

Potential use of phytobiotics as an alternative to antibiotics in livestock

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ABSTRACT

The use of antibiotics as antibiotic growth promoters (AGP) in the livestock industry has contributed significantly to increasing livestock productivity. However, overuse and unregulated use have led to the development of antimicrobial resistance (AMR), which is currently a concern to world health. AGP is restricted by laws in many nations, which promotes the hunt for sustainable and efficient substitutes. Phytobiotics, which are derived from plants and include essential oils, extracts, and pure active compounds such as flavonoids, alkaloids, terpenoids, and tannins, have attracted attention due to their multifunctional properties. Phytobiotics work through a variety of mechanisms, such as immune system modulation, intestinal microbiota composition regulation, antimicrobial activity that stops the growth of pathogens, antioxidant effects that shield cells from oxidative damage, and stimulation of the secretion of digestive enzymes. According to scientific data, adding phytobiotics to pig, ruminant, and poultry feed can lower the prevalence of infectious illnesses while also increasing feed conversion efficiency, animal product quality, and production performance. Its efficacy is affected by the kind of plant, bioactive constituent content, extraction technique, formulation, and interactions with other feed ingredients. Despite the promising potential of phytobiotics, issues include production costs, heterogeneity in composition due to different plant sources, and standardization of raw material quality. Innovations in formulation, including the application of nanotechnology or mixes with organic acids and probiotics, offer chances to improve efficacy and stability. The livestock industry could use phytobiotics as a safe, sustainable, and eco-friendly antibiotic substitute in the post-AGP age if the right technology is applied and a scientific evidence-based strategy is taken.

Introduction

Antibiotic use has been widespread in the livestock business for many years in an attempt to enhance efficiency, growth, and the prevention and treatment of livestock illnesses (Matheou *et al.*, 2025). The use of antibiotics as antibiotic growth promoters (AGP) helps to improve intestinal health and nutritional absorption by lowering the number of harmful microorganisms in the digestive tract (Miyakawa *et al.*, 2024). However, the widespread and unchecked use of antibiotics has led to major issues, particularly with the rise in antimicrobial resistance (AMR) (Ahmed *et al.*, 2024a). This resistance reduces the ability of antibiotics to treat diseases in animals and increases the possibility that it will spread to people through the environment and food chain (Salam *et al.*, 2023).

The World Health Organization (WHO) and other international health agencies have acknowledged the occurrence of antibiotic resistance as a global threat (World Health Organization, 2014). AMR increases infection-related mortality, lengthens the duration of sickness, and raises medical expenses, all of which worsens public health issues (Ferraz, 2024). Antibiotic resistance in animal husbandry can have a detrimental effect on food safety and impede sustainable production (Kaur *et al.*, 2024). As a result, numerous nations have passed laws restricting or outright banning the use of AGP, including the European Union, which has done so since 2006 (Millet and Maertens, 2011). Several other nations have enacted comparable laws to lessen the effects of this resistance (Donley, 2019; Perera and Ravindran, 2025).

The livestock and research communities have started searching for safe and efficient substitutes to preserve cattle health and productivity in response to limitations on the use of antibiotics in feed (Ghimpețeanu *et*

al., 2022). A viable substitute is the application of phytobiotics, which are feed additives made from natural bioactive compounds or plant extracts (Obianwuna *et al.*, 2024). Phytobiotics are known to have various pharmacological properties, such as antimicrobial, antioxidant, anti-inflammatory, and immunomodulatory, which can help maintain the balance of intestinal microbiota, strengthen the immune system, and improve the digestive function of livestock (Pudota *et al.*, 2025). Phytobiotics provide a more natural and eco-friendlier alternative to synthetic antibiotics without the significant risk of antimicrobial resistance (Rachwał and Gustaw, 2025).

Although studies on phytobiotics have yielded conflicting findings, in general, phytobiotics can improve growth performance, feed conversion efficiency, the quality of livestock products (e.g., meat, milk, and eggs), and lower the prevalence of diseases, particularly those associated with digestive tract disorders (Kikusato, 2021). Numerous phytobiotic active ingredients, including alkaloids, flavonoids, terpenoids, tannins, and saponins, function in a variety of ways, from preventing the growth of harmful bacteria to boosting the action of digestive enzymes (Kumar *et al.*, 2023a). However, the effectiveness of phytobiotics is greatly influenced by the plant source, extraction method, dosage, and interaction with other feed components (Ivanova *et al.*, 2024).

The aim of this review article was to comprehensively review the potential of phytobiotics as an alternative to antibiotics in livestock production, including definitions, classifications, mechanisms of action, scientific evidence for their application, as well as challenges and opportunities for their development. It is envisaged that by comprehending the properties and advantages of phytobiotics, the livestock sector would be able to adopt safe, sustainable, and efficient substitutes to lessen reliance

on synthetic antibiotics and lower the risk of antibiotic resistance. The explanation in this article provides a scientific basis for researchers and practitioners to optimize the use of phytobiotics in modern livestock production systems that are environmentally friendly and healthy.

Definition of phytobiotics

Phytobiotics, sometimes referred to as phytochemicals or phytobiotics in international literature, are a class of bioactive compounds that are extracted from different plant parts, including leaves, roots, bark, seeds, and flowers, and are added to feed to enhance the welfare, health, and productivity of livestock (Obianwuna *et al.*, 2024). Phytobiotics are organic components that comprise secondary plant compounds with a variety of biological activities, such as immunomodulatory, antioxidant, and antibacterial properties, as well as beneficial effects on digestion (Rachwał and Gustaw, 2025).

Phytobiotics are classified as complex mixtures of different classes of bioactive compounds, including terpenoids (volatile components and essential oils), alkaloids, glycosides, phenolics (flavonoids, phenolic acids, and tannins), and saponins (Abdelli *et al.*, 2021). Each of these compounds contributes to a particular mechanism of action in the livestock's body. These compounds can be extracted using contemporary chemical techniques, such as water or organic solvents, or they can be steam-distilled to produce essential oils (Awad *et al.*, 2021).

The use of phytobiotics in animal feed emerged in response to growing global concerns regarding the use of synthetic antibiotic growth promoters (AGPs), which have been widely banned or restricted in many countries due to the risk of developing antimicrobial resistance and negative impacts on human and animal health (Abd El-Ghany, 2020). A safer and more sustainable natural alternative, phytobiotics work through a variety of mechanisms, such as enhancing digestive enzymes, innate and adaptive immune responses, and gut microbiota modulation, which boosts probiotic bacterial populations and inhibits pathogen growth (Wang *et al.*, 2024).

From a physiological standpoint, phytobiotics are crucial for enhancing the gastrointestinal mucosa's integrity, boosting the release of digesting enzymes, and decreasing intestinal inflammation through immunomodulatory and antioxidant properties (Kikusato, 2021). This combined effect boosts resistance to infection and environmental stress in addition to improving cattle production performance and nutrient use efficiency (Gumowski *et al.*, 2025).

From a conceptual standpoint, phytobiotics are a subset of a more general natural feed additive. They are constantly being researched in a number of scientific studies to determine their therapeutic potential, low risk of adverse effects, and best use in a variety of livestock, including pigs, ruminants, and poultry (Galamatis *et al.*, 2025; Pandey *et al.*, 2023; Nastoh *et al.*, 2024). This strategy promotes the sustainable livestock paradigm, which focuses on lowering the usage of artificial chemicals while enhancing the safety of food products and animal health.

Sources and forms of phytobiotics

Phytobiotics are bioactive compounds obtained from various parts of plants such as leaves, roots, stems, seeds, flowers, and even bark (Riaz *et al.*, 2023). The bioactive potential of these phytobiotics is influenced by the distinct secondary metabolite composition of each plant portion, including phenolics, alkaloids, terpenoids, tannins, and saponins (Kaushik *et al.*, 2021). This variety of sources makes it possible to choose particular phytobiotic types based on the intended use in the field of animal nutrition and health.

Various techniques are utilized in the phytobiotic extraction process, depending on the target compound's chemical characteristics and the plant compound being used. The most popular method for isolating polar to semi-polar compounds is solvent extraction with ethanol,

methanol, or water (Plaskova and Mlcek, 2023). This method is effective and somewhat easy to use for producing crude extracts that contain intricate blends of bioactive compounds. Furthermore, more specialized compound fractions can be separated through extraction using organic solvents, allowing for the concentration of components with specific biological activity (Lee *et al.*, 2024).

In addition to crude extracts, phytobiotics are also accessible in the form of essential oils—volatile fractions derived through steam distillation or other specialized extraction procedures (Zhang *et al.*, 2023). The volatile terpenoid and phenolic compounds found in essential oils have potent antibacterial and antioxidant properties (Masyita *et al.*, 2022). However, encapsulation technology is frequently required for feed applications due to the volatile and lipophilic character of essential oils, which necessitate specific consideration for stability and bioavailability (Fontana *et al.*, 2025).

Furthermore, the extraction and purification of pure bioactive compounds such as alkaloids (e.g., berberine), flavonoids (quercetin), terpenoids (carvacrol and thymol), tannins, and saponins offers new prospects for more quantitative and exact applications (El-Saadony *et al.*, 2025). The efficiency of phytobiotics as a substitute for antibiotics and immunomodulators in livestock production is increased by the use of these pure compounds, which enable improved dose control and analysis of particular mechanisms of action (Zaikina *et al.*, 2022).

As a result, the range of phytobiotic sources and forms, bolstered by suitable extraction techniques, offers versatility in the creation of safe and efficient natural feed additive solutions to sustainably enhance animal productivity and health. Figure 1 shows the diverse plant sources of phytobiotics, the bioactive compounds they contain, various extraction methods (solvent extraction, organic solvent extraction, and steam distillation for essential oils), encapsulation technology for stabilization, and the application of purified compounds as natural feed additives to enhance livestock nutrition and health.

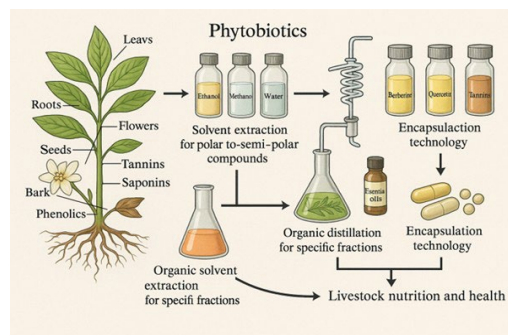


Figure 1. Phytobiotic sources, extraction methods, and applications in animal nutrition.

Classification of phytobiotics

A class of bioactive compounds called phytobiotics is made from plants and is added to feed as a natural way to increase the productivity and health of animals (Ivanova *et al.*, 2024). To understand the characteristics, working mechanisms, and potential applications systematically, phytobiotics can be classified based on two main aspects, namely plant origin and the type of active compounds contained in them. Table 1 shows the classification of phytobiotics based on two main aspects that are important for understanding their application and mechanism of action. Classification based on plant origin highlights the form of the phytobiotic (essential oil, extract, and powder) and examples of source plants, while classification based on the type of active compound groups phytobiotics according to the main chemical components that contribute to their biological activity. The combination of these two classifications provides a comprehensive overview for the development and selection of suitable phytobiotics in the animal feed industry.

Table 1. Classification of phytobiotics based on plant origin and type of active compound.

Classification	Types of phytobiotics	Examples of plant sources	Main components	Main biological activities
Based on origin	Essential oils	Oregano, Thyme, Rosemary, and Cinnamon	Terpenoids and volatile phenolics	Antimicrobial and antioxidant
	Plant extracts	Neem, Moringa, and Ginger	Flavonoids, alkaloids, and tannins	Antimicrobial and immunomodulator
	Plant powder/Flour	Garlic, Turmeric, and Cinnamon	Various bioactive compounds	Antimicrobial, antioxidant, and digestive stimulation
Based on the type of active compound	Alkaloid	<i>Berberis</i> spp. and <i>Sanguinaria canadensis</i>	Berberine and sanguine	Antimicrobial and analgesic
	Flavonoid	Berries, Green Tea, and Shallots	Quercetin and kaempferol	Antioxidant and immunomodulator
	Terpenoid	Essential oils of various plants	Carvacrol, Thymol	Antimicrobial and anti-inflammatory
	Tannin	Bark and leaves of certain plants	Hydroxy tannins and condensates	Antimicrobial and antioxidant
	Saponin	<i>Quillaja saponaria</i> and Fenugreek	Saponin	Immunostimulation and antimicrobials

Table 2. *In vivo* and *in vitro* studies on the effectiveness of phytobiotics on livestock production.

Types of livestock	Types of phytobiotics	Effectiveness parameters	Main results	Reference
Poultry	Oregano essential oil	FCR, egg production, and carcass quality	Increased FCR up to 5%, increased egg production, and decreased pathogenic bacteria	(Zhang <i>et al.</i> , 2021)
	Garlic extract	Digestive enzyme activity, and gut microbiota	Increased amylase and protease activity, increased probiotic bacteria, and reduced <i>E. coli</i>	(Abd El-Ghany, 2024)
	Moringa leaf extract	Immunity, body weight, and mortality	Increased specific antibodies, 12% weight gain, and decreased mortality	(Rehman <i>et al.</i> , 2018)
	Oregano essential oil	Antimicrobial activity against <i>Salmonella</i> spp.	Inhibition of <i>Salmonella</i> growth by up to 90% at low concentrations	(Ebani <i>et al.</i> , 2019)
	<i>Quillaja saponaria</i>	Inhibition of growth of <i>Clostridium perfringens</i>	Significant inhibition of pathogenic bacterial growth and increase in <i>Lactobacillus</i> population	(Bafundo <i>et al.</i> , 2021)
Ruminants	Cinnamon and lemongrass extract	Milk production, rumen fermentation, and methane emissions	8% increase in milk production, 15% reduction in methane emissions, and increase in propionate	(Castro-Montoya <i>et al.</i> , 2015)
	Thyme essential oil	Rumen microbial activity and fiber digestion	Reduction of methanogenic bacteria population and increase in fiber fermentation efficiency	(Baraz <i>et al.</i> , 2018)
	Flavonoids from Moringa	Oxidative stress and blood lipid profile	Decreased oxidative stress, improved lipid profile, and decreased inflammation	(Liu <i>et al.</i> , 2023)
	Lemongrass extract	Rumen fermentation and methane gas production	Reduction of methane production by 20%, increase of propionate in <i>in vitro</i> fermentation	(Singh <i>et al.</i> , 2018)
Pig	Allicin (garlic)	Growth, diarrhea incidence, and gut health	Average daily weight gain of 10%, 30% reduction in diarrhea, improvement in intestinal morphology	(Huang <i>et al.</i> , 2011)
	<i>Quillaja saponaria</i> extract	Immunity and growth performance	Increased immunoglobulin production, feed efficiency increased by 7%	(Turner <i>et al.</i> , 2002)
	Moringa leaf flavonoids	Antioxidant and anti-inflammatory activity	75% free radical inhibition, decreased expression of proinflammatory cytokines	(Mukumbo <i>et al.</i> , 2014)

Classification based on plant origin

This classification groups phytobiotics based on the form and plant source from which the bioactive compounds are obtained. Commonly used forms of phytobiotics include:

Essential Oils: Plant volatile fractions that contain lipophilic and aromatic compounds such as volatile phenolics and terpenoids (Maleš *et al.*, 2022). Essential oils are potent antioxidants and antimicrobials (Bibow and Oleszek, 2024). Examples of plants that yield essential oils are cinnamon (*Cinnamomum verum*) (Shu *et al.*, 2024), thyme (*Thymus vulgaris*) (Pandur *et al.*, 2022), oregano (*Origanum vulgare*) (Nurzyńska-Wierdak and Walasek-Janusz, 2025), and rosemary (*Rosmarinus officinalis*) (Rahbardar and Hosseinzadeh, 2020).

