



LITERATURE REVIEW: OPPORTUNITIES WITH PHYTOBIOTICS FOR HEALTH AND GROWTH OF PIGS

Yesid Garavito-Duarte, Zixiao Deng, Sung Woo Kim*

Department of Animal Science, North Carolina State University, Raleigh, NC 27695, USA

*Corresponding author: sungwoo_kim@ncsu.edu

Abstract

Phytobiotics are plant-derived substances rich in bioactive compounds such as phenolics, organosulfur compounds, terpenes, and aldehydes. Phytobiotics can be classified based on their origin or chemical structure, with the main categories being essential oils, oleoresins, and herbs and spices. Phytobiotics have gained interest due to their positive effects on animal health, including anti-inflammatory, antioxidant, and antimicrobial properties resulting in improved growth performance. This review explores the mode of action of phytobiotics based on their bioactive compounds and highlights their impacts on intestinal health and growth performance in pigs. The inclusion of phytobiotics in pig diets has shown promise in mitigating negative impacts caused by environmental and dietary challenges by reducing inflammatory and oxidative stress responses, enhancing intestinal barrier function, and exhibiting antimicrobial properties against pathogens like *Escherichia coli*. Collectively, phytobiotics showed a diverse biological activity through different mode of actions, resulting in improved growth performance and overall health in pigs, making phytobiotics a valuable feed additive in pig nutrition and production.

Key words: phytobiotics, mode of action, bioactive compounds, pig health

Concerns about microbial resistance in human pathogens due to the continuous use of antibiotics as performance enhancers in animals have led to restrictions on antimicrobial growth promoters, which have been extensively used in animal agriculture over the past 50 years. This restriction has led to more infections by pathogens, creating a need for alternatives solutions. In this context, phytobiotics are gaining interest as viable alternatives to antibiotics as growth promoters (Park et al., 2016 a; Mohammadi Gheisar and Kim, 2018; Ferdous et al., 2019).

Phytobiotics, also known as phytochemicals, or botanicals, are plant-derived specific biologically active compounds. These bioactive compounds in phytobiotics include phenolics, organosulfur compounds, terpenes, and aldehydes (Pandey et al., 2023). The content and properties of these compounds vary depending on different factors, including the part of the plant used (seeds, leaf, root, etc.), harvesting season, geographical origin, and the processing method (cold pressing, steam distillation, extraction with solvents, etc.) (Windisch et al., 2008). Research has shown that various phytobiotics have positive effects on animal health, including anti-inflammatory, antioxidant, and anti-bacterial properties (Rossi et al., 2020). Phytobiotics also improved growth performance (Hanczakowska and Swiatkiewicz, 2012; Ferdous et al., 2019; Pandey et al., 2023), enhanced meat quality (Buryakov et al., 2023 b; Juhász et al., 2023), and improved milk composition (Buryakov et al., 2023 a). Phytobiotics leave minimal residues, with no resistance

concerns and minimal side effects (Yitbarek, 2015; Alghirani et al., 2021; Iwiński et al., 2023).

Incorporating phytobiotics into pig production could enhance pork quality by promoting pig health. Their anti-inflammatory, antimicrobial, and antioxidant properties help to combat environmental stressors, toxin exposure, and enteric infections, which negatively influence both animal welfare and meat quality (Martínez-Miró et al., 2016). Understanding the properties of phytobiotics is crucial for addressing these challenges (Sun and Kim, 2017; Rossi et al., 2020). This review explores the classification, and bioactive compounds of phytobiotics, based on existing literature, and explores their potential benefits as feed additives to enhance pig health and growth.

Classification of phytobiotics

Although there is not a definitive classification for phytobiotics, Windisch et al. (2008) suggest that phytobiotics can be classified based on their origin and transformation, such as essential oils, oleoresins, herbs, and spices.

Essential oils are complex mixtures of secondary plant metabolites. They include aliphatic hydrocarbons (e.g., thymol, carvacrol, eugenol, and gaiacol), aromatic aldehydes (e.g., cinnamaldehyde, cuminal, and phellandral), and terpenes (e.g., linalool, geraniol, thujanol, borneol, menthol, citronnillol, and α -terpineol) (Bakkali et al., 2008; Brenes and Roura, 2010; Christaki et al., 2012). Oleoresins are natural mixtures of oils and resins extract-

ed from various plants. They contain a wide range of essential oil concentrations and consist mainly of complex blends of monoterpenes, sesquiterpenes and diterpenes (Dussault et al., 2014; Celedon and Bohlmann, 2019). Unlike essential oils, oleoresins contain natural antioxidants from the corresponding spices, making them more stable (Shaikh et al., 2006). Spices and herbs, known for their intense smell or taste, are derived from flowering, nonwoody, and nonpersistent plants. The beneficial properties of spices and herbs are largely attributed to secondary metabolites such as cinnamaldehyde, piperine, and curcumin (Korošec et al., 2009; Tajodini et al., 2015). The compounds in phytobiotics can act as palatable and digestive stimulants, positively influencing physiological functions that support health, welfare, and growth performance (Lin et al., 2020; Wang et al., 2022).

Phytobiotics can also be classified based on their chemical structure, composition, solubility in organic solvents or water, and biosynthetic pathways. One classification method separates phytobiotics into key groups based on their biosynthetic pathway: phenolic compounds, terpenes, and aldehydes (Singh, 2017; González Mera et al., 2019). Phenolic compounds constitute the largest class of phytobiotics, characterized by aromatic rings that can react with peroxy radicals (Rossi et al., 2020). These compounds are commonly found in essential oils derived from plants such as basil (*Ocimum basilicum*), clove (*Syzygium aromaticum*), sage (*Salvia officinalis*), thyme (*Thymus vulgaris*) (Li et al., 2023; Vlaicu et al., 2023). Terpenes are aromatic compounds with unsaponifiable lipids with volatile properties (Houketchang and Kuietche, 2023). Common plant sources of terpenes include Japanese cinnamon (*Cinnamomum tenuifolium*), mint (*Mentha* sp.), Tasmanian bluegum (*Eucalyptus globulus*) (Karpiński, 2020; Guerrero et al., 2022; Reuben et al., 2022). Aldehydes are formyl compounds containing a carbonyl functional group and are known for their anti-inflammatory and antioxidant properties. Among the most common aldehydes are vanillin and cinnamaldehyde which are derived from plants such as cinnamon (*Cinnamomum*) and vanilla (*Vanilla planifolia*) (Rossi et al., 2020; Khamtawee et al., 2021; Yeh et al., 2021).

Phytobiotics and their biological activities

Among all the bioactive compounds in phytobiotics, phenolics, aldehydes, and terpenes are fundamental compounds. These compounds are known for their antioxidant, inflammatory, and antibacterial properties (Pannee et al., 2014; Álvarez-Martínez et al., 2021; Kamelan Kafi et al., 2022). The beneficial effects of these bioactive compounds in phytobiotics are further illustrated in Figure 1.

