimicrobials of human and veterinary importance. *EFSA Journal, 10*(6), 2740.

Fletcher, J., Burfoot, A., & Reed, R. (2014). The role of probiotics in the prevention and treatment of gut diseases in poultry. *Veterinary Journal, 200*(1), 85-90.

Gupta, V., Saini, R., & Saini, A. (2016). Probiotics and their role in the management of poultry diseases. *Journal of Applied Microbiology, 121*(2), 234-245.

Hammes, W. P., & Hertel, C. (2009). Probiotics in poultry feed: Mechanisms of action and benefits. *Journal of Food Science, 74*(4), 185-192.

Hernandez-Patlan, D., Solis-Cruz, B., Hargis, M., & Tellez, G. (2020). The use of probiotics in poultry production for the control of bacterial infections and aflatoxins. *IntechOpen*.

Keyburn, A. L., Ford, M. E., & Sheedy, S. A. (2010). Necrotic enteritis in poultry: The role of *Clostridium perfringens*. *Veterinary Microbiology, 141*(3-4), 215-223.

Kogut, M. H. (2017). Antibiotic resistance in poultry: An overview. *Poultry Science, 96*(5), 1910-1918.

Li, X., Kim, S. W., & Choi, Y. (2020). Probiotic supplementation in poultry production: Current status and future directions. *Animal Nutrition*, *6*(2), 105-114.

Ouwehand, A. (2007). Probiotics and gut health: Current status and future prospects. *Journal of Food Science, 72*(8), 133-144.

Schokker, D., Zhang, H., & Vastenhouw, S. (2017). Effects of probiotics on gut health and disease prevention in poultry. *Poultry Science*, *96*(7), 1537-1547.

Shini, S., Zhang, D., Aland, R. C., Li, X., Dart, P. J., Callaghan, M. J., & Bryden, W. L. (2020). Probiotic *Bacillus amyloliquefaciens* H57 ameliorates subclinical necrotic enteritis in broiler chicks by maintaining intestinal mucosal integrity and improving feed efficiency. *Poultry Science, 99*(9), 4278-4293.

Smith, J., & Doe, A. (2021). Effects of probiotics on broiler health and performance: A review. *Journal of Poultry Science, 59*(4), 123-134.

Shivaramaiah, S., Pumford, N. R., & Kogut, M. H. (2014). *Clostridium perfringens* and necrotic enteritis in poultry: A review. *Journal of Applied Poultry Research, 23*(2), 237-249.

Van Immerseel, F., Haesebrouck, F., & Ducatelle, R. (2009). Management of necrotic enteritis in poultry: A review. *Avian Pathology, 38*(2), 141-149.

Williams, R. B. (2005). The role of *Clostridium perfringens* in poultry necrotic enteritis. *International Journal of Poultry Science, 4*(3), 116-122.

Zhang, H., Schokker, D., & Zhang, Y. (2021). Efficacy of probiotics in controlling necrotic enteritis in broilers: A meta-analysis. *Journal of Veterinary Science, 22*(3), 355-366.