Plant Extracts: Complex combinations of bioactive compounds can be found in extracts made from plant parts using solvents like water or ethanol (Plaskova and Mlcek, 2023). Examples include extracts from ginger (*Zingiber officinale*) (Saldaña-Olguin *et al.*, 2024), neem bark (*Azadirachta indica*) (Wylie and Merrell, 2022), and moringa leaves (*Moringa oleifera*) (Gomes *et al.*, 2025).

Plant Powder and Flour: Dried plant forms that are ground into powder to be mixed directly into feed, such as garlic powder (Basuini *et al.*, 2024), turmeric (El-Saadony *et al.*, 2023), and cinnamon (Kowalska *et al.*, 2021).

Classification based on the type of active compound

This classification is based on the main chemical components in phytobiotics that determine their biological mechanisms:

Alkaloid: A nitrogen-containing heterocyclic molecule that has antibacterial and nerve-stimulating pharmacological properties (Yan *et al.*, 2021). Examples: berberine from *Berberis* spp. (Neag *et al.*, 2018) and sanguinarine from *Sanguinaria canadensis* (Croaker *et al.*, 2016).

Flavonoids: A class of polyphenols with immunomodulatory and antioxidant properties (Ullah *et al.*, 2020). Examples include quercetin, kaempferol, and hesperidin which are found in berries (Pap *et al.*, 2021), green tea (Sun *et al.*, 2022), and onions (Marefati *et al.*, 2021).

Terpenoids: Essential oils contain a lot of isoprene-derived hydrocarbon compounds that have antibacterial and anti-inflammatory properties (Câmara *et al.*, 2024). Examples: carvacrol (Agliassa and Maffei, 2018), thymol (Meeran *et al.*, 2017), and menthol (Bergman *et al.*, 2019).

Tannins: Polyphenolic compounds that can bind proteins and heavy metals, acting as antimicrobials and antioxidants (Huang *et al.*, 2018). The bark and leaves contain two different kinds of tannins: hydroxy tannins and condensate tannins (Okuda and Ito, 2011).

to plant origin (essential oils, extracts, and powders) and the type of active compound (alkaloids, flavonoids, terpenoids, tannins, and saponins), providing a comprehensive overview of their sources and bioactive components for applications in animal feed.

Mechanism of action of phytobiotics

Phytobiotics are natural feed additives with multifunctional mechanisms of action that improve livestock health and productivity. The primary mechanisms of phytobiotic action include antimicrobial activity, antioxidant effects, immunomodulation, stimulation of digestive processes, and regulation of gut microbiota balance. A thorough understanding of these mechanisms is essential for optimizing the use of phytobiotics as an alternative to antibiotics in livestock production.

Antimicrobial activity

Antimicrobial activity is a fundamental mechanism of phytobiotics that contributes significantly to the control of pathogens in the digestive system of livestock (Obianwuna *et al.*, 2024). The chemical characteristics of phytobiotic bioactive compounds, such as flavonoids, terpenoids, alkaloids, phenolic compounds, and essential oils, enable them to directly affect the structure and function of pathogenic microorganisms, including bacteria, fungus, and protozoa (Rachwał and Gustaw, 2025).

Lipophilic essential oil molecules can interact with the lipid bilayer to molecularly incorporate into the cytoplasmic membrane of microorganisms (Yamine *et al.*, 2022). Microbial cell homeostasis is upset by this integration because it increases membrane permeability, which leads to the leakage of proteins, critical metabolites, and vital ions (such as K^+ and H^+) (Murínová and Dercová, 2014). The loss of electrochemical gradients and a reduction in the membrane potential necessary for bioenergetic processes are the ultimate outcomes of increased membrane permeability, which also causes cell death (Zong *et al.*, 2024).

Phenolic compounds and alkaloids are known to physically disrupt membranes and to impede the action of important enzymes in microbial metabolic pathways, such as those involved in protein and nucleic acid production (Lobiuc *et al.*, 2023). Therefore, phytobiotics can interfere with the microbial protein synthesis and DNA and RNA replication activities, which are essential for the growth and survival of harmful microbes (Rachwał and Gustaw, 2025). Furthermore, several phytobiotic compounds also function as agents that disrupt quorum sensing, a microbial cellular communication mechanism involved in the production of biofilms (Samrot *et al.*, 2021). Biofilms provide protection to microbes from environmental stress, including exposure to antibiotics and the host immune system (Uruén *et al.*, 2020). Phytobiotics make infections more vulnerable to the body's defenses and therapies by preventing the production of biofilms (Roy *et al.*, 2018).

Studies conducted both *in vitro* and *in vivo* have demonstrated that phytobiotics successfully inhibit a number of significant livestock pathogens, including *Salmonella enterica* (Iwiński *et al.*, 2022), *Clostridium perfringens* (Hussein *et al.*, 2020), *Escherichia coli* (Chodkowska *et al.*, 2022), and *Campylobacter jejuni* (Hamad *et al.*, 2023), lowering the prevalence of infectious diseases and enhancing gut health. This effectiveness often depends on the concentration of the bioactive compound, the type of target microorganism, and the microenvironmental conditions in the digestive tract (Firmino *et al.*, 2021).

Antioxidant effect

Phytobiotics include flavonoids, tannins, phenolic acids, carotenoids, and vitamin C, among other bioactive compounds with strong antioxidant potential (Pudota *et al.*, 2025). These compounds are crucial in scavenging free radicals and reactive oxygen species (ROS) that are generated either naturally or in reaction to environmental stress, infection, or animal

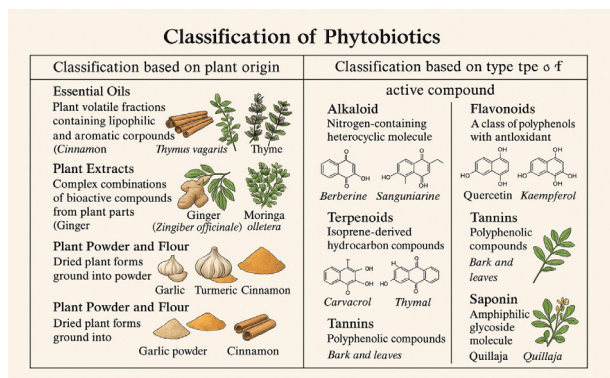


Figure 2. Classification of phytobiotics based on plant origin and active compound type.

Saponin: An amphiphilic glycoside molecule with antibacterial and immunostimulating properties that produces foam (Timilsena *et al.*, 2023). Plants that produce saponins include fenugreek (*Trigonella foenum-graecum*) (Visuvanathan *et al.*, 2022) and *Quillaja saponaria* (Fleck *et al.*, 2019). Figure 2 illustrates the classification of phytobiotics according

metabolism (de Oliveira *et al.*, 2025).

The oxidation reactions that free radicals and ROS can cause biomacromolecular compounds including lipids, proteins, and nucleic acids can lead to genetic mutations, enzyme failure, damage to cell membranes, and overall disruption of cellular function (Juan *et al.*, 2021). Oxidative stress is the term for this buildup of damage, which weakens immunity, reduces physiological function, and makes people more vulnerable to metabolic and infectious diseases (Dash *et al.*, 2025).

Antioxidant compounds in phytobiotics work through several main molecular mechanisms. First, they operate as donors of electrons or hydrogen, which helps free radicals become less reactive molecules and halt the harmful chain reaction of radicals (Phaniendra *et al.*, 2015). Second, phytobiotics can activate cellular signaling pathways, including the nuclear factor erythroid 2-related factor 2-Antioxidant Response Element (Nrf2-ARE) pathway, which activates endogenous antioxidant enzymes like glutathione peroxidase, catalase, and superoxide dismutase (SOD) (Ngo and Duenwald, 2022). Protection against chronic oxidative stress is strengthened when this pathway is activated since it raises the total antioxidant defense capacity of the cell (Suraweera *et al.*, 2020).

Furthermore, phytobiotics might lessen tissue damage linked to chronic inflammation by blocking the activity of prooxidative enzymes including cyclooxygenase and NADPH oxidase, which contribute to the production of ROS and inflammatory mediators (Kumar *et al.*, 2023b). Particularly in intestinal epithelial tissue, which is vulnerable to oxidative damage, this combination of effects not only preserves the integrity of cell structure and function but also enhances the process of tissue regeneration and differentiation (Sahoo *et al.*, 2023).

Physiologically, phytobiotic antioxidants can make animals more resilient to environmental stressors like heat, infections from pathogens, and unfavorable feeding conditions (Mountzouris and Brouklogiannis, 2024). Phytobiotics also support healthy immunological responses and effective metabolic processes by lowering oxidative stress, which enhances cattle production performance (Adetunji *et al.*, 2025).

Immunomodulation

As immunomodulators, phytobiotics have a significant role in influencing the overall response and operation of the livestock immune system at both the innate and adaptive immunity levels (Yu *et al.*, 2021). Phytobiotics contain bioactive compounds such polyphenols, flavonoids, alkaloids, saponins, and terpenoids that interact with different immune system components through intricate molecular pathways to improve the body's resistance to infection and control the balance of inflammation (Ivanova *et al.*, 2024).

At the innate immune system, phytobiotics can increase the capacity of phagocytes, especially neutrophils and macrophages, to identify, engulf (phagocytose), and eliminate pathogens (Lim *et al.*, 2017). Additionally, this stimulation of macrophages promotes the controlled production of inflammatory mediators like chemokines and cytokines (including interleukin-1 β and tumor necrosis factor- α) that attract additional immune cells to the infection site (Duque and Descoteaux, 2014). Furthermore, phytobiotics have the ability to boost the activity of Natural Killer (NK) cells, which use cytotoxic mechanisms to help eradicate tumor or virus-infected cells (Rizzello *et al.*, 2011).

Phytobiotics have an impact on T and B cell differentiation and proliferation at the adaptive immunological level (Li *et al.*, 2022). Bioactive compounds can boost particular immune responses to antigens by influencing signaling pathways that control lymphocyte clonal growth and differentiation (Mitra *et al.*, 2022). Increased cytotoxic T lymphocytes (CTL) improve the capacity to eliminate infected cells, whereas increased T helper lymphocyte activity (Th1 and Th2) aids in B cell antibody generation and macrophage activation (Xie *et al.*, 2023). Additionally, phytobiotics have the ability to boost the synthesis of certain antibodies, which are crucial for humoral immunity over the long term (Obianwuna *et al.*, 2024).

Phytobiotic-induced immunomodulation also includes controlling the ratio of pro-inflammatory to anti-inflammatory responses to avoid tissue damage from excessive inflammation (Di Sotto *et al.*, 2020). Certain phytobiotic compounds have the ability to boost the synthesis of anti-inflammatory cytokines, like transforming growth factor- β (TGF- β) and interleukin-10, which inhibit the expression of inflammatory mediators and preserve tissue homeostasis (Chan *et al.*, 2024). This process is crucial for avoiding persistent inflammation, which can impair cattle performance and lead to health issues (Kikusato, 2021).

Additionally, phytobiotics have the ability to stimulate the expression of critical surface molecules on immune cells, including toll-like receptors (TLR) and major histocompatibility complex (MHC), which improve antigen detection and immune response activation (Wlaźlak *et al.*, 2023). Through these pathways, phytobiotics boost the development of particular adaptive immunity and immunological memory in addition to enhancing non-specific defenses (Al Mahmud *et al.*, 2023).

Stimulation of the digestive process

Phytobiotics, which contain various bioactive compounds such as essential oils, flavonoids, alkaloids, and saponins, play an important role in improving the efficiency of digestion and nutrient absorption in livestock through multifaceted mechanisms involving interactions with the gastrointestinal system (Pudota *et al.*, 2025).

One of the primary processes is the stimulation of the release of exocrine digestive enzymes, such as lipase, amylase, and protease, which break down proteins, lipids, and carbohydrates into simpler molecules that the intestinal mucosa can absorb (Yang *et al.*, 2025). It is believed that the bioactive compounds found in phytobiotics alter the activity of gastrointestinal mucosal glands and pancreatic secretory cells by activating cellular receptors and signaling pathways, including the cyclic adenosine monophosphate (cAMP) and protein kinase C (PKC) pathways (Zimmermann and Wagner, 2021). The process of nutrient breakdown is directly accelerated by this rise in enzyme production, which raises the amount of substrates available for absorption (Salinas *et al.*, 2021).

Furthermore, phytobiotics help to enhance the intestinal mucosa's composition and functionality (Duarte and Kim, 2022). The intestinal barrier is maintained by the trophic effects of some phytochemicals, which also enhance intestinal epithelial integrity, promote enterocyte proliferation and differentiation, and boost the production of junctional proteins like tight junctions (Peng *et al.*, 2023). The absorptive surface area is increased by this improvement in mucosal health, enabling more efficient absorption of macro and micronutrients (Stojanović *et al.*, 2021).

Phytobiotics also affect intestinal motility by regulating enteric nerve activity and stimulating the smooth muscle of the intestinal wall (Liu *et al.*, 2022). The process of digestion and absorption is optimized, food transit is enhanced, and nutrient interaction with the intestinal epithelial surface is increased due to this increase in motility (Zheng *et al.*, 2022). Certain phytobiotic compounds have the ability to control the release of gastrointestinal hormones, including cholecystokinin and gastrin, which are involved in controlling enzyme secretion and motility (Basit *et al.*, 2020).

From a microbiota perspective, phytobiotics can alter the gut microbiota's makeup by promoting the development of advantageous microbes that aid in fiber fermentation and the synthesis of metabolites like short-chain fatty acids (SCFA) (Meyers *et al.*, 2022). These SCFAs support intestinal mucosal growth and serve as a vital source of energy for epithelial cells, enhancing the barrier's ability to absorb substances and absorb them (Nireeksha *et al.*, 2025).

Through this intricate process, digestion and nutrient absorption are enhanced, improving growth performance, feed usage efficiency, and overall animal health (Lian *et al.*, 2024). The use of phytobiotics in feed formulation by considering the right dosage and combination can significantly increase animal productivity and welfare (Doski and Yaseen, 2023).

Regulation of gut microbiota balance

The health and metabolism of animals are significantly influenced by the diverse collection of bacteria known as the gut microbiota (Barathan *et al.*, 2024). The bioactive compounds found in phytobiotics, including flavonoids, essential oils, tannins, and saponins, work as ecological modulators of the microbiota's composition and activity, supporting livestock systemic health and gastrointestinal homeostasis (Gumowski *et al.*, 2025).