Phytobiotics are known for their antioxidant properties. These properties could protect feed lipids from oxidative damage, such as antioxidants used commonly in diets (e.g., alpha tocopherol) (Windisch et al., 2008). Certain bioactive compounds, such as phenolics and flavonoids, possess structures that allow electron delocalization. This enables them to interact with free radicals

and prevent the propagation of free radical chain reactions (Tsao and Deng, 2004). By neutralizing these radicals, these compounds help to prevent oxidative stress. Phytobiotic compounds such as quercetin, sulforaphane, and resveratrol can help to neutralize reactive oxygen species (ROS) by indirectly stimulating antioxidant enzymes like catalase, and superoxide dismutase, which reduce ROS production (Martel et al., 2020).

Phytobiotics could exert anti-inflammatory effects by inhibiting the nuclear factor kappa-light-chain-enhancer of activated β cells (NF- κ B) pathway (Figure 2), a fundamental regulator of inflammatory and immune responses (Surh, 2008; Liu et al., 2012). According to Liu et al. (2012), phytobiotics such as carvacrol, cinnamaldehyde, eugenol, and garlic could inhibit proinflammatory cytokine tumor necrosis factor- α (TNF- α) production, a proinflammatory cytokine induced by lipopolysaccharide (LPS) in porcine alveolar macrophages, whereas also reducing interleukin 1 β (IL-1 β) secretion. Similarly, terpenes exhibit anti-inflammatory properties by inhibiting lipoxygenase and cyclooxygenase enzymes, which play a role in the arachidonic acid pathway. This pathway involves the metabolism of arachidonic acid, released from cell membrane phospholipids in response to inflammation, leading to inflammatory mediators such as prostaglandins and leukotrienes production (Miguel, 2010). Thus, terpenoids potentially reduce the production of these inflammatory mediators (Frankič et al., 2009; Al-Yasiry and Kiczorowska, 2016). Bioactive compounds in phytobiotics, such as chlorogenic acid, flavonoids, and astragalus polysaccharides, can inhibit inflammation by influencing intracellular signaling and reducing pro-inflammatory cytokines production. These anti-inflammatory effects involve inhibiting toll-like receptor 4 (TLR4), a transmembrane receptor that detects pathogens and triggers inflammation after interaction with LPS in the cell membrane of enterocytes (Poltorak et al., 1998; Bhatia et al., 2022). Additionally, TLR4 affects nucleotide-binding oligomerization domain (NODs) proteins (Dong et al., 2019; Kikusato, 2021; Shen et al., 2024), which recognize bacterial components and activate inflammatory responses (Almeida-da-Silva et al., 2023).

The inclusion of cinnamaldehyde has been shown to enhance phagocytic activity and improve the cellular immune response (Yang et al., 2019; Krauze et al., 2021). The enhancement of immune response occurs by stimulation of complement receptor-mediated phagocytosis and increasing TNF- α and interferon- γ production (Al-Yasiry et al., 2018; El-Sheikh et al., 2019). The inclusion of cinnamaldehyde stimulates interactions between lymphocytes and macrophages, thereby initiating and regulating the immune response (Brabb et al., 2012; Li et al., 2020; Morsi et al., 2022). Krauze et al. (2021) observed that cinnamon oil exerts immunomodulatory properties by stimulating nonspecific immunity, particularly through macrophages activation (Abd El-Hack et al., 2022). This activation enhances the phagocytic and bactericidal functions of macrophages.

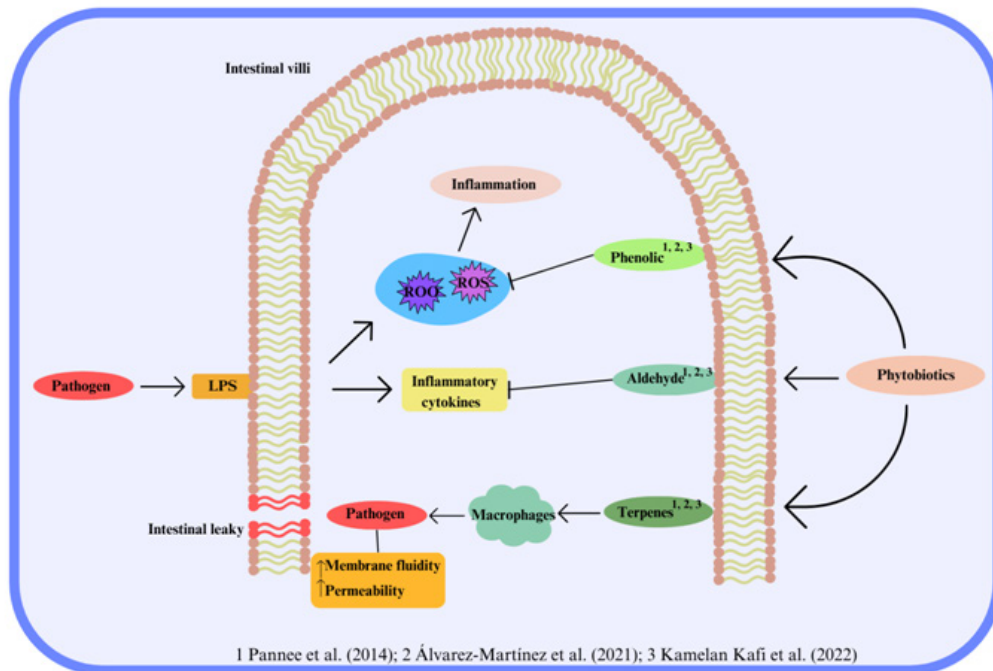


Figure 1. Mechanism of action of common compounds of phytobiotics. Phenolic compounds react with peroxy (ROO) and lipid peroxy (ROS) radicals; aldehyde compounds inhibit pro-inflammatory mediators; terpenes increase the membrane fluidity and increase permeability on bacterial cell wall in pathogens such as *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus*

