



Bacteriophage as a Novel Feed Additive in Poultry: A Comprehensive Review

Kishore Gottam¹, M.M. Pawar¹, S.S. Patil¹, C.P. Modi¹, D.J. Raval¹, D.H. Limbachiya¹

10.18805/ag.R-2816

ABSTRACT

The global restriction of antibiotic use in poultry production has driven the search for effective alternatives. Bacteriophages, viruses that specifically infect bacteria, are gaining attention as promising feed additives due to their safety, specificity and antimicrobial efficacy. This review outlines the biological characteristics of bacteriophages, their applications in poultry for therapy, food safety, disinfection and performance enhancement. It also discusses current research findings, potential commercial products and challenges related to phage resistance and gut microbiota interaction. Bacteriophages show promise as alternatives to antibiotics, but further research on stability, dosage and resistance mechanisms is essential for widespread use.

Key words: Antimicrobial resistance, Bacteriophage, Feed additive.

Poultry plays a significant role in generating income and providing livelihood to millions of farmers in India. As per 20th Livestock Census, poultry population in India was 851.81 million (BAHS, 2019). In India, the meat production from poultry was 4.995 million tonnes and egg production were 138.38 billion during year 2022-23 (BAHS, 2023). Poultry meat and eggs are important sources of nutrients, contributing significantly to human nutrition. The uses of in-feed antibiotics in chickens are aimed at improving production performance, controlling enteric diseases and reducing the production cost (Eid *et al.*, 2020). However, the use of antibiotics as growth promoters have been associated with antibiotic residues in animal products leading to bacterial resistance to these drugs, posing a global health challenge (Anee *et al.*, 2021). Now days, there is increasing health awareness, consumers are demanding high-quality, safe and nutritious food products. In light of this, several alternatives have been studied recently to replace antibiotic growth promoters in chickens to improve growth performance, product quality and health (Gosai *et al.*, 2023; Qiu *et al.*, 2023). Bacteriophage as a newer feed additive in chickens has been investigated as an alternative to replace antibiotic growth promoters (Shaufi *et al.*, 2024).

Bacteriophages have been studied as a viable alternative to antibiotic growth promoters. This review discusses the biological mechanisms, applications and advantages of bacteriophages in poultry farming.

This review was prepared through a systematic evaluation of published literature retrieved from Google Scholar, Scopus, ScienceDirect and Web of Science. Keywords including bacteriophage, phage therapy, poultry, broiler, layer, feed additive and antibiotic alternative were used. Studies published between 2010 and 2024 focusing on poultry performance, gut health, immunity, pathogen reduction and food safety were included.

¹Department of Animal Nutrition, College of Veterinary Science and A.H., Kamdhenu University, Sardarkrushinagar-385 506, Gujarat, India.

Corresponding Author: Kishore Gottam, Department of Animal Nutrition, College of Veterinary Science and A.H., Kamdhenu University, Sardarkrushinagar-385 506, Gujarat, India.
Email: gottamkishore@gmail.com

ORCIDs: 0000-0003-0318-0599, 0000-0002-0797-3580, 0009-0004-3945-6758, 0009-0004-9464-5463

How to cite this article: Gottam, K., Pawar, M.M., Patil, S.S., Modi, C.P., Raval, D.J. and Limbachiya, D.H. (2026). Bacteriophage as a Novel Feed Additive in Poultry: A Comprehensive Review. *Agricultural Reviews*. **47(5)**: 851-854. doi: 10.18805/ag.R-2816.

Submitted: 21-07-2025 **Accepted:** 09-02-2026 **Online:** 24-02-2026

Bacteriophages: Biology and mechanism of action

Bacteriophages are bacteria-infecting viruses which multiply in a specific bacterial host. They are ubiquitous and classified into two categories: virulent and temperate. Discovered independently by Twort (1915) and d'Herelle (1917), with an estimated global population of 10³¹ particles (Kazi and Annapure, 2016). They are naturally present in water, soil, plants and even the human gut microbiome.

Phages are categorized into two main types based on their life cycles:

1. Lytic (Virulent) phages: These infect bacteria, replicate inside and subsequently lyse the bacterial cell to release new phages (Loc-Carrillo and Abedon, 2011).

2. Lysogenic (Temperate) phages: These integrate their DNA into the host bacterial genome, remaining dormant until triggered to enter the lytic cycle (Shaufi *et al.*, 2024).

Lytic phages, due to their ability to destroy bacterial cells, are considered for therapeutic use in livestock production.

Application of bacteriophages in poultry production

Bacteriophages are being explored as a novel feed additive in poultry to address various challenges such as bacterial infections and food contamination. Their main applications are categorized into the following:

Phage therapy in poultry disease management

Phage therapy utilizes bacteriophages to target and eliminate bacterial pathogens like *Campylobacter jejuni*, *Salmonella enterica* and *Escherichia coli*, which are of zoonotic concern (Wernicki *et al.*, 2017). Lytic phages, with their specific host-targeting abilities, offer an advantage over antibiotics, which indiscriminately kill both harmful and beneficial bacteria (Abedon *et al.*, 2017).

In a European food safety authority (EFSA) report, campylobacteriosis, salmonellosis and shiga toxin-producing *E. coli* infections were the most common zoonotic diseases linked to poultry (EFSA, 2019). Bacteriophage therapy has shown efficacy in reducing these bacterial pathogens in poultry, mitigating risks to public health (Dlamini *et al.*, 2023).

Phages have been used experimentally to control diseases such as necrotic enteritis, salmonellosis and colibacillosis. Targeted phage therapy can lower pathogen loads in the gastrointestinal tract, reduce mortality and minimize economic losses due to infectious outbreaks (Sarrami *et al.*, 2022).