In terms of microbiology, phytobiotics have specific actions that restrict the growth of potentially harmful microbes including *Salmonella enterica*, *Escherichia coli*, and *Clostridium perfringens*, which are known to induce inflammation and intestinal dysbiosis (Rachwał and Gustaw, 2025). Pathogen growth is inhibited by phytobiotic substances in two ways: directly, by destroying microbial cell membranes, and indirectly, by competing with helpful microorganisms for nutrients and space (Fanai *et al.*, 2024). As a result of the concurrent inhibition of pathogens, probiotic bacteria like *Lactobacillus* sp. and *Bifidobacterium* sp. have an ecological advantage in colonizing the gut mucosa (Rafique *et al.*, 2023).

The production of significant secondary metabolites, particularly SCFAs like acetate, propionate, and butyrate, is impacted by the growth in the population of advantageous microorganisms (Deleu *et al.*, 2021). These SCFAs serve as the primary source of energy for enterocytes, promote intestinal epithelial cell growth and differentiation, and enhance the function of the mucosal barrier by upregulating the expression of junctional proteins, also known as tight junction proteins (Portincasa *et al.*, 2022). As a result, the intestinal epithelium's permeability and integrity are preserved, avoiding the spread of harmful bacteria and endotoxins throughout the body, which can cause inflammation (Di Vincenzo *et al.*, 2024).

Additionally, SCFA metabolites have immunomodulatory effects locally. For instance, butyrate can stimulate the development of regulatory T cells (Tregs), which help to preserve gut immunological balance by reducing excessive inflammatory reactions (Nireeksha *et al.*, 2025). Additionally, phytobiotics help goblet cells produce more mucus, which strengthens the mucosa's defenses against pathogen invasion (Obianwu-na *et al.*, 2024).

Phytobiotics lower the likelihood of dysbiosis, which is frequently linked to gastrointestinal issues, persistent inflammation, and poorer output performance, by holistically modifying the gut microbiota (Martinez *et al.*, 2021). Overall, these benefits enhance gut health, promote an adaptable and regulated immune response, and improve digestion and nutrient absorption efficiency (Zhao *et al.*, 2023).

According to recent molecular and metagenomic research, supplementing phytobiotics can change the microbiota's composition in a way that makes it more resilient and stable, allowing it to adjust to pathogenic and environmental stress (Ren *et al.*, 2019). This method lowers the danger of antibiotic resistance and dependence on antibiotics, making it a crucial tactic in sustainable animal health management. Figure 3 illustrates the multifunctional mechanisms of phytobiotics in livestock, covering antimicrobial activity, antioxidant effects, immunomodulation, stimulation of digestive processes, and regulation of gut microbiota balance.

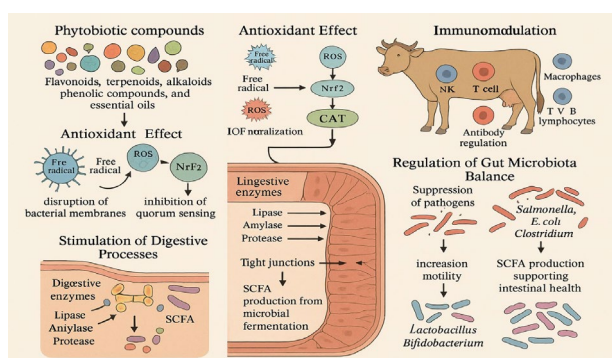


Figure 3. Mechanisms of action of phytobiotics in livestock health and productivity.

Scientific evidence and applications of phytobiotics in livestock production

The use of phytobiotics as a natural alternative to antibiotics in livestock production has been extensively researched through both *in vivo* and *in vitro* studies. Numerous scientific evidence indicates that phytobiotics can improve the production performance and health of various livestock species, including poultry, ruminants, and swine. Table 2 summarizes the results of *in vivo* and *in vitro* studies evaluating the effectiveness of various phytobiotics in poultry, ruminant, and swine production. These studies provide empirical evidence of the benefits of phytobiotics in improving production performance while maintaining animal health.

Application of phytobiotics in poultry

The application of phytobiotics as feed additives for poultry has drawn a lot of interest in an attempt to sustainably increase animal health and production efficiency (Wang *et al.*, 2024). Numerous experiments have demonstrated that adding phytobiotic supplements can raise the Feed Conversion Ratio (FCR), a measure of improved nutrient utilization efficiency that leads to a more optimal conversion of feed into animal products, including meat and eggs (Aljumaah *et al.*, 2020; Iwiński *et al.*, 2023; Kikusato, 2021). This rise in FCR is associated with better gastrointestinal health, which is mediated by changes in the gut microbiota (Zhang *et al.*, 2021).

Phytobiotics function by inhibiting the growth of harmful bacteria, including *Escherichia coli*, a common source of gastrointestinal illnesses in chickens, and *Clostridium perfringens*, the causative agent of necrotic enteritis (Sayed *et al.*, 2023). The incidence of digestive disorders and intestinal mucosal inflammation, which can obstruct nutrient absorption, are both decreased when these microorganisms are reduced in quantity (Abd El-Ghany, 2024). Simultaneously, phytobiotics support the growth of probiotic bacteria such as *Lactobacillus* and *Bifidobacterium* which play a role in maintaining the balance of the intestinal microbiota ecosystem (Chandrasekaran *et al.*, 2024). These helpful microorganisms improve the local immunological response, boost the formation of short-chain fatty acids that promote epithelial cell regeneration, and fortify the intestinal mucosal barrier (Rehman *et al.*, 2018).

Phytobiotics not only influence the microbiota but also directly enhance the quality of poultry products. It has been demonstrated that the usage of aromatic plant extracts, such as thyme (*Thymus vulgaris*) and oregano (*Origanum vulgare*), improves carcass metrics, such as meat texture and a healthier lipid profile, and increases egg production and eggshell quality (Migliorini *et al.*, 2019; Yasin *et al.*, 2025). The antibacterial qualities of phytobiotics, which lessen the burden of infection, and the stimulation of the release of digestive enzymes, such as lipases, amylases, and proteases, which enhance digestion and nutrient absorption, are the processes behind these effects (Oni and Oke, 2025). Furthermore, phytobiotics' antioxidants shield tissue cells from oxidative stress, promoting healthy metabolic processes (Ebani *et al.*, 2019).

The use of phytobiotics in poultry not only boosts output by improving gut health and feed efficiency, but it also enhances the quality of the finished product. As a result, phytobiotics provide a sustainable and efficient natural substitute for synthetic antibiotics in the poultry industry (Bafundo *et al.*, 2021).

Application of phytobiotics in ruminants

The potential of phytobiotics to enhance efficiency of rumen fermentation and the general metabolic health of animals has led to a great deal of research in ruminant nutrition (Ahmed *et al.*, 2024b). A community of symbiotic bacteria participates in the intricate biological process of rumen fermentation, which breaks down high-fiber materials into metabolic products like volatile fatty acids (VFA) that ruminants can consume

(McCann *et al.*, 2014). Through the modulation of rumen microbiota composition, phytobiotic supplementation in rations can increase the efficiency of fiber degradation and produce a more beneficial proportion of VFA. For instance, it can increase the production of acetone acetate and propionate, which are vital sources of energy for livestock (Baraz *et al.*, 2018).

Additionally, methane (CH₄) emissions, a major greenhouse gas generated during methanogenic fermentation in the rumen, are decreased by phytobiotics (Ugbogu *et al.*, 2019). Methane causes a significant loss of metabolic energy for cattle in addition to having a detrimental effect on the environment (Liu *et al.*, 2023). Condensed tannins and essential oils from acacia (*Acacia* spp.), lemongrass (*Cymbopogon citratus*), and cinnamon (*Cinnamomum verum*) are among the bioactive compounds found in phytobiotics that are known to inhibit methanogenic activity while lowering the population of methane-producing bacteria without interfering with other crucial fermentation-related microorganisms (Denninger *et al.*, 2020; Pinski *et al.*, 2015; Vázquez-Carrillo *et al.*, 2023).

Phytobiotics have important immunomodulatory and anti-inflammatory functions in preserving the systemic health of ruminants, in addition to their impact on gas emissions and rumen microbiota (Ahmed *et al.*, 2024b). Chronic inflammation and oxidative stress are major factors that reduce reproductive performance, milk production, and livestock growth (Sammad *et al.*, 2020). Phytobiotics contain phenolic and flavonoid chemicals that act as antioxidants, reducing oxidative stress, neutralizing free radicals, and suppressing the release of proinflammatory cytokines and other inflammatory mediators (Singh *et al.*, 2018). Therefore, adding phytobiotics to livestock can make them more resilient to diseases and environmental stressors (Rachwał and Gustaw, 2025).

Regarding milk production, a number of studies have documented higher milk output and quality in dairy cows fed phytobiotic supplements, which has been linked to better animal health and digestive efficiency (AlSuwaiegh *et al.*, 2022; Hashemzadeh-Cigari *et al.*, 2014; Wang *et al.*, 2024). Higher antioxidant content and a healthier lipid profile are further indicators of higher-quality milk (Castro-Montoya *et al.*, 2015). This demonstrates how phytobiotics have the ability to improve livestock products' nutritional content in addition to boosting productivity (Khan *et al.*, 2019).

The multipurpose strategy of adding phytobiotics to ruminant feed not only boosts production efficiency but also helps to improve animal wellbeing and lessen environmental effects (Nastoh *et al.*, 2024). Further research is needed to determine the optimal dosage, combination of phytobiotics, and the molecular mechanisms underlying these effects so that commercial applications can be carried out effectively and sustainably.

Application of phytobiotics in pigs

Using phytobiotics instead of antibiotics to improve pig health and productivity has gained significant attention, particularly during crucial stages like post-weaning when diarrhea and digestive issues are common (Liu *et al.*, 2024). Pigs are more vulnerable to infection by gastrointestinal pathogens like *Salmonella* spp. and *Escherichia coli* during this time because their immune systems and gut flora are still developing (Sung *et al.*, 2025). Phytobiotics play an important role in stabilizing the gut microbiota ecosystem by suppressing the proliferation of pathogenic bacteria while supporting the growth of beneficial probiotic bacteria, such as *Lactobacillus* and *Bifidobacterium* (Ji *et al.*, 2023). These modifications to the microbiota's makeup help to improve nutrition absorption efficiency and lower the prevalence of diarrhea (Huang *et al.*, 2011).

Phytobiotics have important immunomodulatory effects in pigs in addition to modifying the microbiota. It has been demonstrated that bioactive compounds such saponins from quillaja bark extract (*Quillaja saponaria*) and allicin, which is produced from garlic (*Allium sativum*), improve humoral and cellular immune responses (Abd El-Ghany, 2024; Fleck *et al.*, 2019). These processes, which together strengthen the body's

defenses against infections, include phagocyte activity, the development of certain antibodies, and the stimulation of the production of anti-inflammatory cytokines (Obianwuna *et al.*, 2024). As a result, phytobiotics not only lower the prevalence of infectious disorders but also lessen the necessity for therapeutic antibiotic use, which increases the danger of developing antibiotic resistance (Turner *et al.*, 2002).

Additionally, phytobiotics promote intestinal health by lowering mucosal inflammation and strengthening the intestinal epithelial barrier (Vancamelbeke and Vermeire, 2017). Phytobiotics contain antioxidant chemicals that shield intestinal tissue from oxidative damage, which frequently happens during times of environmental stress and feed transition (Duarte and Kim, 2022). Kondisi ini berperan penting dalam mempertahankan fungsi pencernaan optimal dan penyerapan nutrisi yang efisien, yang pada gilirannya berkontribusi pada peningkatan pertumbuhan dan performa babi secara keseluruhan (Mukumbo *et al.*, 2014).

Numerous *in vivo* investigations have demonstrated that supplementing post-weaning pigs with phytobiotics can enhance their average daily gain (ADG), feed efficiency, and gastrointestinal health (Gheisar and Kim, 2017; Holanda *et al.*, 2021; Pandey *et al.*, 2023). Furthermore, changes in hematological and biochemical indicators that indicate a better state of systemic health are linked to the usage of phytobiotics (Madesh *et al.*, 2025). This data supports the use of phytobiotics as a safe and effective feed additive alternative to antibiotics, promoting sustainable livestock practices that minimize the need for synthetic antibiotics. Figure 4 illustrates the application of phytobiotics as natural alternatives to antibiotics in poultry, ruminants, and pigs, highlighting their roles in improving gut health, enhancing nutrient utilization, reducing methane emissions, strengthening immune responses, and ultimately contributing to better animal productivity and product quality.

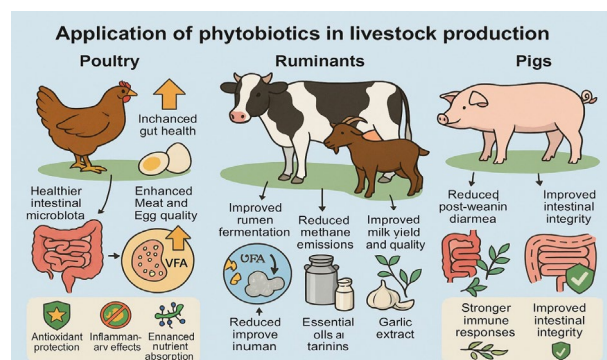


Figure 4. Application of phytobiotics in livestock production.

Factors affecting the effectiveness of phytobiotics

The effectiveness of phytobiotics as natural feed additives depends heavily on various factors related to their chemical composition, formulation, and usage conditions. A thorough understanding of these factors is essential for phytobiotics to provide optimal benefits in improving livestock health and performance. The following is a detailed explanation of the main factors influencing phytobiotic effectiveness.

Variation of active compound composition

The chemical composition of phytobiotics is a key factor that greatly influences their effectiveness in livestock applications. Phytobiotics contain bioactive substances such alkaloids, flavonoids, terpenoids, tannins, and saponins that have a variety of biological characteristics and chemical structures (Musa *et al.*, 2023). These compounds have a wide range of activities, from immunomodulatory to antioxidant and antibacterial. However, the composition and relative concentration of these compounds are greatly influenced by various biotic and abiotic factors, including the

plant species, the part of the plant used (roots, leaves, flowers, and bark), the extraction technique applied, as well as environmental conditions during plant growth such as temperature, humidity, light intensity, and soil type (Riaz *et al.*, 2023).

The quality and quantity of active phytobiotic substances vary because plants develop different secondary metabolites in response to their surroundings (Alem, 2024). For instance, plants that grow in environments with high levels of biotic stress (such as pathogen attack) or abiotic stress (such as drought and extremely high temperatures) typically create more secondary defensive chemicals (Khan *et al.*, 2025). The chemical profile of the extract is also determined by the extraction technique, including the solvent (oil, ethanol, methanol, and water) (Sultana *et al.*, 2009). Hydrophilic and lipophilic substances will be extracted differently, which will affect the bioactive potential that is discovered (Domínguez-Valencia *et al.*, 2023).