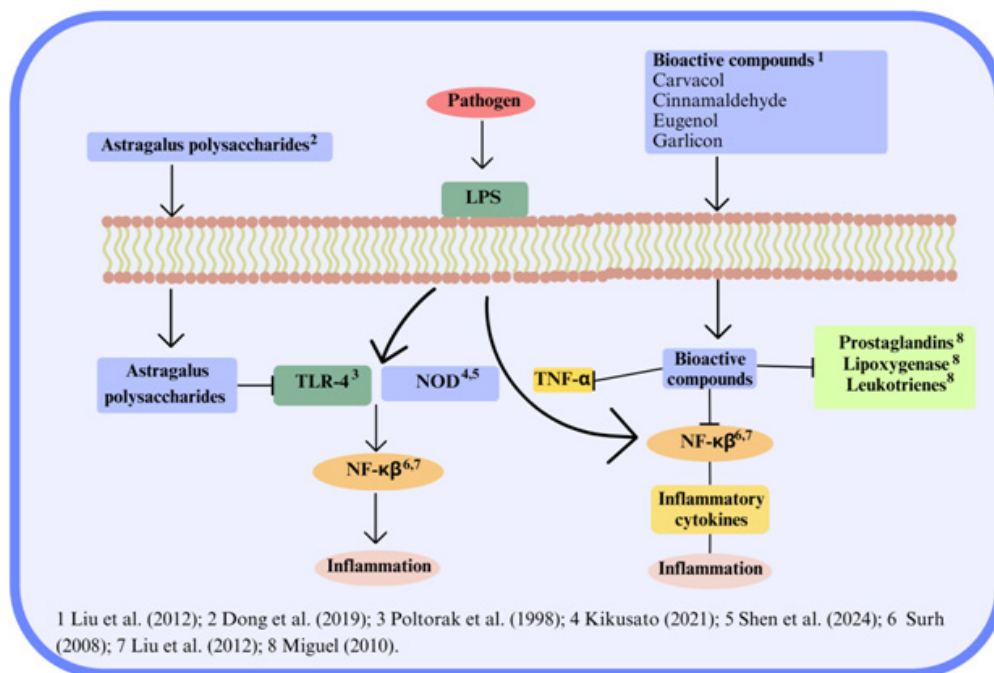


Figure 2. Anti-inflammatory mechanism of phytobiotics. Phytobiotics inhibit the binding of pathogens cell walls LPS to TLR4 and TNF- α , altering the NF- κ B signaling, blocking the inflammation process, reducing the secretion of inflammatory cytokines

Phytobiotics such as carvacrol, geraniol, terpineol, eugenol, and citronella exhibit antimicrobial properties. These bioactive compounds reduce the negative charge of the cell surface of *Escherichia coli* (*E. coli*) and *Staphylococcus aureus*, inducing bacterial cellular damage (Lopez-Romero et al., 2015). Phytobiotics

with nonpolar compounds, like α -amyrin, lupeol, and β -sitosterol, can induce ROS production, disrupting both the outer and inner cytoplasmic membrane structures (Han and Lee, 2022). The oxidative stress from ROS results in membrane depolarization, leading to various disruptions: membrane separation from the cell

wall, cell membrane lysis, leakage and polarization of cytoplasmic content, and cell distortion. These disruptions compromise membrane integrity and exert antimicrobial properties of phytobiotics (Famuyide et al., 2020; Han and Lee, 2022; Abo-Elghiet et al., 2023). Dong et al. (2019) observed that astragalus polysaccharides inhibit the binding of *Salmonella typhimurium* LPS to TLR4. Normally, TLR4 detects LPS and triggers a signaling cascade (Poltorak et al., 1998) that degrades the inhibitor of nuclear factor kappa β protein (I κ β), allowing NF- κ β to enter the nucleus and activate genes encoding pro-inflammatory cytokines (Diomedea et al., 2017). By blocking this pathway, astragalus polysaccharides reduce the production of these inflammatory mediators (Dong et al., 2019). Overall, phytobiotics offer a multiple approach to enhancing animal health through their diverse biological activities, including antioxidant, anti-inflammatory, and antimicrobial effects leading to an enhanced performance.

Impact on intestinal health and growth performance in pigs

With the ban on antimicrobial growth promoters in pork production due to concerns over antibiotic resistance and public health (Monger et al., 2021), there is an increasing need for alternatives like natural feed additives such as phytobiotics (Kommera et al., 2006). Selected studies have demonstrated the positive effects of various phytobiotics on pig health and growth performance. Summarized in Table 1, studies from 2015 show that the inclusion of phytobiotics in pig diets resulted in an average increase of 21% in ADG, 4% in ADFI, and 17% in feed efficiency (Figure 3 A–C).

Pigs experience significant stress during the weaning period, one of the most critical phases of production (Lallès et al., 2004; Shen et al., 2012; Zheng et al., 2021). Weaning stress often leads to intestinal and immune dysfunctions, which could result in post weaning diarrhea (PWD), dehydration, increased mortality, and reduced growth performance (Kick et al., 2012; Campbell et al., 2013; Duarte et al., 2023). The PWD is primarily linked to intestinal dysbiosis as pigs rapidly adapt to new environments and diets, and it is commonly associated with enterotoxigenic *E. coli* infection in weaned pigs (Castillo et al., 2007; Duarte et al., 2023; Jang et al., 2023). To mitigate these negative effects, dietary interventions during the weaning period are essential. Phytobiotics, for example, have shown potential to improve pig health during nursery period by enhancing immune responses, balancing intestinal microbiota, and enhancing intestinal morphology, which collectively support better growth performance (Fresno Rueda et al., 2021; Moita et al., 2021; Duarte and Kim, 2022). Pigs also face several stressors during different production phases, such as transport and heat stress, which could negatively impact health and growth performance (Jócsák et al., 2020). Mycotoxins, commonly found in cereals grains and feedstuffs, can also compromise the

immune response, elevate oxidative stress, and increase the production of inflammatory markers (Holanda et al., 2021). In response to these challenges, phytobiotics have been used for their potential benefits. For instance, the inclusion of 0.25% oregano essential oil in finishing diets for growing pigs under transportation stress reduced the cortisol levels, a key stress marker, by 38% (Zhang et al., 2015). Similarly, under heat stress conditions, the inclusion of 10% of betaine reduced the respiration rate by 18% and reduced colonic permeability by 33%. Additionally, 1.5% isoquinoline alkaloid from *Macleaya cordata* decreased colonic permeability by 52% in growing pigs (Le et al., 2020).

Research has demonstrated that inclusion of phytobiotics can enhance the integrity of intestinal epithelium, supporting the barrier that controls nutrient and water absorption whereas also limiting the entry of pathogens (Williams et al., 2015). The integrity of the intestinal epithelium is maintained by tight junctions and adherens junctions, regulated by transmembrane proteins like occludin and claudins, facilitated by the zonula occludens (ZO) protein family (Hartsock and Nelson, 2008; Rahimi, 2017). For example, Zhao et al. (2023) demonstrated that the inclusion of a blend of essential oils (5% cinnamaldehyde, 5% carvacrol and 0.8% thymol) to the diet of pigs weaned at 28 days improved intestinal barrier function. The blend doubled the mRNA expression of genes related with intestinal epithelial integrity, such as zonula occludens-1 (ZO-1), claudin-1, and claudin-5, in both the duodenum and ileum of weaned pigs. Similarly, Duarte and Kim (2022) observed that including 0.05% of thymol and carvacrol extracted from oregano increased the expression of occludin in jejunal tissue by 15%. Pigs challenged with F18⁺ *E. coli* and fed a diet containing 0.01% of microencapsulated blend of thymol and carvacrol improved claudin-1 expression in the ileal mucosa by 63% (Chang et al., 2022). Additionally, feeding weaned pigs challenged with F18⁺ *E. coli* a diet containing 0.04% of a phytobiotic premixture with over 10% flavonoids doubled claudin-1 expression in the ileal mucosa (Chang et al., 2022). Studies have shown that phytobiotics promote cellular growth (Patra et al., 2019), and improve intestinal morphology in pig models (Moita et al., 2021; Duarte and Kim, 2022; Moniruzzaman et al., 2023). The inclusion of essential oils from a blend of castor oil and cashew nutshell liquid enhances the intestinal morphology by increasing the villus height by 17%. A diet with 0.01% of a microencapsulated blend of thymol and carvacrol led to an 8% increase in villus height (Chang et al., 2022). In the same study conducted by Chang et al. (2022), the inclusion of 0.04% premixture of grape seed and grape marc extract, green tea, and hops containing more than 10% of flavonoids improved intestinal morphology by increasing villus height by 11%. These enhancements in intestinal morphology may lead to increased feed efficiency, improving growth performance in pigs.

