



Gut Health Challenges Upon Replacement of AGPs and Anticoccidials in Poultry Production

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The global poultry industry has expanded considerably to meet the growing demand for affordable animal protein. This intensification has historically been associated with considerable use of antimicrobials. Poultry production has therefore become an important sector in discussions concerning antimicrobial use and antimicrobial resistance. Maintaining optimal intestinal health is essential for efficient nutrient utilization, disease resistance and overall production performance. Gut health depends on the interaction of an intact epithelial barrier, balanced intestinal microbiota, efficient digestion and absorption, appropriate immune responses and effective management. These processes are particularly vulnerable during the early stages of life when the gastrointestinal tract is still developing.

For decades, antibiotic growth promoters (AGPs) and ionophore anticoccidials have been widely used in commercial broiler production to improve feed efficiency and control enteric diseases. AGPs help suppress undesirable bacterial populations, whereas ionophore anticoccidials provide important protection against *Eimeria* spp. and can indirectly reduce *Clostridium perfringens*-associated necrotic enteritis. Their long-term use, however, has raised concerns regarding antimicrobial resistance, residues, environmental contamination and food safety, resulting in progressive restrictions on antimicrobial use in several production systems.

The transition towards antibiotic-free and reduced-antimicrobial production systems creates new challenges for maintaining intestinal homeostasis. Removal of AGPs and anticoccidials may increase susceptibility to dysbiosis, coccidiosis and necrotic enteritis, impair intestinal barrier function and ultimately reduce production efficiency. Therefore, successful antimicrobial-free poultry production requires an integrated approach involving nutrition, vaccination, biosecurity, management and targeted feed additives.

Major regulatory milestones governing the use of AGPs in poultry production across different countries and regions:

Country/Region	Year/Timeline	Regulatory Action
European Union (EU)	1997, 1999, 1 January 2006	Complete ban on antibiotic growth promoters (AGPs).
Sweden	1981, 1986	Swedish farmers voluntarily stopped using AGPs in 1981, and a nationwide ban was implemented in 1986.
United States (North America)	Ongoing (voluntary approach)	Voluntary withdrawal of medically important antibiotics for growth promotion.
India	2019, October 2024 (effective 1 April 2025)	Ban on colistin (2019). Subsequently, the FSSAI introduced regulations in October 2024 (effective 1 April 2025) prohibiting 27 antibiotics across all production stages for poultry, meat, eggs, milk, and aquaculture.

Major Gut Health Challenges Following AGP and Anticoccidial Withdrawal

1. Microbiota Dysbiosis and Intestinal Barrier Disruption

AGP withdrawal can alter the microbial equilibrium of the gastrointestinal tract by reducing the selective suppression of opportunistic bacteria. Changes in microbial composition may favor the proliferation of undesirable bacterial populations and disturb normal intestinal functions. Such microbial shifts can affect digestion, nutrient utilization and resistance to enteric diseases. The consequences extend beyond changes in microbial composition. *Eimeria* spp. and *C. perfringens* can damage the intestinal epithelium and compromise barrier integrity. Reduced expression of tight-junction proteins and impaired mucus production may increase intestinal permeability, promote inflammation and reduce the protective capacity of the gut. Consequently, nutrients may be less efficiently absorbed and luminal antigens and pathogens may gain greater access to underlying tissues.

2. Resurgence of Necrotic Enteritis

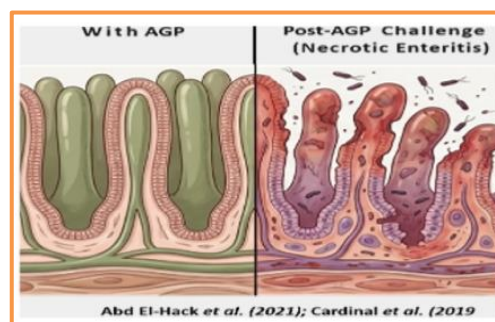
Necrotic enteritis (NE), primarily associated with *C. perfringens*, is an important challenge following the withdrawal of antimicrobial growth promoters. In the absence of antimicrobial suppression, favorable intestinal conditions can promote proliferation of *C. perfringens*, resulting in both clinical and subclinical disease. Subclinical NE may cause prolonged reductions in weight gain and feed efficiency, whereas severe infections can result in intestinal damage, mortality and economic losses. The relationship between intestinal microbial imbalance and NE is particularly important because disruption of the normal gut ecosystem can create conditions favorable for *C. perfringens* multiplication. Thus, controlling NE in antibiotic-free production requires strategies that address both the pathogen and the intestinal environment supporting its proliferation.