This variation makes it difficult to standardize phytobiotic products. Phytobiotic products may exhibit inconsistent biological efficacy if the active chemical content is not standardized, making field application outcomes uncertain (Zaikina *et al.*, 2022). As a result, in order to guarantee product quality, rigorous standardization procedures must be developed in addition to conducting meticulous quantitative and qualitative analyses of bioactive compounds employing contemporary chromatography and spectroscopic techniques (Wang *et al.*, 2023).

Moreover, depending on the species, age, physiological state, and overall health of the animal, variations in the makeup of these active chemicals may also result in distinct biological reactions in livestock (Tedeschi *et al.*, 2021). This necessitates modifying the phytobiotic formula in accordance with the particular requirements of the livestock and the intended usage, such as boosting immune, enhancing digestion, or managing particular infections (Kikusato, 2021). Therefore, improving the use of phytobiotics in contemporary livestock production systems requires a thorough understanding of the differences in the composition of active compounds and their bioactivity processes.

Dosage and dosage form

Phytobiotic dosage is a crucial parameter that directly influences its biological effectiveness in livestock applications (Chodkowska *et al.*, 2022). The dose-response relationship must be considered when determining the ideal dosage since too-low dosages may result in subtherapeutic effects, which would prevent the best possible antibacterial, immunomodulatory, or digestive stimulating effects (Adepu and Ramakrishna, 2021). However, overdosing can result in toxicity, metabolic problems, and even potentially harmful side effects for the health of cattle, like gastrointestinal mucosal irritation or shifts in the microbiota's equilibrium (Tu *et al.*, 2020). Each phytobiotic must therefore undergo pharmacodynamic and toxicological research in order to determine a safe and effective dosage range and to guarantee that results can be replicated in the field (Borgert *et al.*, 2021).

The stability and bioavailability of the active ingredients in phytobiotics are significantly influenced by the dosage form in addition to the dose (Rachwał and Gustaw, 2025). There are several ways to offer phytobiotics, including as a dry powder, liquid extract, essential oil, or pure chemical (Magklaras *et al.*, 2025). Each form has physicochemical properties that influence the kinetics of active ingredient release in the animal digestive system, solubility, and penetration of microbial cell membranes (Sokol *et al.*, 2025). For instance, lipophilic essential oils have better antibacterial activity than hydrophilic solvent-based extracts because they can more easily pass through microbial lipid membranes (Nazzaro *et al.*, 2013). Nevertheless, essential oils are also more prone to oxidation and volatility, necessitating specific formulation methods to preserve their stability throughout feed processing and storage (Movahedi *et al.*, 2024).

The type of cattle, age, physiological state, and application goal must all be taken into consideration when choosing the right dosage form

(Malkawi *et al.*, 2022). For instance, calibrated amounts of liquid extracts may be safer and easier to absorb than dry preparations in young livestock with delicate digestive tracts (Hristov *et al.*, 2019). However, dry powder or pellet form might be more cost-effective and feasible for long-term use in adult livestock (Nath *et al.*, 2023). Nanoencapsulation and matrix carriers are two formulation technology advancements that are beginning to be developed to improve the stability and controlled release of phytobiotic bioactive substances, maximizing their efficacy without raising dosage (Pateiro *et al.*, 2021).

The key elements in the effective use of phytobiotics as a substitute for natural antibiotics are dosage management and the choice of the right phytobiotic dosage form (Galamatis *et al.*, 2025). Modern livestock production requires a multidisciplinary strategy that integrates chemistry, pharmacology, formulation technology, and animal nutrition research to guarantee the efficacy, safety, and consistency of phytobiotics.

Interactions with other feeds or additives

The way phytobiotics interact with feed ingredients and other additives is a crucial factor that can have a big impact on how biologically successful they are in livestock production systems (Ren *et al.*, 2019). The diverse chemical properties of phytobiotic bioactive compounds, which are often secondary plant metabolites like flavonoids, tannins, terpenoids, and saponins, allow them to interact both chemically and physically with different molecules in feed (Roy *et al.*, 2022). These interactions can be synergistic, antagonistic, or even neutral depending on the type of compound and environmental conditions in the livestock's digestive tract.

Certain phytobiotic compounds, such as tannins, can produce protein-tannin complexes that decrease the availability of vital proteins in feed because of their high affinity for protein (Besharati *et al.*, 2022). This can reduce the nutritional value of feed and have a negative impact on livestock growth if not properly controlled. Moreover, tannins have the ability to bind digestive enzymes, which lowers enzyme activity and digestive effectiveness (Cosme *et al.*, 2025). Therefore, the dosage and type of phytobiotics containing tannins must be formulated carefully to minimize this antagonistic effect (Ahmed *et al.*, 2024b).

However, there may be a positive and reciprocal relationship between phytobiotics and feed additives including probiotics, prebiotics, vitamins, and digestive enzymes (Windisch *et al.*, 2008). For example, phytobiotics can increase the growth of probiotic microorganisms in the digestive tract by providing substrates or creating a more conducive environment through reducing pathogens (Ding *et al.*, 2021). Similarly, combining phytobiotics and feed enzymes can boost nutrient absorption and accelerate the breakdown of complex feed constituents (Rafiq *et al.*, 2022). The stability and activity of phytobiotics can be diminished by temperature, pH, and chemical interactions, thus it is important to take into account the possibility of chemical degradation or alteration of active phytobiotic substances when mixing with other additives (Selionova *et al.*, 2025).

A comprehensive understanding of these interactions is necessary for optimal feed composition in order to guarantee the stability and efficacy of phytobiotics. The active phytobiotic components can be shielded from deterioration and their controlled release in the digestive system regulated by modern formulation methods like microencapsulation or the use of certain carriers (Sun *et al.*, 2023). As a result, the combination of phytobiotics with other feed ingredients presents both a problem and a chance to create synergy that will greatly enhance the performance and health of livestock.

Stability during storage and processing of feed

The uniformity and efficacy of the finished product are significantly influenced by the stability of the bioactive components in phytobiotics during feed processing and storage (Sokol *et al.*, 2025). Essential oils, flavonoids, tannins, and saponins are examples of active chemicals that are

highly vulnerable to environmental conditions such as high temperatures, light, oxygen, and humidity (Gutiérrez-Del-Río *et al.*, 2021). These circumstances can lead to oxidation, hydrolysis, and volatility processes, which can degrade chemicals and reduce biological activity (Zhang *et al.*, 2024). For instance, during the feed pelletization process, essential oils that are high in volatile compounds readily evaporate at high temperatures, but during storage, flavonoids and tannins may deteriorate as a result of oxidation accelerated by light and oxygen (Gharby *et al.*, 2022).

The chemical structure of bioactive compounds may be harmed by feed processing techniques that use high heat and pressure, such as drying, pelletization, and extrusion (Kour *et al.*, 2021). Thermal processing can alter chemical structure, denaturize active molecules, and lower the concentration of substances that have antibacterial, antioxidant, or immunomodulatory properties (Miškec *et al.*, 2025). Furthermore, lipids and phenolic compounds can oxidize more quickly when exposed to oxygen during mixing and storage, which drastically lowers their phytobiotic potential (Geng *et al.*, 2023). Therefore, controlling the processing parameters is very important to minimize damage to active compounds.

Modern formulation and packaging solutions have been developed to improve phytobiotic stability in order to solve these issues (Yao *et al.*, 2024). Microencapsulation methods that employ protective matrices like proteins, lipids, or polysaccharides can restrict the direct exposure of active substances to light and oxygen while also regulating the release of bioactive compounds into the livestock's digestive tract (Mehta *et al.*, 2022). The shelf life of phytobiotic products has also been successfully increased by packing them in airtight and light-proof containers (Vasile and Baican, 2021). Furthermore, stability can be added without producing hazardous residues by using natural preservatives that are compatible (Baptista *et al.*, 2020).

In order for phytobiotics to offer the best possible benefits as a substitute for natural antibiotics, it is crucial to have a solid understanding of the variables that affect their stability during processing and storage as well as the use of suitable protection measures. This promotes the sustainability of the livestock sector as well as the development of high-quality feed that is safe and effective for the health of animals. Figure 5 shows the main factors determining the effectiveness of phytobiotics as natural feed additives, including the variation of active compound composition, dosage and dosage form, interactions with other feed ingredients or additives, and stability during storage and feed processing, which collectively affect their bioactivity, safety, and consistency in livestock production systems.

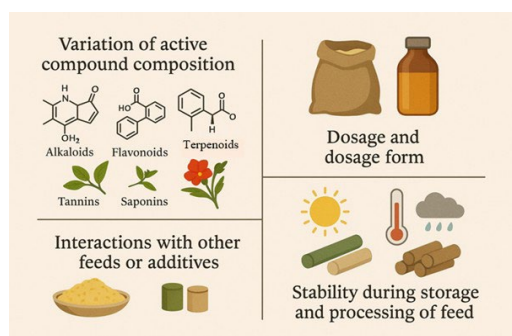


Figure 5. Key factors influencing the effectiveness of phytobiotics in livestock feed applications.

Challenges and opportunities for developing phytobiotics as an alternative to antibiotics

The development of phytobiotics as alternatives to antibiotics in livestock production faces numerous challenges while offering significant opportunities for innovation and the application of cutting-edge technologies. A thorough understanding of these aspects is crucial to accelerating the widespread and sustainable adoption of phytobiotics.

Challenges of phytobiotic development

Variability in the quality of the natural raw materials employed is one of the primary obstacles in the development of phytobiotics. Phytobiotic-producing plants' bioactive component composition is heavily impacted by genetic factors, the growth environment, harvest timing, and extraction technique (Riaz *et al.*, 2023). These differences result in inconsistent biological activity of the finished product, which might lower clinical efficacy and user confidence. Therefore, standardization of raw materials through rigorous quantitative and qualitative chemical analysis, certification of raw material sources, and development of reproducible extraction protocols are essential to ensure consistent quality and safety of phytobiotic products (Wang *et al.*, 2023).

Phytobiotic manufacturing costs continue to be a major obstacle, particularly when considering industrial production. Advanced technology and costly solvents are frequently needed for the extraction and purification of active chemicals, and the cultivation of plants that produce phytobiotics is not necessarily agronomically ideal (Altemimi *et al.*, 2017). Furthermore, given the seasonality and varying environment, the year-round supply of reliable raw materials is a challenge. It is imperative to cut costs while boosting supply by implementing current agronomic techniques, plant genetic engineering, and environmentally friendly, cost-effective green extraction processes to increase production efficiency (Usman *et al.*, 2023).

Opportunities for phytobiotic development

Innovative opportunities in the development of phytobiotics lie in utilizing synergism with other additives such as probiotics and organic acids. This combination can provide a synergistic effect that improves digestive tract health and livestock immune response more effectively than single use (Ren *et al.*, 2019). Pathogens can be suppressed by phytobiotics, probiotics can boost the beneficial microbiota, and organic acids can lower intestinal pH and foster the growth of helpful microorganisms (Ji *et al.*, 2023). The development of multifunctional feed additive products with a wide range of potential applications is made possible by research into the best combination formulation and molecular interaction mechanisms of this synergy (Perera and Ravindran, 2025).

Innovative opportunities in phytobiotic formulation are provided by nanotechnology, such as the nanoencapsulation of bioactive substances, which can enhance the stability, bioavailability, and regulation of phytobiotic release in the gastrointestinal tract (Guía-García *et al.*, 2022). The formulation of phytobiotics can be revolutionized by nanotechnology. For example, bioactive chemicals can be nanoencapsulated to enhance the stability, bioavailability, and regulation of phytobiotic release in the gastrointestinal system (Rachwał and Gustaw, 2025). Furthermore, the controlled release formulation prolongs the effect and lessens the need for recurrent administration by allowing the phytobiotics to be released gradually based on the physiological parameters of the animals (Li *et al.*, 2023). Translating these breakthroughs into marketable goods requires interdisciplinary research that integrates materials science, biotechnology, and animal nutrition.

Conclusion

Phytobiotics show great potential as sustainable natural alternatives to AGPs in livestock production. It has been demonstrated that a variety of phytobiotic mechanisms of action, including as antioxidant, immunomodulatory, digestive stimulation, and antibacterial properties, greatly enhance the health and productivity of livestock. Advances in formulation and packaging technologies present chances to maximize the effectiveness of phytobiotics, despite issues with dose, stability of active compounds, and uniformity of raw materials. Further research focused on understanding molecular mechanisms, developing innovative formu-

lations, and conducting large-scale field trials is highly recommended to strengthen industrial applications. Phytobiotics can be a strategic option to assist the production of livestock that is healthy, productive, and environmentally friendly when used in an integrative and evidence-based manner.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