Table 1. Impact on intestinal health and growth performance in pigs fed with phytobiotics

Initial BW (kg)	Days fed	Dietary information	Health and growth performance ¹	Reference
1	2	3	4	5
77.8	28	Oregano essential oil (0.25%)	Decreased cortisol levels in serum by 38%, malondialdehyde in liver by 43.9%, and increased superoxide dismutase in liver by 22%.	(Zhang et al., 2015)
6.4	21	Encapsulated oregano essential oil (0.05%)	Increased jejunal villus height by 6.3%, decreased tumor necrosis factor alpha 13.4%, immunoglobulin G by 16.2%, and protein carbonyl by 69%; tended to increase ADG by 15%.	(Park et al., 2016 a)
27.9	42	Encapsulated oregano essential oil (0.05%)	Decreased immunoglobulin G and protein carbonyl by 15.8% and 23.6%, respectively; increased feed efficiency by 3%.	(Park et al., 2016 b)
12.0	28	<i>Oregano vulgaris</i> and <i>Thymus vulgaris</i> watery extracts (0.02%)	Decreased pH in ileal digesta by 8%; increased ADG by 25% and feed efficiency by 15%.	(Nowak et al., 2017)
27.3	14	<i>Macleaya cordata</i> extract (1.5%)	Decreased respiration rate by 7%, rectal temperature, bilirubin in urine by 32% and permeability in the colon by 52%.	(Le et al., 2020)
Weaned piglets aged 30 days	15	Natural extracts of <i>Oreganum vulgare</i> , <i>Cinnamomum cassia</i> and <i>Capsicum annuum</i> ; hydrogenated rapeseed oil (0.015%)	Decreased activity of serum alanine and aspartate aminotransferases by 32.4% and 29.1%, respectively, decreased activity of serum alkaline phosphatase by 40% and gamaglutamyltranspeptidase by 27.5%.	(Lukashchuk et al., 2020)
25.0	95	Lyophilized garlic (0.5%) and dandelion root powder (5%)	Decreased content of fat and cholesterol levels by 2.6% and 13.5%, respectively in backfat, <i>longissimus lumborum</i> muscle by 7.2% and 30.6%, respectively, and liver by 2.9% and 8.6%, respectively. Increased the loin eye area and lean meat yield by 7.2% and 12.2%, respectively. Increased ADG by 7% and feed efficiency by 6%.	(Samolińska et al., 2020)
6.0	21	Plant polyphenols (0.8%)	Increased <i>Lactobacillaceae</i> by 5.6%, <i>Peptostreptococcaceae</i> by 1.6%, and <i>Veillonellaceae</i> by 3.5%, decreased <i>Streptococcaceae</i> by 8.4% and <i>Erysipelotrichaceae</i> by 3.8%, increased lactate producers.	(Fresno Rueda et al., 2021)
7.0	34	Castor oil and cashew nutshell liquid (0.075% to 0.150%)	Decreased <i>Helicobacteraceae</i> by 25.8%, increased <i>Lactobacillus kitatonis</i> by 3.5%, tended to decrease protein carbonyl by 18%, tended to increase the villus height and crypt depth by 13% and 11.6%, respectively in jejunum.	(Motta et al., 2021)
7.3	42	<i>Allium</i> extract (0.02%)	Decreased microbiota alpha diversity, changed beta diversity; increased ADG by 13% and feed efficiency by 10%.	(Rabelo-Ruiz et al., 2021)
11.3	63	Blend of <i>Cinnamomum zeylanicum</i> (0.03%) and <i>Trachyspermum copiticum</i> (0.04%) essential oils; plant extracts of <i>Mikania micrantha</i> (0.28%) and <i>Garcinia lanceifolia</i> (0.14%)	Decreased cholesterol by 14.4%, increased immunoglobulin M by 12%, decreased interleukin 1β by 6.54%, increased <i>Lactobacilli</i> population by 3.5%, decreased enterobacterial populations by 30%; no difference in growth performance.	(Samanta et al., 2021)
6.4; 27.9	21; 42	Oregano extracts (0.05%)	Decreased tumor necrosis factor alpha by 15.6%, immunoglobulin G by 25%, and protein carbonyl by 18.2%, increased villus height by 6.6%; increased ADG, ADFI, and feed efficiency by 14%, 7% and 5%, respectively.	(Duarte and Kim, 2022)
8.01	16	Mixture of bitter citrus extract, thymol, carvacrol, grape seed, grape marc extract, green tea and hops (0.1%)	Increased gross energy digestibility by 2.5%, villus height by 8.4% and increased ADG 11%	(Chang et al., 2023)
32.7	70	Combination of chicory and extracts of carob pulp and fenugreek (0.1%)	Increased <i>Bifidobacterium</i> and <i>Lactobacillus</i> by 3% and 1.21%, respectively. Decreased <i>Bacteroidaceae</i> and <i>Campylobacteraceae</i> by 0.15% and 8.6%; increased ADG by 3%.	(Juhász et al., 2023)

Table 1 – contd.

1	2	3	4	5
73.8	40	Curcumin nanospheres (0.2%)	Decreased glutamic-pyruvic transaminase by 45.7%, glutamic-oxaloacetic transaminase by 46.2%, triglycerides by 16.3%, and total cholesterol levels by 5.5%; increased high density lipoprotein 27.7%, decreased <i>Escherichia coli</i> by 40.4% and ammonia gas by 64.9%, increased villus height by 3.2%, crypt depth and goblet cell in jejunum by 3.3% and 5%, respectively, decreased tumor necrosis factor alpha, increased immunoglobulin A and tight junction protein expression; increased ADG by 27%.	(Moniruzzaman et al., 2023)
6.3	56	Fenugreek, clove, thyme, nutmeg and cumin leaves (1.0% to 1.5%)	Decreased <i>Escherichia coli</i> and <i>Salmonella</i> spp. by 68.2% and 64.4%, respectively. Increased <i>Lactobacillus</i> spp. by 60%, double increased immunoglobulins A, G and M; increased ADG, ADFI, and feed efficiency by 80%, 22% and 32%, respectively.	(Alagbe et al., 2024)
8.0	21	Premixture of grape seed and grape marc extract, green tea, and hops (0.04%)	Reduced tumor necrosis factor alpha and IL-6 by 58.3% and 17.5%, respectively, fecal score and increased ADG by 17%.	(Chang et al., 2022)
8.1	42	A blend of essential oil containing cinnamaldehyde, carvacrol and thymol (0.1%)	Increased body ADG by 14%, increased the mRNA expression of tight junction protein; reduced IL-1 β , IL-6, and tumor necrosis factor alpha by 18.2%, 46.2% and 39.1%, respectively. Decreased serum diamine oxidase, endothelin and D-lactic acid by 38.3%, 29.7%, and 10%, respectively.	(Zhao et al., 2023)
6.4	28	Ground herbs-based phytobiotics (1%) and essential oil-based phytobiotics (1%)	Reduced <i>Veillonellaceae</i> , <i>Prevotellaceae</i> , <i>Lachnospiraceae</i> by 73.9%, 91.1%, and 77.8%, respectively. Tended to decrease protein carbonyl levels by 44.4% and no difference in growth performance.	(Duarte et al., 2024)

¹Values compared with control treatments.