Bacteriophage as a feed additive

Recent studies demonstrate that bacteriophages can be administered as a feed additive to improve growth performance, modulate gut microbiota and reduce pathogen loads in poultry (Shaafi *et al.*, 2023; Huff *et al.*, 2002). For example, Upadhaya *et al.* (2021) found that bacteriophage supplementation enhanced broiler weight gain and positively impacted the gut microbiome, particularly increasing the relative abundance of *Lactobacillus*.

Food biocontrol and decontamination

Bacteriophages are used as bio-preservatives to reduce bacterial contamination in meat products. Commercial products like ListShield™ and Listex™ have been developed to target *Listeria monocytogenes* in ready-to-eat foods (Bigot *et al.*, 2018). Phage-based treatments can decontaminate poultry carcasses without affecting the organoleptic properties of the food. Phages also serve as disinfectants in hatcheries and transport systems, reducing surface contamination and biofilm formation (Atterbury *et al.*, 2003). Commercial phage-based sprays have shown efficacy in reducing surface contamination without altering the product's quality or appearance (Garcia *et al.*, 2008).

Advantages of bacteriophages over antibiotics

Phages offer several advantages over traditional antibiotics:

- **High specificity:** Phages target specific bacterial strains

without disturbing the host's beneficial microbiota (Wernicki *et al.*, 2017).

- **Reduced resistance development:** Phage cocktails can be designed to minimize the risk of bacterial resistance (Allen *et al.*, 2013).
- **Safety and tolerability:** Bacteriophages do not replicate in animal cells, ensuring minimal toxicity or side effects (Pirnay *et al.*, 2011).
- **Self-replicating:** Amplifies at the site of infection, sustaining its activity naturally (Upadhaya *et al.*, 2021).
- **Low risk of dysbiosis:** Unlike antibiotics, does not disrupt gut microbial balance (Shaafi *et al.*, 2024; Huff *et al.*, 2010; Waseh *et al.*, 2010).
- **Minimal environmental impact:** No chemical residues; does not contribute to environmental pollution (Kazi and Annapure, 2016).
- **Versatile applications:** Used in feed, water, sprays and as surface sanitizers (Dlamini *et al.*, 2023).

Challenges and Limitations

Despite their potential, several challenges limit the widespread adoption of bacteriophages in poultry production:

- **Bacterial Resistance:** Bacteria may develop resistance to specific phages, although this can be mitigated by using phage cocktails.
- **Stability and Storage:** Phage viability may be compromised under extreme storage conditions, requiring careful formulation and preservation (Burrowes *et al.*, 2011).
- **Regulatory Hurdles:** The use of bacteriophages in food production is subject to stringent regulatory approval processes, which vary across regions (Garcia *et al.*, 2008).
- **Immune neutralization:** Host immune system may inactivate phages before they act (Kazi and Annapure, 2016).
- **Risk of horizontal gene transfer:** Lysogenic phages can potentially spread antimicrobial resistance genes (ARGs) (Pirnay *et al.*, 2011).

Further research is needed to determine optimal dosing strategies, administration methods and long-term impacts of bacteriophage use in poultry.

Recent research findings

Several recent studies provide promising insights into the use of bacteriophages in poultry farming:

- Upadhaya *et al.* (2021) reported that supplementation of a bacteriophage cocktail (0.05%) significantly improved body weight gain and feed conversion ratio in broiler chickens, with performance comparable to antibiotic growth promoters. The same study also observed increased populations of beneficial *Lactobacillus* species in the gut.
- Shaafi *et al.* (2024) found that broilers fed diets supplemented with phage cocktails exhibited improved growth performance and enhanced gut microbial diversity. Further research by Shaafi *et al.* (2024) demonstrated synergistic effects when bacteriophages were combined with probiotics, resulting in better feed efficiency and intestinal health.

- Dlamini *et al.* (2023) evaluated encapsulated Salmonella-specific bacteriophages and observed a significant reduction in intestinal Salmonella counts, along with improved intestinal histomorphology and meat quality traits, although growth responses varied with dosage.
- Sarrami *et al.* (2022) reported enhanced immune response markers and modulation of gut health-related gene expression in broilers receiving bacteriophage supplementation.
- Phage-based interventions have also shown effectiveness in reducing *Campylobacter jejuni* and *Escherichia coli* colonization in poultry, thereby lowering zoonotic risk and improving food safety (Wernicki *et al.*, 2017; Atterbury *et al.*, 2003; Clavijo *et al.*, 2018).
- These findings suggest that bacteriophage therapy can effectively substitute for antibiotics as a growth promoter in poultry, offering an eco-friendly and safe alternative.

Future prospects

Despite encouraging results, phage therapy in poultry remains an emerging field. Research is ongoing to:

- Optimize phage dose, frequency and administration methods.
- Develop stable, commercial-grade phage formulations.
- Combine phages with other feed additives (e.g., probiotics, prebiotics, enzymes) for synergistic benefits (Asrore *et al.*, 2023).
- Study long-term effects on antibiotic resistance genes and microbiome composition (Shaafi *et al.*, 2024).

CONCLUSION

Bacteriophages represent a promising, targeted and eco-friendly alternative to antibiotics in poultry production. They have shown significant potential in improving growth performance, enhancing disease resistance and ensuring food safety. Despite initial skepticism, numerous studies have demonstrated their effectiveness, especially in the context of rising multidrug resistance. However, challenges such as narrow host range, potential for resistance development and regulatory complexities remain. Continued research is essential to address these limitations, particularly in understanding phage-bacterium interactions, determining optimal dosages and exploring the influence of diet composition on phage efficacy. With more studies and better understanding, bacteriophages could become an important part of poultry health management.

Disclaimers

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish, or preparation of the manuscript.

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