- Abd El-Ghany, W.A., 2020. Phytobiotics in Poultry Industry as Growth Promoters, Antimicrobials and Immunomodulators – A Review. *J. World Poult. Res.* 10, 571–579. doi: 10.36380/jwpr.2020.65.
- Abd El-Ghany, W.A., 2024. Potential Effects of Garlic (*Allium sativum* L.) on the Performance, Immunity, Gut Health, Anti-Oxidant Status, Blood Parameters, and Intestinal Microbiota of Poultry: An Updated Comprehensive Review. *Animals (Basel)* 14, 498. doi: 10.3390/ani14030498.
- Abdelli, N., Solà-Oriol, D., Pérez, J.F., 2021. Phytogetic Feed Additives in Poultry: Achievements, Prospective and Challenges. *Animals (Basel)* 11, 3471. doi: 10.3390/ani11123471.
- Adepu, S., Ramakrishna, S., 2021. Controlled Drug Delivery Systems: Current Status and Future Directions. *Molecules* 26, 5905. doi: 10.3390/molecules26195905.
- Adetunji, A.O., Price, J., Owusu, H., Adewale, E.F., Adesina, P.A., Saliu, T.P., Zhu, Z., Xedzro, C., Asiamah, E., Islam, S., 2025. Mechanisms by which phytogetic extracts enhance livestock reproductive health: current insights and future directions. *Front. Vet. Sci.* 12, 1568577. doi: 10.3389/fvets.2025.1568577.
- Agliassa, C., Maffei, M.E., 2018. *Origanum vulgare* Terpenoids Induce Oxidative Stress and Reduce the Feeding Activity of *Spodoptera littoralis*. *Int. J. Mol. Sci.* 19, 2805. doi: 10.3390/ijms19092805.
- Ahmed, M.G., Elwakeel, E.A., El-Zarkouny, S.Z., Al-Sagheer, A.A., 2024b. Environmental impact of phytobiotic additives on greenhouse gas emission reduction, rumen fermentation manipulation, and performance in ruminants: an updated review. *Environ. Sci. Pollut. Res. Int.* 31, 37943–37962. doi: 10.1007/s11356-024-33664-5.
- Ahmed, S.K., Hussein, S., Qurbani, K., Ibrahim, R.H., Fareeq, A., Mahmood, K.A., Mohamed, M.G., 2024a. Antimicrobial resistance: Impacts, challenges, and future prospects. *J. Med. Surg. Public Health* 2, 100081. doi: 10.1016/j.jgmed.2024.100081.
- Al Mahmud, A., Siddiqui, S.A., Karim, M.R., Al-Mamun, M.R., Akhter, S., Sohel, M., Hasan, M., Bellah, S.F., Amin, M.N., 2023. Clinically proven natural products, vitamins and mineral in boosting up immunity: A comprehensive review. *Heliyon* 9, e15292. doi: 10.1016/j.heliyon.2023. e15292.
- Alem, W.T., 2024. Effect of herbal extracts in animal nutrition as feed additives. *Heliyon* 10, e24973. doi: 10.1016/j.heliyon.2024.e24973.
- Aljumaah, M.R., Suliman, G.M., Abdullatif, A.A., Abudabos, A.M., 2020. Effects of probiotic feed additives on growth traits, blood biochemistry, and meat characteristics of broiler chickens exposed to *Salmonella typhimurium*. *Poult. Sci.* 99, 5744–5751. doi: 10.1016/j.psj.2020.07.033.
- AlSuwaigh, S.B., Almoatham, A.M., Alyousef, Y.M., Mansour, A.T., Al-Sagheer, A.A., 2022. Influence of Functional Feed Supplements on the Milk Production Efficiency, Feed Utilization, Blood Metabolites, and Health of Holstein Cows during Mid-Lactation. *Sustainability* 14, 8444. doi: 10.3390/su14148444.
- Altemimi, A., Lakhssassi, N., Baharlouei, A., 2017. Watson DG, Lightfoot DA. Phytochemicals: Extraction, Isolation, and Identification of Bioactive Compounds from Plant Extracts. *Plants (Basel)* 6, 42. doi: 10.3390/plants6040042.
- Awad, A.M., Kumar, P., Ismail-Fitry, M.R., Jusoh, S., Ab Aziz, M.F., Sazili, A.Q., 2021. Green Extraction of Bioactive Compounds from Plant Biomass and Their Application in Meat as Natural Antioxidant. *Antioxidants (Basel)* 10, 1465. doi: 10.3390/antiox10091465.
- Bafundo, K.W., Duerr, I., McNaughton, J.L., Johnson, A.B., 2021. The Effects of a Quillaja/Yucca Saponin Combination on Performance, *Clostridium perfringens* Counts and Percentage of Salmonella Positive Broiler Chickens. *EC Vet. Sci.* 6, 40–45. doi: 10.31080/ecve.2021.06.00371.
- Baptista, R.C., Horita, C.N., Sant'Ana, A.S., 2020. Natural products with preservative properties for enhancing the microbiological safety and extending the shelf-life of seafood: A review. *Food Res. Int.* 127, 108762. doi: 10.1016/j.foodres.2019.108762.
- Barathan, M., Ng, S.L., Lokanathan, Y., Ng, M.H., Law, J.X., 2024. The Profound Influence of Gut Microbiome and Extracellular Vesicles on Animal Health and Disease. *Int. J. Mol. Sci.* 25, 4024. doi: 10.3390/ijms25074024.
- Baraz, H., Jahani-Azizabadi, H., Azizi, O., 2018. Simultaneous use of thyme essential oil and disodium fumarate can improve *in vitro* ruminal microbial fermentation characteristics. *Vet. Res. Forum* 9, 193–198. doi: 10.30466/VRF.2018.30828.
- Basit, M.A., Kadir, A.A., Loh, T.C., Aziz, S.A., Salleh, A., Zakaria, Z.A., Idris, S.B., 2020. Comparative Efficacy of Selected Phytobiotics with Halquinol and Tetracycline on Gut Morphology, Ileal Digestibility, Cecal Microbiota Composition and Growth Performance in Broiler Chickens. *Animals* 10, 2150. doi: 10.3390/ani10112150.
- Basuini, M.F.E., Shaban, M.M.E.A., El-Hais, A.M., Soliman, A.A., Abu-Elala, N.M., Teiba, I.I., Alhoshy, M., Sallam, G.R., Shadrack, R.S., Mzengeza, K., Shehata, A.I., 2024. Exploring the Dual Benefits of Fermented and Non-Fermented Garlic Powder on Growth, Antioxidative Capacity, Immune Responses, and Histology in Gray Mullet (*Liza ramada*). *Fishes* 9, 401. doi: 10.3390/fishes9100401.
- Bergman, M.E., Davis, B., Phillips, M.A., 2019. Medically Useful Plant Terpenoids: Biosynthesis, Occurrence, and Mechanism of Action. *Molecules* 24, 3961. doi: 10.3390/molecules24213961.
- Besharati, M., Maggolino, A., Palangi, V., Kaya, A., Jabbar, M., Eseceli, H., De Palo, P., Lorenzo, J.M., 2022. Tannin in Ruminant Nutrition: Review. *Molecules* 27, 8273. doi: 10.3390/molecules2738273.
- Bibow, A., Oleszek, W., 2024. Essential Oils as Potential Natural Antioxidants, Antimicrobial, and Antifungal Agents in Active Food Packaging. *Antibiotics (Basel)* 13, 1168. doi: 10.3390/antibiotics13121168.
- Borgert, C.J., Fuentes, C., Burgoon, L.D., 2021. Principles of dose-setting in toxicology studies: the importance of kinetics for ensuring human safety. *Arch. Toxicol.* 95, 3651–3664. doi: 10.1007/s00204-021-03155-4.
- Câmara, J.S., Perestrelo, R., Ferreira, R., Berenguer, C.V., Pereira, J.A.M., Castilho, P.C., 2024. Plant-Derived Terpenoids: A Plethora of Bioactive Compounds with Several Health Functions and Industrial Applications—A Comprehensive Overview. *Molecules* 29, 3861. doi: 10.3390/molecules29163861.
- Castro-Montoya, J., Peiren, N., Cone, J.W., Zweifel, B., Fievez, V., De Campeneere, S., 2015. *In vivo* and *in vitro* effects of a blend of essential oils on rumen methane mitigation. *Livest. Sci.* 180, 134–142. doi: 10.1016/j.livsci.2015.08.010.
- Chan, S., Xiong, P., Zhao, M., Zhang, S., Zheng, R., Ye, J., Chan, K.I., Li, C., Zhong, Z., 2024. Anti-inflammatory effects of natural products from vitamin C-rich fruits. *Food Front.* 5, 2383–2422. doi: 10.1002/fft2.433.
- Chandrasekaran, P., Weiskirchen, S., Weiskirchen, R., 2024. Effects of Probiotics on Gut Microbiota: An Overview. *Int. J. Mol. Sci.* 25, 6022. doi: 10.3390/ijms25116022.
- Chodkowska, K.A., Iwiński, H., Wódz, K., Nowak, T., Różański, H., 2022. *In vitro* Assessment of Antimicrobial Activity of Phytobiotics Composition towards of Avian Pathogenic *Escherichia coli* (APEC) and Other *E. coli* Strains Isolated from Broiler Chickens. *Antibiotics (Basel)* 11, 1818. doi: 10.3390/antibiotics11121818.
- Cosme, F., Aires, A., Pinto, T., Oliveira, I., Vilela, A., Gonçalves, B., 2025. A Comprehensive Review of Bioactive Tannins in Foods and Beverages: Functional Properties, Health Benefits, and Sensory Qualities. *Molecules* 30, 800. doi: 10.3390/molecules30040800.
- Croaker, A., King, G.J., Pyne, J.H., Anoopkumar-Dukie, S., Liu, L., 2016. *Sanguinaria canadensis*: Traditional Medicine, Phytochemical Composition, Biological Activities and Current Uses. *Int. J. Mol. Sci.* 17, 1414. doi: 10.3390/ijms17091414.
- Dash, U.C., Bhol, N.K., Swain, S.K., Samal, R.R., Nayak, P.K., Raina, V., Panda, S.K., Kerry, R.G., Dutaray, A.K., Jena, A.B., 2025. Oxidative stress and inflammation in the pathogenesis of neuro-logical disorders: Mechanisms and implications. *Acta Pharm. Sin B* 15, 15–34. doi: 10.1016/j.apsb.2024.10.004.
- de Oliveira, I., Santos-Buelga, C., Aquino, Y., Barros, L., Heleno, S.A., 2025. New frontiers in the exploration of phenolic compounds and other bioactives as natural preservatives. *Food Biosci.* 68(1), 106571. doi: 10.1016/j.food.2025.106571.
- Deleu, S., Machiels, K., Raes, J., Verbeke, K., Vermeire, S., 2021. Short chain fatty acids and its producing organisms: An overlooked therapy for IBD? *EBioMedicine* 66, 103293. doi: 10.1016/j.ebiom.2021.103293.
- Denninger, T.M., Schwarm, A., Birkinshaw, A., Terranova, M., Dohme-Meier, F., Münger, A., Eggerschwiler, L., Bapst, B., Wegmann, S., Clauss, M., Kreuzer, M., 2020. Immediate effect of Acacia mearnsii tannins on methane emissions and milk fatty acid profiles of dairy cows. *Anim. Feed Sci. Technol.* 261, 114388. doi: 10.1016/j.anifeeds.2019.114388.
- Di Sotto, A., Vitalone, A., Di Giacomo, S., 2020. Plant-Derived Nutraceuticals and Immune System Modulation: An Evidence-Based Overview. *Vaccines (Basel)* 8, 468. doi: 10.3390/vaccines8030468.
- Di Vincenzo, F., Del Gaudio, A., Petito, V., Lopetuso, L.R., Scaldaferrì, F., 2024. Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. *Intern. Emerg. Med.* 19, 275–293. doi: 10.1007/s11739-023-03374-w.
- Ding, S., Yan, W., Ma, Y., Fang, J., 2021. The impact of probiotics on gut health via alternation of immune status of monogastric animals. *Anim. Nutr.* 7, 24–30. doi: 10.1016/j.aninu.2020.11.004.
- Domínguez-Valencia, R., Cittadini, A., Pateiro, M., Munekata, P.E.S., Lorenzo, J.M., 2023. Elderberry Lipophilic and Hydrophilic Bioactive Compounds: Characterization and Extract Encapsulation. *Foods* 12, 4233. doi: 10.3390/foods12234233.
- Donley, N., 2019. The USA lags behind other agricultural nations in banning harmful pesticides. *Environ. Health* 18, 44. doi: 10.1186/s12940-019-0488-0.
- Doski, J.M.M., Yaseen, K.K., 2023. The effects of different levels of postbiotic and phytobiotic combination as feed additives on carcass, lipid profile, meat quality, and tibia bone in broiler chickens. *Kirkuk Univ. J. Agric. Sci.* 14, 227–241. doi: 10.58928/ku23.14324.
- Duarte, M.E., Kim, S.W., 2022. Phytobiotics from Oregano Extracts Enhance the Intestinal Health and Growth Performance of Pigs. *Antioxidants* 11, 2066. doi: 10.3390/antiox11102066.
- Duque, G.A. and Descoteaux, A., 2014. Macrophage cytokines: involvement in immunity and infectious diseases. *Front. Immunol.* 5, 491. doi: 10.3389/fimmu.2014.00491.
- Ebani, V.V., Nardoni, S., Bertelloni, F., Tosi, G., Massi, P., Pistelli, L., Mancianti, F., 2019. *In vitro* Antimicrobial Activity of Essential Oils Against *Salmonella enterica* Serotypes Enteritidis and Typhimurium Strains Isolated from Poultry. *Molecules* 24, 900. doi: 10.3390/molecules24050900.
- El-Saadony, M.T., Saad, A.M., Mohammed, D.M., Korma, S.A., Alshahrani, M.Y., Ahmed, A.E., Ibrahim, E.H., Salem, H.M., Alkafas, S.S., Saif, A.M., Elkafas, S.S., Fahmy, M.A., Abd El-Mageed, T.A., Abady, M.M., Assal, H.Y., El-Tarabily, M.K., Mathew, B.T., AbuQamar, S.F., El-Tarabily, K.A., Ibrahim, S.A., 2025. Medicinal plants: bioactive compounds, biological activities, combating multidrug-resistant microorganisms, and human health benefits - a comprehensive review. *Front. Immunol.* 16, 1491777. doi: 10.3389/fimmu.2025.1491777.
- El-Saadony, M.T., Yang, T., Korma, S.A., Sityohy, M., Abd El-Mageed, T.A., Selim, S., Al Jaouni, S.K., Salem, H.M., Mahmood, Y., Soliman, M.M., Mo'men, S.A.A., Mosa, W.F.A., El-Wafai, N.A., Abou-Aly, H.E., Sityohy, B., Abd El-Hack, M.E., El-Tarabily, K.A., Saad, A.M., 2023. Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Front. Nutr.* 9, 1040259. doi: 10.3389/fnut.2022.1040259.
- Fanaei, A., Bohia, B., Lalremruati, F., Lalhriatpuii, N., Lalrokimi, Lalmanpuii, R., Singh, P.K., Zothanpui, 2024. Plant growth promoting bacteria (PGPB)-induced plant adaptations to stresses: an updated review. *PeerJ* 12, e17882. doi: 10.7717/peerj.17882.
- Ferraz, M.P., 2024. Antimicrobial Resistance: The Impact from and on Society According to One Health Approach. *Societies* 14, 187. doi: 10.3390/soc14090187.
- Firmino, J.P., Galindo-Villegas, J., Reyes-López, F.E., Gisbert, E., 2021. Phytogetic Bioactive Compounds Shape Fecal Mucosal Immunity. *Front. Immunol.* 12, 695973. doi: 10.3389/fimmu.2021.695973.
- Fleck, J.D., Betti, A.H., da Silva, F.P., Troian, E.A., Olivaro, C., Ferreira, F., Verza, S.G., 2019. Saponins from *Quillaja saponaria* and *Quillaja brasiliensis*: Particular Chemical Characteristics and Biological Activities. *Molecules* 24, 171. doi: 10.3390/molecules24010171.
- Fontana, L.B., Henn, G.S., Dos Santos, C.H., Specht, L., Schmitz, C., de Souza, C.F.V., Lehn, D.N., 2025. Encapsulation of Zootechnical Additives for Poultry and Swine Feeding: A Systematic Review. *ACS Omega* 10, 6294–6305. doi: 10.1021/acsomega.4c08080.
- Galamatis, D., Panitsidis, I., Mantzios, T., Sioutas, G., Stylianaki, I., Papadopoulos, E., Raj, J., Vasiljević, M., Bošnjak-Neumüller, J., Blake, D., Tsiouris, V., Giannenas, I., 2025. Assessment of a Natural Phytobiotic Mixture as Feed Additive for Broiler Chicken: Studies on Animal Performance, Gut Health, and Antioxidant Status After Experimental Infection with *Eimeria* spp. *Poultry* 4, 4. doi: 10.3390/poultry4010004.
- Geng, L., Liu, K., Zhang, H., 2023. Lipid oxidation in foods and its implications on proteins. *Front. Nutr.* 10(1), 1192199. doi: 10.3389/fnut.2023.1192199.
- Gharby, S., Oubannin, S., Bouzid, H.A., Bijla, L., Iboukri, M., Gagour, J., Koubachi, J., Sakar, E.H., Majourhat, K., Lee, L.H., Harhar, H., Bouyahya, A., 2022. An Overview on the Use of Extracts from Medicinal and Aromatic Plants to Improve Nutritional Value and Oxidative Stability of Vegetable Oils. *Foods* 11, 3258. doi: 10.3390/foods11103258.
- Gheisar, M.M., Kim, I.H., 2017. Phytobiotics in poultry and swine nutrition – a review. *Ital. J. Anim. Sci.* 17, 92–99. doi: 10.1080/1828051X.2017.1350120.
- Ghimpeanu, O.M., Pogurschi, E.N., Popa, D.C., Dragomir, N., Drăgoțoiu, T., Mihai, O.D., Petcu, C.D., 2022. Antibiotic Use in Livestock and Residues in Food-A Public Health Threat: A Review. *Foods* 11, 1430. doi: 10.3390/foods11101430.
- Gomes, S.M., Miranda, R., Santos, L., 2025. Enhancing the Biological Properties of White Chocolate: *Moringa oleifera* Leaf Extract as a Natural Functional Ingredient. *Foods* 14, 359. doi: 10.3390/foods14030359.
- Guía-García, J.L., Charles-Rodríguez, A.V., Reyes-Valdés, M.H., Ramírez-Godina, F., Robledo-Olivo, A., García-Osuna, H.T., Cerqueira, M.A., Flores-López, M.L., 2022. Micro and nanoencapsu-