Phytobiotics have also been shown to regulate both humoral immunity and cytokine expression in pigs, helping to coordinate immune responses and manage inflammation (Fossum, 1998; Choi et al., 2006). Herbs, such as garlic, echinacea, and liquorice, could improve the activity of lymphocytes, macrophages, and natural killer cells, and stimulate interferon synthesis (Frankič et al., 2009). Phytobiotics derived from oregano, fenugreek, clove, thyme, nutmeg and cumin, have demonstrated immunostimulant properties by increasing the immunoglobulin levels (Park et al., 2016 a; Alagbe et al., 2024). Similarly, the inclusion of 0.05% of thymol and carvacrol from oregano to weaned pigs reduced TNF- α concentration by 16%, reduced plasma protein carbonyl levels by 30%, and increased villus height in the jejunum by 6% (Duarte and Kim, 2022). Additionally, a blend of thymol and carvacrol reduced TNF- α and IL-6 levels by 36% and 34%, respectively, and improved immune response by increasing IgA levels by 19% (Chang et al., 2022). The inclusion of essential oils from a blend of castor oil and cashew nutshell liquid decreases the concentration of protein carbonyl by 22% in nursery pigs (Moita et al., 2021). Besides their immune-response properties, phytobiotics also help to reduce oxidative stress by mitigating the effects of ROS, which can damage proteins, lipids, or DNA and produce carbonyl groups such as aldehydes and ketones (Dalle-Donne et al., 2003). The antioxidant properties of phytobiotics depend on their specific compounds. For instance, astilbin from *Engelhardtia chrysolepis*, has been shown to decrease lactate dehydrogenase and malondialdehyde levels, both markers of oxidative stress (Jovanovic et al., 2010; Khoubnasabjafari et al., 2015; Xu et al., 2020). On the other hand, baicalin, extracted from *Scutellaria baicalensis*, has been found to alleviate oxidative stress in pigs by enhancing the activity of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, which protects cells from oxidative damage (Liao et al., 2020; Strycharz-Dudziak et al., 2020).

The phytobiotics have shown antibacterial effects, particularly when eugenol, cinnamaldehyde, thymol and carvacrol are combined, as observed against *E. coli* (Pei et al., 2009). Phytobiotics supplementation using a combination of chicory, carob pulp extracts, and fenugreek, castor oil, and cashew nutshell liquid has been shown to reduce the potential pathogens like *E. coli* whereas increasing beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* (Moita et al., 2021; Juhász et al., 2023; Alagbe et al., 2024). This microbiota modulation could provide a favorable metabolic equilibrium between lactate production and utilization, leading to a healthier intestinal environment. The inclusion of plant polyphenols in the diets of weaned pigs resulted in an increased relative abundance of *Lactobacillus* in the intestinal mucosa-associated microbiota (Fresno Rueda et al., 2021). *Lactobacillus* synthesizes lactic acid, which inhibits pathogens such as *E. coli* and *Enterobacter* (Hou et al., 2015; Moita et al., 2021). The inclusion of essential oils from a blend of

castor oil and cashew nutshell liquid reduced the relative abundance of *Helicobacter* sp. (Moita et al., 2021). The antibacterial activity of essential oils seems to be associated with their ability to disrupt bacteria cell membranes due to their hydrophobic nature (Burt, 2004). In the case of spices and herbs, piperine, the major active compound in black pepper, has been shown to cause the physical and morphological alterations in the cell wall and membrane of *E. coli* in pigs (Srinivasan, 2007; Zhang et al.,

2016). Phytobiotics positively influence several aspects of pig health, including immune response, intestinal microbiota balance, and intestinal morphology. These benefits collectively enhance overall growth performance. By mitigating the negative impacts of stressors, phytobiotics support the integrity of the intestinal epithelium, promote cellular growth, and improve metabolic health. This makes them promising components of pig nutrition.