3. Increased Coccidiosis and *Eimeria*–*Clostridium perfringens* Interaction

Removal of ionophore anticoccidials eliminates an important layer of protection against *Eimeria* infection. Coccidial damage to intestinal epithelial cells can create favorable conditions for *C. perfringens* proliferation, thereby increasing the risk and severity of necrotic enteritis. This interaction makes simultaneous control of coccidiosis and bacterial dysbiosis particularly important in antimicrobial-free systems. Recent evidence has shown that birds raised without anticoccidials may develop greater coccidial lesion severity, altered microbial diversity and deterioration of intestinal morphology, ultimately affecting nutrient utilization and intestinal function.

4. Dysbacteriosis and Wet Litter

Dysbacteriosis following antimicrobial withdrawal can alter intestinal fermentation and increase intestinal water excretion. Increased intestinal viscosity and moisture may contribute to wet litter, which can subsequently increase ammonia production and predispose birds to footpad dermatitis and hock burns. These effects demonstrate that intestinal disturbances can extend beyond nutrient utilization and disease susceptibility to influence environmental conditions and bird welfare. AGP and anticoccidial replacement initiates number of microbial, structural, immunological, and metabolic issues that destabilize intestinal homeostasis, compromise nutrient utilization, disease resistance and reduce production efficiency. These interrelated challenges underscore the critical role these compounds previously served while emphasizing urgent need for sustainable nutritional and management innovations capable of restoring intestinal integrity and supporting productivity in antibiotic free systems.



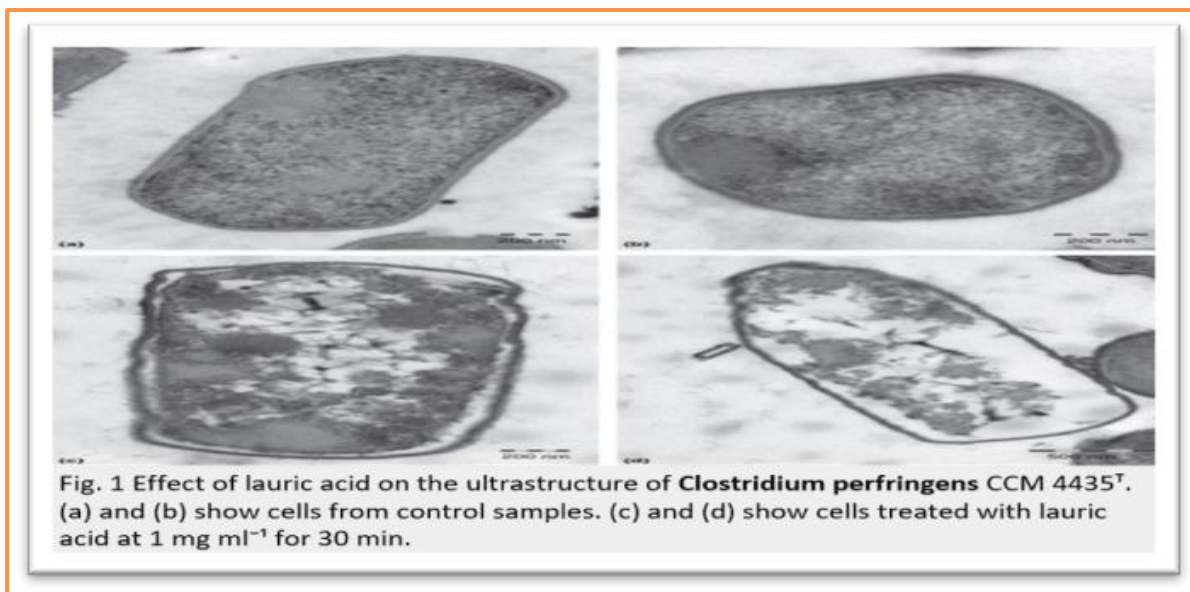
Alternatives for Maintaining Gut Health Without AGPs and Anticoccidials

Successful antibiotic-free poultry production cannot depend on a single replacement product. Improved biosecurity, appropriate vaccination, balanced nutrition and targeted feed additives must work together to maintain intestinal health and production performance. Important