- lation of bioactive compounds for agri-food applications: A review. *Ind. Crop. Prod.* 186, 115198. doi: 10.1016/j.indcrop.2022.115198.
- Gutiérrez-Del-Río, I., López-Ibáñez, S., Magadán-Corpas, P., Fernández-Calleja, L., Pérez-Valero, Á., Tuñón-Granda, M., Miguélez, E.M., Villar, C.J., Lombó, F., 2021. Terpenoids and Polyphenols as Natural Antioxidant Agents in Food Preservation. *Antioxidants (Basel)* 10, 1264. doi: 10.3390/antiox10081264.
- Gumowski, M., Ceccopieri, C., Madej, J.P., Leicht, K., Korzeniowska, M., Lipińska, A., Sierżant, K., Konkol, D., Różański, H., Asghar, M.U., Korczyński, M., 2025. The use of phytochemicals in the form of complexed organometallic phytoncides and micronized herbs in the nutrition of Ross 308 broiler chickens: Effects on growth performance, meat quality, and immune response. *Anim. Feed Sci. Technol.* 326, 116391. doi: 10.1016/j.anifeeds.2025.116391.
- Hamad, G.M., Gerges, M., Mehany, T., Hussein, S.M., Eskander, M., Tawfik, R.G., El-Halmouch, Y., Mansour, A.M., Hafez, E.E., Esatbeyoglu, T., Elghazaly, E.M., 2023. Estimating the Prevalence of Foodborne Pathogen *Campylobacter jejuni* in Chicken and Its Control via Sorghum Extracts. *Pathogens* 12, 958. doi: 10.3390/pathogens12070958.
- Hashemzadeh-Cigari, F., Khorvash, M., Ghorbani, G.R., Kadivar, M., Riasi, A., Zebeli, Q., 2014. Effects of supplementation with a phytochemical-rich herbal mixture on performance, udder health, and metabolic status of Holstein cows with various levels of milk somatic cell counts. *J. Dairy Sci.* 97, 7487–7497. doi: 10.3168/jds.2014-7989.
- Holanda, D.M., Kim, Y.J., Parnsen, W., Kim, S.W., 2021. Phytochemicals with Adsorbent to Mitigate Toxicity of Multiple Mycotoxins on Health and Growth of Pigs. *Toxins* 13, 442. doi: 10.3390/toxins13070442.
- Hristov, A.N., Bannink, A., Crompton, L.A., Huhtanen, P., Kreuzer, M., McGee, M., Nozière, P., Reynolds, C.K., Bayat, A.R., Yáñez-Ruiz, D.R., Dijkstra, J., Kebreab, E., Schwarm, A., Shingfield, K.J., Yu, Z., 2019. Inverted review: Nitrogen in ruminant nutrition: A review of measurement techniques. *J. Dairy Sci.* 102, 5811–5852. doi: 10.3168/jds.2018-15829.
- Huang, Q., Liu, X., Zhao, G., Hu, T., Wang, Y., 2018. Potential and challenges of tannins as an alternative to in-feed antibiotics for farm animal production. *Anim. Nutr.* 4, 137–150. doi: 10.1016/j.aninu.2017.09.
- Huang, R.H., Qiu, X.S., Shi, F.X., Hughes, C.L., Lu, Z.F., Zhu, W.Y., 2011. Effects of dietary allicin on health and growth performance of weanling piglets and reduction in attractiveness of faeces to flies. *Animal* 5, 304–311. doi: 10.1017/S1751731110001953.
- Hussein, E.O.S., Ahmed, S.H., Abudabos, A.M., Aljumaah, M.R., Alkhulaili, M.M., Nassan, M.A., Suliman, G.M., Naiel, M.A.E., Swelum, A.A., 2020. Effect of Antibiotic, Phytochemical and Probiotic Supplementation on Growth, Blood Indices and Intestine Health in Broiler Chicks Challenged with *Clostridium perfringens*. *Animals* 10, 507. doi: 10.3390/ani10030507.
- Ivanova, S., Sukhikh, S., Popov, A., Shishko, O., Nikonov, I., Kapitonova, E., Krol, O., Larina, V., Noskova, S., Babich, O., 2024. Medicinal plants: A source of phytochemicals for the feed additives. *J. Agric. Food Res.* 16, 101172. doi: 10.1016/j.jafr.2024.101172.
- Iwinski, H., Chodkowska, K.A., Drabik, K., Batkowska, J., Karwowska, M., Kurocka, P., Szumowski, A., Szumny, A., Różański, H., 2023. The Impact of a Phytochemical Mixture on Broiler Chicken Health and Meat Safety. *Animals* 13, 2155. doi: 10.3390/ani13132155.
- Iwinski, H., Wódcz, K., Chodkowska, K., Nowak, T., Różański, H., 2022. *In vitro* Evaluation of Antimicrobial Effect of Phytochemicals Mixture on *Salmonella* spp. Isolated from Chicken Broiler. *Antibiotics (Basel)* 11, 868. doi: 10.3390/antibiotics11070868.
- Ji, J., Jin, W., Liu, S.J., Jiao, Z., Li, X., 2023. Probiotics, prebiotics, and postbiotics in health and disease. *MedComm (2020)* 4, e420. doi: 10.1002/mco2.420.
- Juan, C.A., de la Lastra, J.M.P., Plou, F.J., Pérez-Lebeña, E., 2021. The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies. *Int. J. Mol. Sci.* 22, 4642. doi: 10.3390/ijms22094642.
- Kaur, K., Singh, S., Kaur, R., 2024. Impact of antibiotic usage in food-producing animals on food safety and possible antibiotic alternatives. *Microbe* 4, 100097. doi: 10.1016/j.microb.2024.100097.
- Kaushik, B., Sharma, J., Yadav, K., Kumar, P., Shourie, A., 2021. Phytochemical Properties and Pharmacological Role of Plants: Secondary Metabolites. *Biosci. Biotechnol. Res. Asia* 18, 23–35. doi: 10.13005/bbra/2894.
- Khan, A., Kanwal, F., Ullah, S., Fahad, M., Tariq, L., Altaf, M.T., Riaz, A., Zhang, G., 2025. Plant Secondary Metabolites-Central Regulators Against Abiotic and Biotic Stresses. *Metabolites* 15, 276. doi: 10.3390/metabo15040276.
- Khan, I.T., Bule, M., Ullah, R., Nadeem, M., Asif, S., Niaz, K., 2019. The antioxidant components of milk and their role in processing, ripening, and storage: Functional food. *Vet. World* 12, 12–33. doi: 10.14202/vetworld.2019.12-33.
- Kikusato, M., 2021. Phytochemicals to improve health and production of broiler chickens: functions beyond the antioxidant activity. *Anim. Biosci.* 34, 345–353. doi: 10.5713/ab.20.0842.
- Kour, J., Singh, S., Saxena, D.C., 2021. Retention of bioactive compounds during extrusion processing and storage. *Food Chem. X* 13, 100191. doi: 10.1016/j.fochx.2021.100191.
- Kowalska, J., Tyburski, J., Matysiak, K., Jakubowska, M., Łukaszek, J., Krzyńska, J., 2021. Cinnamon as a Useful Preventive Substance for the Care of Human and Plant Health. *Molecules* 26, 5299. doi: 10.3390/molecules26175299.
- Kumar, A., Nimal, P., Kumar, M., Jose, A., Tomer, V., Oz, E., Proestos, C., Zeng, M., Elobied, T., Sneha, K., Oz, F., 2023a. Major Phytochemicals: Recent Advances in Health Benefits and Extraction Method. *Molecules* 28, 887. doi: 10.3390/molecules28020887.
- Kumar, H., Dhalaria, R., Guleria, S., Cimler, R., Sharma, R., Siddiqui, S.A., Valko, M., Nepovimova, E., Dhanjal, D.S., Singh, R., Kumar, V., Pathera, A.K., Verma, N., Kaur, T., Manickam, S., Alover, S.Y., Kuča, K., 2023b. Anti-oxidant potential of plants and probiotic spp. in alleviating oxidative stress induced by H₂O₂. *Biomed. Pharmacother.* 165, 115022. doi: 10.1016/j.biopha.2023.115022.
- Lee, J.E., Jayakody, J.T.M., Kim, J.I., Jeong, J.W., Choi, K.M., Kim, T.S., Seo, C., Azimi, I., Hyun, J.M., Ryu, B.M., 2024. The Influence of Solvent Choice on the Extraction of Bioactive Compounds from Asteraceae: A Comparative Review. *Foods* 13, 3151. doi: 10.3390/foods13193151.
- Li, B., Zhang, C., Zhu, Y., Sun, P., Fan, S., Wang, W., Tian, Y., Lu, H., 2023. Development of Novel Formulation for Sustained Release of Drug to Prevent Swainsonine-Containing Plants Poisoning in Livestock. *Animals* 13, 2646. doi: 10.3390/ani13162646.
- Li, Y., Ye, Z., Zhu, J., Fang, S., Meng, L., Zhou, C., 2022. Effects of Gut Microbiota on Host Adaptive Immunity Under Immune Homeostasis and Tumor Pathology State. *Front. Immunol.* 13, 844335. doi: 10.3389/fimmu.2022.844335.
- Lian, X., Shi, M., Liang, Y., Lin, Q., Zhang, L., 2024. The Effects of Unconventional Feed Fermentation on Intestinal Oxidative Stress in Animals. *Antioxidants (Basel)* 13, 305. doi: 10.3390/antiox13030305.
- Lim, J.J., Grinstein, S., Roth, Z., 2017. Diversity and Versatility of Phagocytosis: Roles in Innate Immunity, Tissue Remodeling, and Homeostasis. *Front. Cell. Infect. Microbiol.* 7, 191. doi: 10.3389/fcimb.2017.00191.
- Liu, H.Y., Zhu, C., Zhu, M., Yuan, L., Li, S., Gu, F., Hu, P., Chen, S., Cai, D., 2024. Alternatives to antibiotics in pig production: looking through the lens of immunophysiology. *Stress Biol.* 4, 1. doi: 10.1007/s44154-023-00134-w.
- Liu, J., Wang, Y., Liu, L., Ma, G., Zhang, Y., Ren, J., 2023. Effect of Moringa leaf flavonoids on the production performance, immune system, and rumen fermentation of dairy cows. *Vet. Med. Sci.* 9, 917–923. doi: 10.1002/vms3.993.
- Liu, Q., Luo, Y., Ke, X., 2022. Interaction between the Gut Microbiota and Intestinal Motility. *Evid Based Complement Alternat. Med.* 2022, 3240573. doi: 10.1155/2022/3240573.
- Lobiuc, A., Pavál, N.E., Mangalagiu, I.I., Gheorghita, R., Teliban, G.C., Amăriucă-Mantu, D., Stoleru, V., 2023. Future Antimicrobials: Natural and Functionalized Phenolics. *Molecules* 28, 1114. doi: 10.3390/molecules28031114.
- Madesh, M., Yan, J., Jinan, G., Hu, P., Kim, I.H., Liu, H.Y., Ennab, W., Jha, R., Cai, D., 2025. Phytochemicals in swine nutrition and their effects on growth performance, nutrient utilization, gut health, and meat quality: a review. *Stress Biol.* 5, 11. doi: 10.1007/s44154-024-00209-2.