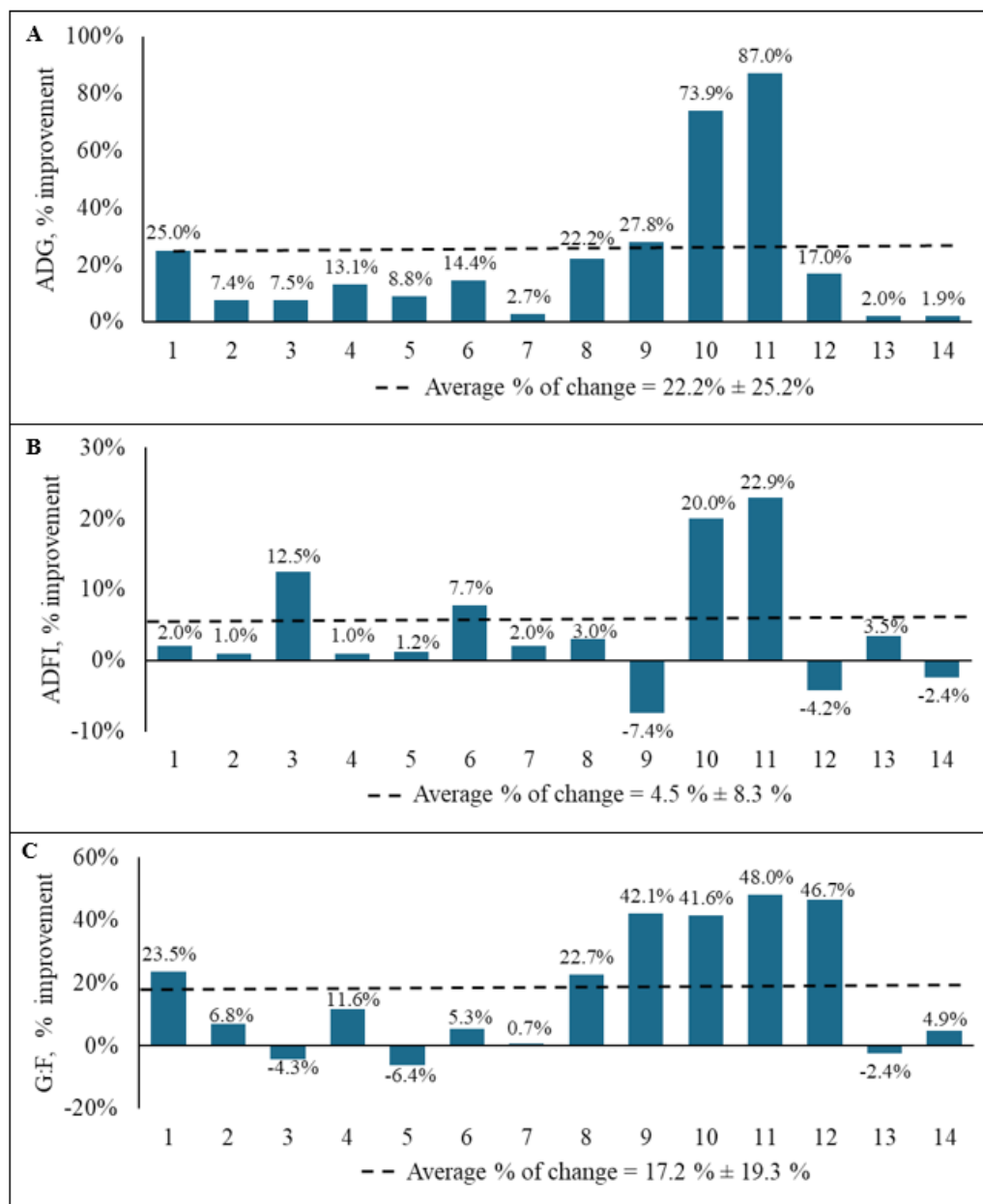


Figure 3. Impacts of phytobiotics on (A) average daily gain (ADG), (B) average daily feed intake (ADFI), and (C) gain to feed ratio (G:F) of pigs compared with control treatments. Selected studies employed phytobiotics and reported outcomes related to growth performance. The selected studies were (1) Nowak et al. (2017), (2) Samolińska et al. (2020), (3) Moita et al. (2021), (4) Rabelo-Ruiz et al. (2021), (5) Samanta et al. (2021), (6) Duarte and Kim (2022), (7) Juhász et al. (2023), (8) Moniruzzaman et al. (2023), (9) Moniruzzaman et al. (2023), (10) Alagbe et al. (2024), (11) Alagbe et al. (2024), (12) Chang et al. (2022), (13) Zhao et al. (2023), (14) Duarte et al. (2024)

Although phytobiotics offer diverse biological activities and potential benefits in pig production, their adoption as feed additives in practice faces several challenges. One major issue is the variability in the composition and efficacy of phytobiotic products. This variability can arise from differences in plant sources, extraction methods, and environmental conditions that affect bioactive compound concentrations (Windisch et al., 2008). Additionally, the lack of standardized formulations and dosages makes it difficult to ensure consistent results across different animal productions. Incorrect dosing, such as using excessive amounts of certain herbs, can lead to potential toxicity. Therefore, it is crucial to use safe and effective doses that maintain consistent levels of active compounds (Krauze, 2021). Some phytobiotic compounds can generate unpleasant odors and flavors, reducing appetite (Kommera et al., 2006; Clouard and Val-Laillet, 2014; Christaki et al., 2022). Moreover, the bioactive compounds of phytobiotics are sensitive to environmental factors such as light, heat, oxygen, and humidity. These factors can lead to oxidation and degradation (Choi et al., 2019; Christaki et al., 2022). Another important consideration is that phytobiotics administered in their free form are often quickly absorbed and metabolized in the stomach. This rapid metabolism limits the amount that reaches the intestine (Van Noten et al., 2020), indicating a need for technology to help to mitigate this issue.

Future prospective

Phytobiotics, which include a diverse range of bioactive compounds such as phenolics, terpenes, and aldehydes, offer beneficial properties in pig production. Their antioxidant, anti-inflammatory, and antibacterial properties are particularly relevant in the context of weaning stress, PWD, environmental and nutritional challenges. Phytobiotics reduce inflammatory and oxidative stress responses, enhance intestinal barrier function, and exhibit antimicrobial properties. However, to fully harness the potential of phytobiotics, certain challenges must be addressed. One important issue is the variability in their composition driven by differences in plant sources, extraction methods, and environmental factors. This variability complicates the development of consistent results. Standardized formulations and dosages are essential to ensure reliable and reproducible effects across different farming systems. Future research should focus on understanding the specific mechanisms of action, identifying optimal combinations of bioactive compounds, and determining appropriate dosages. Addressing these challenges will enable phytobiotics to become a successful alternative to future pig nutrition strategies, enhancing productivity whilst promoting animal welfare and environmental sustainability.

Acknowledgement

Financial supports from North Carolina Agricultural Foundation (Raleigh, NC, USA) and USDA-NIFA Hatch (Washington DC, USA).

References

- Abd El-Hack M.E., El-Saadony M.T., Salem H.M., El-Tahan A.M., Soliman M.M., Youssef G.B. A., Taha A.E., Soliman S.M., Ahmed A.E., El-kott A.F., Al Syaad K.M., Swelum A.A. (2022). Alternatives to antibiotics for organic poultry production: types, modes of action and impacts on bird's health and production. *Poult. Sci.*, 101: 101696.
- Abo-Elghiet F., Rushdi A., Ibrahim M.H., Mahmoud S.H., Rabeh M.A., Alshehri S.A., El Menofy N.G. (2023). Chemical profile, antibacterial, antibiofilm, and antiviral activities of *Pulicaria crispa* most potent fraction: an *in vitro* and *in silico* study. *Molecules*, 28: 4184.
- Al-Yasiry A.R., Kiczorowska B. (2016). Frankincense – therapeutic properties. *Adv. Hyg. Exp. Med.*, 70: 380–391.
- Al-Yasiry A.R., Kiczorowska M., Samolińska W., Kowalczyk-Vasilev E. (2018). Growth performance, digestibility, haematology, biochemistry, and some humoral immunity blood parameters of broiler chickens fed different levels of *Boswellia serrata* resin. *Anim. Prod. Sci.*, 58: 1885–1891.
- Alagbe J.O., Anorue D.N., Shittu M.D., Ramalan S.M., Faniyi T.O., Ajagbe A.D. (2024). Growth performance and physiological response of weaned pigs fed diet supplemented with novel a phyto-genics. *Braz. J. Sci.*, 3: 43–57.
- Alghirani M.M., Chung E.L.T., Jesse F.F.A., Sazili A.Q., Loh T.C. (2021). Could phytobiotics replace antibiotics as feed additives to stimulate production performance and health status in poultry? An overview. *J. Adv. Vet. Res.*, 11: 254–265.
- Almeida-da-Silva C.L.C., Savio L.E.B., Coutinho-Silva R., Ojcius D.M. (2023). The role of NOD-like receptors in innate immunity. *Front. Immunol.*, 14: 1122586.
- Álvarez-Martínez F.J., Barrajón-Catalán E., Herranz-López M., Micol V. (2021). Antibacterial plant compounds, extracts and essential oils: An updated review on their effects and putative mechanisms of action. *Phytomed.*, 90: 153626.
- Bakkali F., Averbeck S., Averbeck D., Idaomar M. (2008). Biological effects of essential oils – a review. *Food Chem. Toxicol.*, 46: 446–475.
- Bhatia R., Sharma S., Bhadada S.K., Bishnoi M., Kondepudi K.K. (2022). Lactic acid bacterial supplementation ameliorated the lipopolysaccharide-induced gut inflammation and dysbiosis in mice. *Front. Microbiol.*, 13: 930928.
- Brabb T., Newsome D., Burich A., Hanes M. (2012). Infectious diseases. In: The laboratory rabbit, guinea pig, hamster, and other rodents, Suckow M.A., Stevens K.A., Wilson R.P. (eds). Academic Press, London, UK. pp. 637–683.
- Brenes A., Roura E. (2010). Essential oils in poultry nutrition: Main effects and modes of action. *Anim. Feed Sci. Technol.*, 158: 1–14.
- Burt S. (2004). Essential oils: their antibacterial properties and potential applications in foods – a review. *Int. J. Food Microbiol.*, 94: 223–253.
- Buryakov N.P., Sycheva L.V., Trukhachev V.I., Zaikina A.S., Buryakova M.A., Nikonov I.N., Petrov A.S., Kravchenko A.V., Fathala M.M., Medvedev I.K., Aleshin D.E. (2023 a). Role of dietary inclusion of phytobiotics and mineral adsorbent combination on dairy cows' milk production, nutrient digestibility, nitrogen utilization, and biochemical parameters. *Vet. Sci.*, 10: 238.
- Buryakov N.P., Zagarin A.Y., Fathala M.M., Aleshin D.E. (2023 b). The role of supplementing a complex phytobiotic feed additive containing (*Castanea sativa* mill) extract in combination with calcium butyrate, zinc–methionine and essential oils on growth indicators, blood profile and carcass quality of broiler chickens. *Vet. Sci.*, 10: 212.
- Campbell J.M., Crenshaw J.D., Polo J. (2013). The biological stress of early weaned piglets. *J. Anim. Sci. Biotechnol.*, 4: 19.
- Castillo M., Martín-Orúe S.M., Nofrarias M., Manzanilla E.G., Gasa J. (2007). Changes in caecal microbiota and mucosal morphology of weaned pigs. *Vet. Microbiol.*, 124: 239–247.
- Celedon J.M., Bohlmann J. (2019). Oleoresin defenses in conifers: chemical diversity, terpene synthases and limitations of oleoresin defense under climate change. *New Phytol.*, 224: 1444–1463.