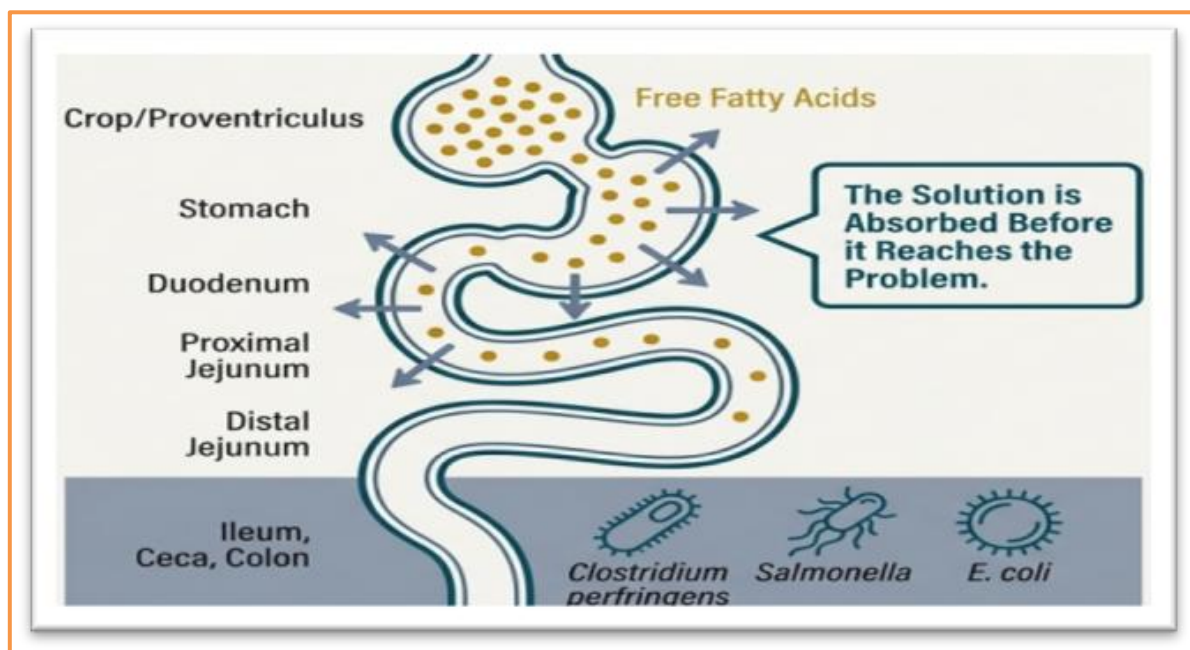
nutritional alternatives include organic acids, esterified fatty acids, postbiotics, probiotics, prebiotics, synbiotics and phytogenic feed additives.

A) Organic Acids (SCFAs and MCFAs)

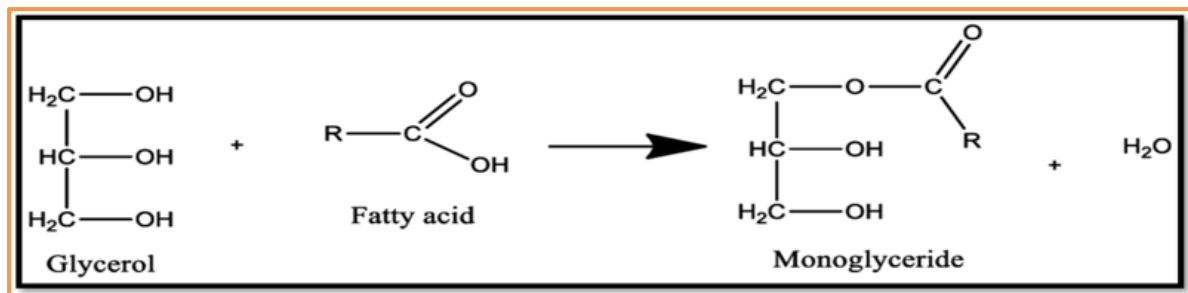
Short-chain fatty acids (SCFAs) and medium-chain fatty acids (MCFAs) are promising alternatives because of their antimicrobial and intestinal health-promoting properties. Important SCFAs include acetate, propionate and butyrate, whereas MCFAs include caproic, caprylic, capric and lauric acids. SCFAs can suppress pathogen growth by altering intracellular pH and bacterial metabolism, while butyrate supports intestinal barrier integrity and tight-junction function. MCFAs exhibit direct antimicrobial activity against important enteric pathogens, including *Salmonella* spp., *Escherichia coli*, *Campylobacter jejuni* and *C. perfringens*. Their supplementation has also been associated with improvements in growth performance and feed efficiency in broilers.



Despite their potential, direct supplementation of free fatty acids has practical limitations. Rapid absorption in the upper gastrointestinal tract may limit their availability in the distal intestine, where antimicrobial activity is often required. Their activity can also be influenced by intestinal pH, while strong odor and palatability issues may restrict practical inclusion levels.



Esterified forms: Particularly monoglycerides and diglycerides, provide an alternative delivery strategy. These compounds consist of fatty acids linked to glycerol and may offer improved stability, palatability and antimicrobial activity throughout the gastrointestinal tract. Monoglycerides of lauric and butyric acids, such as monolaurin and monobutylin, have shown potential for improving intestinal morphology and reducing *C. perfringens*-associated intestinal damage and mortality in challenged broilers.