- Magklaras, G., Tzora, A., Bonos, E., Zacharis, C., Fotou, K., Wang, J., Grigoriadou, K., Giannenas, I., Jin, L., Skoufos, I., 2025. Nutritional Use of Greek Medicinal Plants as Diet Mixtures for Weaned Pigs and Their Effects on Production, Health and Meat Quality. *Appl. Sci.* 15, 9696. doi: 10.3390/app15179696.
- Maleš, I., Pedišić, S., Zorić, Z., Elez-Garofulić, I., Repajić, M., You, L., Vladimir-Knežević, S., Butorac, D., Dragović-Uzelac, V., 2022. The medicinal and aromatic plants as ingredients in functional beverage production. *J. Funct. Foods* 96, 105210. doi: 10.1016/j.jff.2022.105210.
- Malkawi, W.A., AlRafayah, E., AlHazabreh, M., AbuLaila, S., Al-Ghananeem, A.M., 2022. Formulation Challenges and Strategies to Develop Pediatric Dosage Forms. *Children (Basel)* 9, 488. doi: 10.3390/children9040488.
- Marefat, N., Ghorani, V., Shakeri, F., Boskabady, M., Kianian, F., Rezaee, R., Boskabady, M.H., 2021. A review of anti-inflammatory, antioxidant, and immunomodulatory effects of *Allium cepa* and its main constituents. *Pharm. Biol.* 59, 287–302. doi: 10.1080/13880209.2021.1874028.
- Martinez, J.E., Kahana, D.D., Ghuman, S., Wilson, H.P., Wilson, J., Kim, S.C.J., Lagishetty, V., Jacobs, J.P., Sinha-Hikim, A.P., Friedman, T.C., 2021. Unhealthy Lifestyle and Gut Dysbiosis: A Better Understanding of the Effects of Poor Diet and Nicotine on the Intestinal Microbiome. *Front. Endocrinol. (Lausanne)* 12, 667066. doi: 10.3389/fendo.2021.667066.
- Masyita, A., Sari, R.M., Astuti, A.D., Yasir, B., Rumata, N.R., Emran, T.B., Nainu, F., Simal-Gandara, J., 2022. Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. *Food Chem X* 13, 100217. doi: 10.1016/j.fochx.2022.100217.
- Matheou, A., Abousetta, A., Pascoe, A.P., Papakostopoulos, D., Charalambous, L., Panagi, S., Panagiotou, S., Yiallouris, A., Filippou, C., Johnson, E.O., 2025. Antibiotic Use in Livestock Farming: A Driver of Multidrug Resistance? *Microorganisms* 13, 779. doi: 10.3390/microorganisms13040779.
- McCann, J.C., Wickersham, T.A., Loo, J.J., 2014. High-throughput Methods Redefine the Rumen Microbiome and Its Relationship with Nutrition and Metabolism. *Bioinform. Biol. Insights* 8, 109–125. doi: 10.4137/BBI.S15389.
- Meeran, M.F.N., Javed, H., Al Tae, H., Azimullah, S., Ojha, S.K., 2017. Pharmacological Properties and Molecular Mechanisms of Thymol: Prospects for Its Therapeutic Potential and Pharmaceutical Development. *Front. Pharmacol.* 8, 380. doi: 10.3389/fphar.2017.00380.
- Mehta, N., Kumar, P., Verma, A.K., Umaraw, P., Kumar, Y., Malav, O.P., Sazili, A.Q., Domínguez, R., Lorenzo, J.M., 2022. Microencapsulation as a Noble Technique for the Application of Bioactive Compounds in the Food Industry: A Comprehensive Review. *Appl. Sci.* 12, 1424. doi: 10.3390/app12031424.
- Meyers, G.R., Samouda, H., Bohn, T., 2022. Short Chain Fatty Acid Metabolism in Relation to Gut Microbiota and Genetic Variability. *Nutrients* 14, 5361. doi: 10.3390/nu14245361.
- Migliorini, M.J., Boiago, M.M., Stefani, L.M., Zampar, A., Roza, L.F., Barreto, M., Arno, A., Robazza, W.S., Giurattini, J., Galvão, A.C., Boscatto, C., Paiano, D., Da Silva, A.S., de C Tavernari, F., 2019. Oregano essential oil in the diet of laying hens in winter reduces lipid peroxidation in yolks and increases shelf life in eggs. *J. Therm. Biol.* 85, 102409. doi: 10.1016/j.jtherbio.2019.102409.
- Millet, S., Maertens, L., 2011. The European ban on antibiotic growth promoters in animal feed: from challenges to opportunities. *Vet. J.* 187, 143–144. doi: 10.1016/j.tvjl.2010.05.001.
- Miškec, K., Frin, M., Šola, I., 2025. Impact of Different Thermal Processing Techniques on the Phytochemical Composition, Antioxidant Capacity, and DNA-Protective Properties of Broccoli. *Appl. Sci.* 15, 7469. doi: 10.3390/app15137469.
- Mitra, S., Paul, S., Roy, S., Sutradhar, H., Bin Emran, T., Nainu, F., Khandaker, M.U., Almalki, M., Wilairatana, P., Mubarak, M.S., 2022. Exploring the Immune-Boosting Functions of Vitamins and Minerals as Nutritional Food Bioactive Compounds: A Comprehensive Review. *Molecules* 27, 555. doi: 10.3390/molecules27020555.
- Miyakawa, M.E.F., Casanova, N.A., Kogut, M.H., 2024. How did antibiotic growth promoters increase growth and feed efficiency in poultry? *Poult. Sci.* 103, 103278. doi: 10.1016/j.psci.2023.103278.
- Mountouris, K.C., Broukogiannis, I., 2024. Phytochemicals as natural gut health management tools for sustainable poultry production. *Livest. Sci.* 286, 105525. doi: 10.1016/j.livsci.2024.105525.
- Movahedi, F., Nirmal, N., Wang, P., Jin, H., Grøndahl, L., Li, L., 2024. Recent advances in essential oils and their nanoformulations for poultry feed. *J. Anim. Sci. Biotechnol.* 15, 110. doi: 10.1186/s40104-024-01067-8.
- Mukumbo, F.E., Maphosa, V., Hugo, A., Nkukwana, T.T., Mabusela, T.P., Muchenje, V., 2014. Effect of *Moringa oleifera* leaf meal on finisher pig growth performance, meat quality, shelf life and fatty acid composition of pork. *S. Afr. J. Anim. Sci.* 44, 388–400. doi: 10.4314/sajas.v44i4.9.
- Murinov, S., Dercová, K., 2014. Response mechanisms of bacterial degraders to environmental contaminants on the level of cell walls and cytoplasmic membrane. *Int. J. Microbiol.* 2014, 873081. doi: 10.1155/2014/873081.
- Musa, B.B., Ismaila, A., Maman, L., Malami, R., Mohamed, M.A.E., Malami, R., 2023. Effect of Phytochemicals and Antibiotic on Growth Performance, Intestinal Morphology and Nutrients Transporters Expression of Broiler Chickens. *Afr. J. Agric. Food Sci.* 6, 78–91. doi: 10.52589/AJAFS-VMWQKUIP.
- Nastoh, N.A., Waqas, M., Çınar, A.A., Salman, M., 2024. The impact of phytochemical feed additives on ruminant production: A review. *J. Anim. Feed Sci.* 33, 431–453. doi: 10.22358/jafs/191479/2024.
- Nath, P.C., Ojha, A., Debnath, S., Sharma, M., Nayak, P.K., Sridhar, K., Inbaraj, B.S., 2023. Valorization of Food Waste as Animal Feed: A Step towards Sustainable Food Waste Management and Circular Bioeconomy. *Animals (Basel)* 13, 1366. doi: 10.3390/ani13081366.
- Nazzaro, F., Fratianni, F., De Martino, L., Coppola, R., De Feo, V., 2013. Effect of essential oils on pathogenic bacteria. *Pharmaceuticals (Basel)* 6, 1451–1474. doi: 10.3390/ph6121451.
- Neag, M.A., Mocan, A., Echeverría, J., Pop, R.M., Bocsan, C.I., Crişan, G., Buzoianu, A.D., 2018. Berberine: Botanical Occurrence, Traditional Uses, Extraction Methods, and Relevance in Cardiovascular, Metabolic, Hepatic, and Renal Disorders. *Front. Pharmacol.* 9, 557. doi: 10.3389/fphar.2018.00557.
- Ngo, V., Duennwald, M.L., 2022. Nrf2 and Oxidative Stress: A General Overview of Mechanisms and Implications in Human Disease. *Antioxidants (Basel)* 11, 2345. doi: 10.3390/antiox11122345.
- Nireeksha, Luke, A.M., Kumari, N.S., Hegde, M.N., Hegde, N.N., 2025. Metabolic interplay of SCFA's in the gut and oral microbiome: a link to health and disease. *Front. Oral Health* 6, 1646382. doi: 10.3389/froh.2025.1646382.
- Nurzyńska-Wierdak, R., Walasek-Janusz, M., 2025. Chemical Composition, Biological Activity, and Potential Uses of Oregano (*Origanum vulgare* L.) and Oregano Essential Oil. *Pharmaceuticals (Basel)* 18, 267. doi: 10.3390/ph18020267.
- Obianwuna, U.E., Chang, X., Oleforuh-Okohe, V.U., Onu, P.N., Zhang, H., Qiu, K., Wu, S., 2024. Phytochemicals in poultry: revolutionizing broiler chicken nutrition with plant-derived gut health enhancers. *J. Anim. Sci. Biotechnol.* 15, 169. doi: 10.1186/s40104-024-01101-9.
- Okuda, T., Ito, H., 2011. Tannins of Constant Structure in Medicinal and Food Plants—Hydrolyzable Tannins and Polyphenols Related to Tannins. *Molecules* 16, 2191–2177. doi: 10.3390/molecules16032191.
- Oni, A.I., Oke, O.E., 2025. Gut health modulation through phytochemicals in poultry: mechanisms, benefits, and applications. *Front. Vet. Sci.* 12, 1616734. doi: 10.3389/fvets.2025.1616734.
- Pandey, S., Kim, E.S., Cho, J.H., Song, M., Doo, H., Kim, S., Keum, G.B., Kwak, J., Ryu, S., Choi, Y., Kang, J., Choe, J., Kim, H.B., 2023. Cutting-edge knowledge on the roles of phytochemicals and their proposed modes of action in swine. *Front. Vet. Sci.* 10, 1265689. doi: 10.3389/fvets.2023.1265689.
- Pandur, E., Micalizzi, G., Mondello, L., Horváth, A., Sipos, K., Horváth, G., 2022. Antioxidant and Anti-Inflammatory Effects of Thyme (*Thymus vulgaris* L.) Essential Oils Prepared at Different Plant Phenophases on Pseudomonas aeruginosa LPS-Activated THP-1 Macrophages. *Antioxidants (Basel)* 11, 1330. doi: 10.3390/antiox11071330.
- Pap, N., Fidelis, M., Azevedo, L., do Carmo, M.A.V., Wang, D., Mocan, A., Pereira, E.P.R., Xavier-Santos, D., Sant'Ana, A.S., Yang, B., Granato, D., 2021. Berry polyphenols and human health: evidence of antioxidant, anti-inflammatory, microbiota modulation, and cell-protecting effects. *Curr. Opin. Food Sci.* 42, 167–186. doi: 10.1016/j.cofs.2021.06.003.