- Chang S.Y., Song M.H., Lee J.H., Oh H.J., Kim Y.J., An J.W., Go Y.B., Song D.C., Cho H.A., Cho S.Y., Kim D.J., Kim M.S., Kim H.B., Cho J.H. (2022). Phyto-genic feed additives alleviate pathogenic *Escherichia coli*-induced intestinal damage through improving barrier integrity and inhibiting inflammation in weaned pigs. *J. Anim. Sci. Biotechnol.*, 13: 107.
- Chang S.Y., Lee J.H., Oh H.J., An J.W., Song D.C., Cho H.A., Park S.H., Jeon K.H., Cho S.Y., Kim D.J., Kim M.S., Cho J.H. (2023). Effect of different ratios of phyto-genic feed additives on growth performance, nutrient digestibility, intestinal barrier integrity, and immune response in weaned pigs challenged with a pathogenic *Escherichia coli*. *J. Anim. Sci.*, 101: skad148.
- Choi C., Kwon D., Jung K., Ha Y., Lee Y.H., Kim O., Park H.K., Kim S.H., Hwang K.K., Chae C. (2006). Expression of inflammatory cytokines in pigs experimentally infected with *Mycoplasma hyopneumoniae*. *J. Comp. Pathol.*, 134: 40–46.
- Choi J., Wang L., Ammeter E., Lahaye L., Liu S., Nyachoti M., Yang C. (2019). Evaluation of lipid matrix microencapsulation for intestinal delivery of thymol in weaned pigs. *Transl. Anim. Sci.*, 4: 411–422.
- Christaki E., Bonos E., Giannenas I., Florou-Paneri P. (2012). Aromatic plants as a source of bioactive compounds. *Agriculture*, 2: 228–243.
- Christaki S., Moschakis T., Hatzikamari M., Mourtzinis I. (2022). Nanoemulsions of oregano essential oil and green extracts: Characterization and application in whey cheese. *Food Contr.*, 141: 109190.
- Clouard C., Val-Laillet D. (2014). Impact of sensory feed additives on feed intake, feed preferences, and growth of female piglets during the early postweaning period. *J. Anim. Sci.*, 92: 2133–2140.
- Dalle-Donne, I., Rossi R., Giustarini D., Milzani A., Colombo R. (2003). Protein carbonyl groups as biomarkers of oxidative stress. *Clin. Chim. Acta.*, 329: 23–38.
- Diomede F., Zingariello M., Cavalcanti M., Merciaro I., Pizzicannella J., De Isla N., Caputi S., Ballerini P., Trubiani O. (2017). MyD88/ERK/NFkB pathways and pro-inflammatory cytokines release in periodontal ligament stem cells stimulated by *Porphyromonas gingivalis*. *Eur. J. Histochem.*, 61: 2791.
- Dong N., Li X., Xue C., Wang C., Xu X., Bi C., Shan A., Li D. (2019). Astragalus polysaccharides attenuated inflammation and balanced the gut microflora in mice challenged with *Salmonella typhimurium*. *Int. Immunopharmacol.*, 74: 105681.
- Duarte M.E., Kim S.W. (2022). Phytobiotics from oregano extracts enhance the intestinal health and growth performance of pigs. *Antioxidants*, 11: 2066.
- Duarte M.E., Garavito-Duarte Y., Kim S.W. (2023). Impacts of F18+ *Escherichia coli* on intestinal health of nursery pigs and dietary interventions. *Animals*, 13: 2791.
- Duarte Y.R.G., Duarte M.E., Kim S.W. (2024). Evaluation of phyto-genic formulations on intestinal health and the performance of nursery pigs challenged with F18+ *Escherichia coli*. *J. Anim. Sci.*, 102: 122–123.
- Dussault D., Vu K.D., Lacroix M. (2014). *In vitro* evaluation of antimicrobial activities of various commercial essential oils, oleoresin and pure compounds against food pathogens and application in ham. *Meat Sci.*, 96: 514–520.
- El-Sheikh S., Abdalim A., Moursi M., Helal M., Ahmed E. (2019). Effectiveness of phyto-biotic fortified-diet on broilers growth performance and gut, cellular, and humoral immunity signals. *Adv. Anim. Vet. Sci.*, 7: 466–473.
- Famuyide I.M., Fasina F.O., Eloff J.N., McGaw L.J. (2020). The ultra-structural damage caused by *Eugenia zeyheri* and *Syzygium legatii* acetone leaf extracts on pathogenic *Escherichia coli*. *BMC Vet. Res.*, 16: 326.
- Ferdous M.F., Arefin M.S., Rahman M.M., Ripon M.M.R., Rashid M.H., Sultana M.R., Hossain M.T., Ahammad M.U., Rafiq K. (2019). Beneficial effects of probiotic and phytobiotic as growth promoter alternative to antibiotic for safe broiler production. *J. Adv. Vet. Anim. Res.*, 6: 409–415.
- Fossum C. (1998). Cytokines as markers for infections and their effect on growth performance and well-being in the pig. *Domest. Anim. Endocrinol.*, 15: 439–444.
- Frankič T., Voljč M., Salobir J., Rezar V. (2009). Use of herbs and spices and their extracts in animal nutrition. *Acta Agric. Slov.*, 94: 95–102.
- Fresno Rueda A., Samuel R., St-Pierre B. (2021). Investigating the effects of a phytobiotics-based product on the fecal bacterial microbiome of weaned pigs. *Animals*, 11: 1950.
- González Mera I.F., González Falconí D., Morera Córdova V. (2019). Secondary metabolites in plants: Main classes, phytochemical analysis and pharmacological activities. *Bionatura*, 4: 1000–1009.
- Guerrero F., Carmona C., Hernández C., Toledo M., Arriagada A., Espinoza L., Bergmann J., Taborga L., Yañez K., Carrasco Y., Muñoz A.A. (2022). Drivers of flammability of *Eucalyptus globulus* Labill leaves: Terpenes, essential oils, and moisture content. *Forests*, 13: 908.
- Han G., Lee D.G. (2022). Antibacterial mode of action of β -amylin promotes apoptosis-like death in *Escherichia coli* by producing reactive oxygen species. *J. Microbiol. Biotechnol.*, 32: 1547–1552.
- Hanczakowska E., Swiatkiewicz M. (2012). Effect of herbal extracts on piglet performance and small intestinal epithelial villi. *Czech J. Anim. Sci.*, 57: 420–429.
- Hartsock A., Nelson W.J. (2008). Adherens and tight junctions: Structure, function and connections to the actin cytoskeleton. *Biochim. Biophys. Acta Biomembr.*, 1778: 660–669.
- Holanda D.M., Kim Y.I., Parnsen W., Kim S.W. (2021). Phytobiotics with adsorbent to mitigate toxicity of multiple mycotoxins on health and growth of pigs. *Toxins*, 13: 442.
- Hou C., Liu H., Zhang J., Zhang S., Yang F., Zeng X., Thacker P.A., Zhang G., Qiao S. (2015). Intestinal microbiota succession and immunomodulatory consequences after introduction of *Lactobacillus reuteri* 15007 in neonatal piglets. *PLoS one*, 10: 0119505.
- Houketchang N.S.C., Kuietche M.H. (2023). The use of plants as phytobiotics: A new challenge. In: *Phytochemicals in Agriculture and Food*, Marcos S.H., Eva A.H., Mariana P.T. (eds). IntechOpen, London, UK. pp. 6–24.
- Iwiński H., Chodkowska K.A., Drabik K., Batkowska J., Karwowska M., Kuroppa P., Szumowski A., Szumny A., Rózański H. (2023). The impact of a phytobiotic mixture on broiler chicken health and meat safety. *Animals*, 13: 2155.
- Jang K.B., Moita V.H.C., Martinez N., Sokale A., Kim S.W. (2023). Efficacy of zinc glycinate reducing zinc oxide on intestinal health and growth of nursery pigs challenged with F18+ *Escherichia coli*. *J. Anim. Sci.*, 101: skad035.
- Jócsák I., Tossenberger J., Végvári G., Sudár G., Varga-Visi É., Tóth T. (2020). How is the effect of phyto-genic feed supplementation tested in heat stressed pigs? Methodological and sampling considerations. *Agriculture*, 10: 257.
- Jovanovic P., Zoric L., Stefanovic I., Dzunic B., Djordjevic-Jocic J., Radenkovic M., Jovanovic M. (2010). Lactate dehydrogenase and oxidative stress activity in primary open-angle glaucoma aqueous humour. *Bosn. J. Basic Med. Sci.* 10: 83–88.
- Juhász Á., Molnár-Nagy V., Bata Z., Tso K.H., Posta K. (2023). Phytobiotic-prebiotic feed additive containing a combination of carob pulp, chicory, and fenugreek improve growth performance, carcass traits, and fecal microbiota of fattening pigs. *Animals*, 13: 3621.
- Kamelan Kafi M., Bolvari N.E., Mohammad Pour S., Moghadam S.K., Shafaei N., Karimi E., Oskoueian E. (2022). Encapsulated phenolic compounds from *Ferula gummosa* leaf: A potential phytobiotic against *Campylobacter jejuni* infection. *J. Food Process. Preserv.*, 46: 16802.
- Karpiński T.M. (2020). Essential oils of Lamiaceae family plants as antifungals. *Biomolecules*, 10: 103.
- Khamtawee I., Singdamrong K., Tatanan P., Chongpaisarn P., Dumnien N., Pearodwong P., Suwimonterabutr J., Nuntapaitoon M., Tummaruk P. (2021). Cinnamon oil supplementation of the lactation diet improves feed intake of multiparous sows and reduces pre-weaning piglet mortality in a tropical environment. *Livest. Sci.*, 251: 104657.
- Khoubnasabjafari M., Ansarin K., Jouyban A. (2015). Reliability of malondialdehyde as a biomarker of oxidative stress in psychological disorders. *Bioimpacts*, 5: 123–127.
- Kick A.R., Tompkins M.B., Flowers W.L., Whisnant C.S., Almond G.W.