B) Postbiotics as Antimicrobial and Anticoccidial Agents

Postbiotics defined as preparations of inanimate microorganisms and their components conferring host health benefits. This emerged over recent years as mechanistically attractive AGP and anticoccidial alternatives. It integrates multiple antimicrobial pathways into stable ingredients without regulatory concerns or antimicrobial resistance risks. *Saccharomyces cerevisiae*-derived yeast fermentation products and *Lactobacillus*-derived non-viable fermentation products have undergone the most extensive poultry studies. Bioactive compounds postbiotics are SCFAs, organic acids, bacteriocins, β -glucans, mannan polysaccharides, antioxidants, nucleotides, and B- and K-group vitamins. Antimicrobial activity through two major metabolite classes i.e. **a. Organic acids** (lactic, acetic, propionic, and formic acids) reduce luminal pH and suppress pathogen growth by disrupting membrane permeability, intracellular pH homeostasis, electron transport, and cellular morphology. **b. Bacteriocins**- ribosomal synthesized antimicrobial peptides, it remains heat- and pH-stable, targeting susceptible bacterial cytoplasmic membranes. Postbiotics are unlikely to induce cross-resistance with antibiotics because their antimicrobial effects operate through mechanisms distinct from conventional antibiotic-resistance. Broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative pathogens, including *C. perfringens*, without the collateral microbiota disruption associated with in-feed antibiotics. Broilers fed postbiotics through feed and drinking water achieved superior results: FCR of 1.51, mortality of 16%, and European Production Efficiency Factor of 279.33, compared with untreated challenged controls recording 1.96 FCR, 36% mortality, and EPEF of 177.33. The In-Ovo and drinking water administration of *Saccharomyces cerevisiae*-based postbiotics reduced jejunal and ileal necrotic enteritis lesion scores in birds challenged with *Eimeria maxima* and *Clostridium perfringens*, marked by elevated expression of nutrient transporter genes (SGLT1, GLUT2, EAAT3) indicating enhanced nutrient absorption and intestinal function.

C) Vaccination Strategies

One of the most reliable non-chemical control approaches is live coccidiosis vaccination. These vaccinations lower the burden of wild isolate resistance and restore drug-sensitive *Eimeria* populations by exposing birds to controlled, graded coccidial infection. However, vaccine-induced coccidial cycling still damages intestinal epithelium during initial parasite replication stages, potentially predisposing flocks to subclinical necrotic enteritis unless management and biosecurity remain consistently high standard.

D) Probiotics, Prebiotics and Synbiotics

Bacillus subtilis, *Bacillus licheniformis* and *Saccharomyces cerevisiae* alone or in combination with mannan-oligosaccharides and β -glucans showed the potential in reducing the negative effects of necrotic enteritis and coccidiosis while improving the intestinal microbiota. Synbiotic formulations similarly support healthier microbial populations and improve production performance in anticoccidial-free programs.

E) Phytogenic Feed Additives

Essential oils from oregano rich in carvacrol and thymol, alongside citrus peel oils containing limonene, linalool and α -terpinene demonstrate both anticoccidial and antimicrobial activity in vitro and in vivo. The phytogenic compounds modulate intestinal microbiota, immune responses and improve gut morphology. Functional oil blends combining these compounds can partially replace ionophore antimicrobial activity against *Eimeria*-induced dysbiosis, particularly when delivered in protected slow-release formulations.

F) Management and Biosecurity

Improved litter management, reduced stocking density, all-in/all-out systems and thorough cleaning and disinfection reduce *Eimeria* challenge pressure but cannot independently prevent clinical coccidiosis under commercial conditions. These management practices remain essential successful anticoccidial-free production components. There are some other alternative strategies, but they differ in mechanism and response consistency. Feed enzymes chiefly enhance nutrient availability with limited antimicrobial activity. Emerging alternatives such as bacteriophages and antimicrobial peptides offer targeted pathogen control but remain constrained by narrow host specificity, production costs and regulatory limitations.

Conclusion

The elimination of antibiotic growth promoters and anticoccidials significantly disrupts intestinal homeostasis in broiler production, resulting in dysbiosis, increased disease susceptibility and substantial economic losses exceeding USD 15 billion annually. The associated microbiota dysbiosis, resurgence of necrotic enteritis, and compromised barrier integrity present interconnected challenges that require comprehensive interventions rather than isolated solutions. Evidence indicates that esterified fatty acids, particularly monoglycerides of lauric and butyric acid, effectively restore intestinal morphology and reduce pathogenic colonization. Postbiotics provide mechanistically distinct antimicrobial activity without the risk of resistance, achieving production parameters comparable to systems supplemented with antibiotic growth promoters. The combination of live coccidiosis vaccination with strategic probiotic and prebiotic supplementation offers complementary benefits through microbiota modulation and immune enhancement. The industry must recognize this as a fundamental paradigm shift rather than a temporary regulatory adjustment. Continued research into novel delivery systems, antimicrobial peptides, and bacteriophage applications is essential for optimizing the sustainability of antibiotic-free poultry production.