- Pateiro, M., Gómez, B., Munekata, P.E.S., Barba, F.J., Putnik, P., Kovačević, D.B., Lorenzo, J.M., 2021. Nanoencapsulation of Promising Bioactive Compounds to Improve Their Absorption, Stability, Functionality and the Appearance of the Final Food Products. *Molecules* 26, 1547. doi: 10.3390/molecules26061547.
- Peng, J., Li, H., Olaolu, O.A., Ibrahim, S., Ibrahim, S., Wang, S., 2023. Natural Products: A Dependable Source of Therapeutic Alternatives for Inflammatory Bowel Disease through Regulation of Tight Junctions. *Molecules* 28, 6293. doi: 10.3390/molecules28176293.
- Perera, W.N.U., Ravindran, V., 2025. Role of feed additives in poultry nutrition: Historical, current and future perspectives. *Anim. Feed Sci. Technol.* 326, 116371. doi: 10.1016/j.anifeedsci.2025.116371.
- Phaniendra, A., Jestadi, D.B., Periyasamy, L., 2015. Free radicals: properties, sources, targets, and their implication in various diseases. *Indian J. Clin. Biochem.* 30, 11–26. doi: 10.1007/s12291-014-0446-0.
- Pinski, B., Günel, M., AbuGhazaleh, A.A., 2015. The effects of essential oil and condensed tannin on fermentation and methane production under *in vitro* conditions. *Anim. Prod. Sci.* 56, 1707–1713. doi: 10.1071/AN15069.
- Plaskova, A., Mlekč, J., 2023. New insights of the application of water or ethanol-water plant extract rich in active compounds in food. *Front. Nutr.* 10, 1118761. doi: 10.3389/fnut.2023.1118761.
- Portincasa, P., Bonfrate, L., Vacca, M., De Angelis, M., Farella, I., Lanza, E., Khalil, M., Wang, D.Q., Sperandio, M., Di Ciaula, A., 2022. Gut Microbiota and Short Chain Fatty Acids: Implications in Glucose Homeostasis. *Int. J. Mol. Sci.* 23, 1105. doi: 10.3390/ijms23031105.
- Pudota, B.A., Tambireddy, N., Chennu, R., Chethurajupalli, L., Shaik, H., Nadella, R.K., Chatterjee, N.S., Paturi, A.P., 2025 Exploring the perspectives of phytobiotics and their role in aquaculture: Present status and future trends. *Microbe* 8, 100496. doi: 10.1016/j.microb.2025.100496.
- Rachwał, K., Gustaw, K., 2025. Plant-Derived Phytobiotics as Emerging Alternatives to Antibiotics Against Foodborne Pathogens. *Appl. Sci.* 15, 6774. doi: 10.3390/app15126774.
- Rafiq, K., Hossain, M.T., Ahmed, R., Hasan, M.M., Islam, R., Hossen, M.I., Shah, S.N., Islam, M.R., 2022. Role of Different Growth Enhancers as Alternative to In-feed Antibiotics in Poultry Industry. *Front. Vet. Sci.* 8, 794588. doi: 10.3389/fvets.2021.794588.
- Rafique, N., Jan, S.Y., Dar, A.H., Dash, K.K., Sarkar, A., Shams, R., Pandey, V.K., Khan, S.A., Amin, Q.A., Hussain, S.Z., 2023. Promising bioactivities of postbiotics: A comprehensive review. *J. Agric. Food Res.* 14, 100708. doi: 10.1016/j.jafr.2023.100708.
- Rahbardar, M.G., Hosseinzadeh, H., 2020. Therapeutic effects of rosemary (*Rosmarinus officinalis* L.) and its active constituents on nervous system disorders. *Iran J. Basic Med. Sci.* 23, 1100–1112. doi: 10.22038/ijbms.2020.45269.10541.
- Rehman, H.F., Zaneb, H., Masood, S., Yousef, M.S., Ashraf, S., Khan, I., Shah, M., Khilji, M.S., Rehman, H., 2018. Effect of *Moringa oleifera* Leaf Powder Supplementation on Pectoral Muscle Quality and Morphometric Characteristics of Tibia Bone in Broiler Chickens. *Braz. J. Poult. Sci.* 20, 817–823. doi: 10.1590/1806-9061-2017-0609.
- Ren, H., Vahjen, W., Dadi, T., Salu, E.M., Boroojeni, F.G., Zentek, J., 2019. Synergistic Effects of Probiotics and Phytobiotics on the Intestinal Microbiota in Young Broiler Chicken. *Microorganisms* 7, 684. doi: 10.3390/microorganisms7120684.
- Riaz, M., Khalid, R., Afzal, M., Anjum, F., Fatima, H., Zia, S., Rasool, G., Egbuna, C., Mtwewa, A.G., Uche, C.Z., Aslam, M.A., 2023. Phytobioactive compounds as therapeutic agents for human diseases: A review. *Food Sci. Nutr.* 11, 2500–2529. doi: 10.1002/fsn3.3308.
- Rizzello, V., Bonaccorsi, I., Dongarrà, M.L., Fink, L.N., Ferlazzo, G., 2011. Role of natural killer and dendritic cell crosstalk in immunomodulation by commensal bacteria probiotics. *J. Biomed. Biotechnol.* 2011, 473097. doi: 10.1155/2011/473097.
- Roy, A., Khan, A., Ahmad, I., Alghamdi, S., Rajab, B.S., Babalghith, A.O., Alshahrani, M.Y., Islam, S., Islam, M.R., 2022. Flavonoids a Bioactive Compound from Medicinal Plants and Its Therapeutic Applications. *Biomed. Res. Int.* 2022, 5445291. doi: 10.1155/2022/5445291.
- Roy, R., Tiwari, M., Donelli, G., Tiwari, V., 2018. Strategies for combating bacterial biofilms: A focus on anti-biofilm agents and their mechanisms of action. *Virulence*, 9, 522–554. doi: 10.1080/21505594.2017.1313372.
- Sahoo, D.K., Heilmann, R.M., Paital, B., Patel, A., Yadav, V.K., Wong, D., Jergens, A.E., 2023. Oxidative stress, hormones, and effects of natural antioxidants on intestinal inflammation in inflammatory bowel disease. *Front. Endocrinol. (Lausanne)* 14, 1217165. doi: 10.3389/fendo.2023.1217165.
- Salam, M.A., Al-Amin, M.Y., Salam, M.T., Pawar, J.S., Akhter, N., Rabaan, A.A. and Alqumber, M.A.A., 2023. Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare (Basel)* 11, 1946. doi: 10.3390/healthcare11131946.
- Saldaña-Olguin, M., Quispe-Ciudad, B.J., Aguirre, E., 2024. Antioxidant Activity of *Zingiber officinale* R. Extract Using Pressurized Liquid Extraction Method. *AgriEngineering* 6, 3875–3890. doi: 10.3390/agriengineering6040220.
- Salinas, E., Reyes-Pavón, D., Cortes-Perez, N.G., Torres-Maravilla, E., Bitzer-Quintero, O.K., Langella, P., Bermúdez-Humarán, L.G., 2021. Bioactive Compounds in Food as a Current Therapeutic Approach to Maintain a Healthy Intestinal Epithelium. *Microorganisms* 9, 1634. doi: 10.3390/microorganisms9081634.
- Sammad, A., Wang, Y.J., Umer, S., Lirong, H., Khan, I., Khan, A., Ahmad, B., Wang, Y., 2020. Nutritional Physiology and Biochemistry of Dairy Cattle under the Influence of Heat Stress: Consequences and Opportunities. *Animals (Basel)* 10, 793. doi: 10.3390/ani10050793.
- Samrot, A.V., Mohamed, A.A., Faradjeva, E., Jie, L.S., Sze, C.H., Arif, A., Sean, T.C., Michael, E.N., Mun, C.Y., Qi, N.X., Mok, P.L., Kumar, S.S., 2021. Mechanisms and Impact of Biofilms and Targeting of Biofilms Using Bioactive Compounds-A Review. *Medicina (Kaunas)* 57, 839. doi: 10.3390/medicina57080839.
- Sayed, M.A., Shahta, M.A., Kotob, M.H., Ali, N.M., Mahmoud, U.T., Mahmoud, M.A.M., Amen, O., 2023. Evaluate the effect of some phytobiotics on the control of necrotic enteritis in broilers chicken. *Assiut Vet. Med. J.* 69, 89–104. doi: 10.21608/avmj.2023.178952.1107.
- Selionova, M.I., Trukhachev, V.I., Zagarin, A.Y., Kulikov, E.I., Belyaeva, N.P., 2025. Effects of Dietary Supplementation Using Phytobiotics with Different Functional Properties on Expression of Immunity Genes, Intestinal Histology, Growth, and Meat Productivity of Broiler Chickens. *Vet. Sci.* 12, 302. doi: 10.3390/vetsci12040302.
- Shu, C., Ge, L., Li, Z., Chen, B., Liao, S., Lu, L., Wu, Q., Jiang, X., An, Y., Wang, Z., Qu, M., 2024. Antibacterial activity of cinnamon essential oil and its main component of cinnamaldehyde and the underlying mechanism. *Front. Pharmacol.* 15, 1378434. doi: 10.3389/fphar.2024.1378434.
- Singh, R.K., Dey, A., Paul, S.S., Singh, M., Punia, B.S., 2018. Responses of Lemongrass (*Cymbopogon citratus*) Essential Oils Supplementation on *in vitro* Ruminal Fermentation Parameters in Buffalo. *Indian J. Anim. Nutr.* 35, 174–179. doi: 10.5958/2231-6744.2018.00026.9.
- Sokol, M., Gulayev, I., Chirikina, M., Klimentko, M., Kamaeva, O., Yabbarov, N., Mollaveva, M., Nikolskaya, E., 2025. Fully Green Particles Loaded with Essential Oils as Phytobiotics: A Review on Preparation and Application in Animal Feed. *Antibiotics (Basel)* 14, 803. doi: 10.3390/antibiotics14080803.
- Stojanović, O., Altirriba, J., Rigo, D., Spiljar, M., Evrard, E., Roska, B., Fabbiano, S., Zamboni, N., Maechler, P., Rohner-Jeanrenaud, F., Trajkovski, M., 2021. Dietary excess regulates absorption and surface of gut epithelium through intestinal PPARα. *Nat. Commun.* 12, 7031. doi: 10.1038/s41467-021-27133-7.
- Sultana, B., Anwar, F., Ashraf, M., 2009. Effect of extraction solvent/technique on the antioxidant activity of selected medicinal plant extracts. *Molecules* 14, 2167–2180. doi: 10.3390/molecules14062167.
- Sun, J., Dong, S., Li, J., Zhao, H., 2022. A comprehensive review on the effects of green tea and its components on the immune function. *Food Sci. Hum. Well.* 11, 1143–1155. doi: 10.1016/j.fshw.2022.04.008.
- Sun, Q., Yin, S., He, Y., Cao, Y., Jiang, C., 2023. Biomaterials and Encapsulation Techniques for Probiotics: Current Status and Future Prospects in Biomedical Applications. *Nanomaterials (Basel)* 13, 2185. doi: 10.3390/nano13152185.
- Sung, J.Y., Deng, Z., Kim, S.W., 2025. Antibiotics and Opportunities of Their Alternatives in Pig Production: Mechanisms Through Modulating Intestinal Microbiota on Intestinal Health and Growth. *Antibiotics (Basel)* 14, 301. doi: 10.3390/antibiotics14030301.
- Suraweera, T.L., Rupasinghe, H.P.V., Deltaira, G., Xu, Z., 2020. Regulation of Nrf2/ARE Pathway by Dietary Flavonoids: A Friend or Foe for Cancer Management? *Antioxidants (Basel)* 9, 973. doi: 10.3390/antiox9100973.
- Tedeschi, L.O., Muir, J.P., Naumann, H.D., Norris, A.B., Ramirez-Restrepo, C.A., Mertens-Talcott, S.U., 2021. Nutritional Aspects of Ecologically Relevant Phytochemicals in Ruminant Production. *Front. Vet. Sci.* 8, 628445. doi: 10.3389/fvets.2021.628445.
- Timilsena, Y.P., Phosanam, A., Stockmann, R., 2023. Perspectives on Saponins: Food Functionality and Applications. *Int. J. Mol. Sci.* 24, 13538. doi: 10.3390/ijms241713538.
- Tu, P., Chi, L., Bodnar, W., Zhang, Z., Gao, B., Bian, X., Stewart, J., Fry, R., Lu, K., 2020. Gut Microbiome Toxicity: Connecting the Environment and Gut Microbiome-Associated Diseases. *Toxics* 8, 19. doi: 10.3390/toxics8010019.
- Turner, J.L., Drits, S.S., Higgins, J.J., Herkelman, K.L., Minton, J.E., 2002. Effects of a *Quillaja saponaria* extract on growth performance and immune function of weanling pigs challenged with *Salmonella typhimurium*. *J. Anim. Sci.* 80, 1939–1946. doi: 10.2527/2002.8071939x.
- Ugbogu, E.A., Elghandour, M.M.M.Y., Ikpeazu, V.O., Buendia, G.R., Molina, O.M., Arunsi, O.O., Emmanuel, O., Salem, A.Z.M., 2019. The potential impacts of dietary plant natural products on the sustainable mitigation of methane emission from livestock farming. *J. Clean. Prod.* 213, 915–925. doi: 10.1016/j.jclepro.2018.12.233.
- Ullah, A., Munir, S., Badshah, S.L., Khan, N., Ghani, L., Poulson, B.G., Emwas, A.H., Jaremko, M., 2020. Important Flavonoids and Their Role as a Therapeutic Agent. *Molecules* 25, 5243. doi: 10.3390/molecules25225243.
- Uruén, C., Chopo-Escuin, G., Tommassen, J., Mainar-Jaime, R.C., Arenas, J., 2020. Biofilms as Promoters of Bacterial Antibiotic Resistance and Tolerance. *Antibiotics (Basel)* 10, 3. doi: 10.3390/antibiotics10010003.
- Usman, M., Nakagawa, M., Cheng, S., 2023. Emerging Trends in Green Extraction Techniques for Bioactive Natural Products. *Processes* 11, 3444. doi: 10.3390/pr11123444.
- Vancamelbeke, M., Vermeire, S., 2017. The intestinal barrier: a fundamental role in health and disease. *Expert. Rev. Gastroenterol. Hepatol.* 11, 821–834. doi: 10.1080/17474124.2017.1343143.
- Vasile, C., Baican, M., 2021. Progresses in Food Packaging, Food Quality, and Safety-Controlled-Release Antioxidant and/or Antimicrobial Packaging. *Molecules* 26, 1263. doi: 10.3390/molecules26051263.
- Vázquez-Carrillo, M.F., Zaragoza-Guerrero, R., Corona-Gochi, L., González-Ronquillo, M., Castillo-Gallegos, E., Castelán-Ortega, O.A., 2023. Effect of *Cymbopogon citratus* on Enteric Methane Emission, Nutrients Digestibility, and Energy Partition in Growing Beef Cattle. *Agriculture* 13, 745. doi: 10.3390/agriculture13040745.
- Visuvanathan, T., Than, L.T.L., Stanslas, J., Chew, S.Y., Vellasamy, S., 2022. Revisiting *Trigonella foenum-graecum* L.: Pharmacology and Therapeutic Potentialities. *Plants* 11, 1450. doi: 10.3390/plants11111450.
- Wang, H., Chen, Y., Wang, L., Liu, Q., Yang, S., Wang, C., 2023. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. *Front. Pharmacol.* 14, 1265178. doi: 10.3389/fphar.2023.1265178.
- Wang, J., Deng, L., Chen, M., Che, Y., Li, L., Zhu, L., Chen, G., Feng, T., 2024. Phytogenic feed additives as natural antibiotic alternatives in animal health and production: A review of the literature of the last decade. *Anim. Nutr.* 17, 244–264. doi: 10.1016/j.aninu.2024.01.012.
- Windisch, W., Schedle, K., Plitzner, C., Kroismayr, A., 2008. Use of phytogenic products as feed additives for swine and poultry. *J. Anim. Sci.* 86, e140–8. doi: 10.2527/jas.2007-0459.
- Wlazlak, S., Pietrzak, E., Biesek, J., Dunislawski, A., 2023. Modulation of the immune system of chickens a key factor in maintaining poultry production-a review. *Poult. Sci.* 102, 102785. doi: 10.1016/j.psj.2023.102785.
- World Health Organization, 2014. Antimicrobial resistance: global report on surveillance.
- Wylie, M.R., Merrell, D.S., 2022. The Antimicrobial Potential of the Neem Tree *Azadirachta indica*. *Front. Pharmacol.* 13, 891535. doi: 10.3389/fphar.2022.891535.
- Xie, L., Fang, J., Yu, J., Zhang, W., He, Z., Ye, L., Wang, H., 2023. The role of CD4+ T cells in tumor and chronic viral immune responses. *MedComm (2020)* 4, e390. doi: 10.1002/mco2.390.
- Yammine, J., Chihib, N.E., Gharsallaoui, A., Dumas, E., Ismail, A., Karam, L., 2022. Essential oils and their active components applied as free, encapsulated and in hurdle technology to fight microbial contaminations. A review. *Heliyon* 8, e12472. doi: 10.1016/j.heliyon.2022.e12472.
- Yan, Y., Li, X., Zhang, C., Lv, L., Gao, B., Li, M., 2021. Research Progress on Antibacterial Activities and Mechanisms of Natural Alkaloids: A Review. *Antibiotics (Basel)* 10, 318. doi: 10.3390/antibiotics10030318.
- Yang, Y., Kummungsee, T., Okazaki, Y., Watanabe, T., Inoue, J., Iguchi, T., Fukuda, S., Kuroda, M., Nishio, K., Yamaguchi, S., Kato, N., 2025. Potential Roles of Exogenous Proteases and Lipases as Prebiotics. *Nutrients* 17, 924. doi: 10.3390/nut17050924.
- Yao, K.-C., Hsieh, H.-H., Li, K.-Y., Xu, J.-R., Ho, W.-S., Huang, W.-L., Huang, S.-H., Liao, Y.-H., Tseng, Y.-J., 2024. Sustainable Packaging Solutions: Food Engineering and Biodegradable Materials. *Designs* 8, 133. doi: 10.3390/designs8060133.
- Yasin, A., Tamiru, M., Alkhatib, A., Mohammed, A., Tadesse, T., Wamatu, J., Burton, E., 2025. Impact of Dried Thyme Leaf Meal on Production Performance, Egg Quality and Blood Parameters of Laying Hens. *Vet. Med. Sci.* 11, e70146. doi: 10.1002/vms3.70146.
- Yu, K., Choi, I., Yun, C.H., 2021. Immunosecurity: immunomodulators enhance immune responses in chickens. *Anim. Biosci.* 34, 321–337. doi: 10.5713/ab.20.0851.
- Zaikina, A.S., Buryakov, N.P., Buryakova, M.A., Zagarin, A.Y., Razhev, A.A., Aleshin, D.E., 2022. Impact of Supplementing Phytobiotics as a Substitute for Antibiotics in Broiler Chicken Feed on Growth Performance, Nutrient Digestibility, and Biochemical Parameters. *Vet. Sci.* 9, 672. doi: 10.3390/vetsci9120672.
- Zhang, L.Y., Peng, Q.Y., Liu, Y.R., Ma, Q.G., Zhang, J.Y., Guo, Y.P., Xue, Z., Zhao, L.H., 2021. Effects of oregano essential oil as an antibiotic growth promoter alternative on growth performance, antioxidant status, and intestinal health of broilers. *Poult. Sci.* 100, 101163. doi: 10.1016/j.psj.2021.101163.
- Zhang, M., Zhao, J., Dai, X., Li, X., 2023. Extraction and Analysis of Chemical Compositions of Natural Products and Plants. *Separations* 10, 598. doi: 10.3390/separations10120598.
- Zhang, X., Yin, Z., Xiang, S., Yan, H., Tian, H., 2024. Degradation of Polymer Materials in the Environment and Its Impact on the Health of Experimental Animals: A Review. *Polymers (Basel)* 16, 2807. doi: 10.3390/polym16192807.
- Zhao, M., Chu, J., Feng, S., Guo, C., Xue, B., He, K., Li, L., 2023. Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: A review. *Biomed. Pharmacother.* 164, 114985. doi: 10.1016/j.biopha.2023.114985.
- Zheng, Z., Tang, J., Hu, Y., Zhang, W., 2022. Role of gut microbiota-derived signals in the regulation of gastrointestinal motility. *Front. Med. (Lausanne)* 9, 961703. doi: 10.3389/fmed.2022.961703.
- Zimmermann, C., Wagner, A.E., 2021. Impact of Food-Derived Bioactive Compounds on Intestinal Immunity. *Biomolecules* 11, 1901. doi: 10.3390/biom11121901.
- Zong, Y., Li, H., Liao, P., Chen, L., Pan, Y., Zheng, Y., Zhang, C., Liu, D., Zheng, M., Gao, J., 2024. Mitochondrial dysfunction: mechanisms and advances in therapy. *Signal Transduct. Target. Ther.* 9, 124. doi: 10.1038/s41392-024-01839-8.