- (2012). Effects of stress associated with weaning on the adaptive immune system in pigs. *J. Anim. Sci.*, 90: 649–656.
- Kikusato M. (2021). Phytobiotics to improve health and production of broiler chickens: functions beyond the antioxidant activity. *Anim. Biosci.*, 34: 345–353.
- Kommerer S., Mateo R.D., Neher F., Kim S.W. (2006). Phytobiotics and organic acids as potential alternatives to the use of antibiotics in nursery pig diets. *Asian-Australas. J. Anim. Sci.*, 19: 1784–1789.
- Korošec T., Voljč M., Salobir J., Rezar V. (2009). Use of herbs and spices and their extracts in animal nutrition. *Acta Agric. Slov.*, 94: 95–102.
- Krauze M. (2021). Phytobiotics, a natural growth promoter for poultry. In: *Advanced studies in the 21st century animal nutrition*, L. Babinszky, J. Oliveira, E.M. Santos (eds). IntechOpen, London, UK. pp. 37–57.
- Krauze M., Cendrowska-Pinkosz M., Matuszevičius P., Stępniewska A., Jurczak P., Ognik K. (2021). The effect of administration of a phytobiotic containing cinnamon oil and citric acid on the metabolism, immunity, and growth performance of broiler chickens. *Animals*, 11: 339.
- Lallès J.P., Boudry G., Favier C., Le Floch N., Luron I., Montagne L., Oswald I.P., Pié S., Piel C., Sève B. (2004). Gut function and dysfunction in young pigs: physiology. *Anim. Res.*, 53: 301–316.
- Le H.H., Shakeri M., Suleria H.A.R., Zhao W., McQuade R.M., Phillips D.J., Vidacs E., Furness J.B., Dunshea F.R., Artuso-Ponte V., Cottrell J.J. (2020). Betaine and isoquinoline alkaloids protect against heat stress and colonic permeability in growing pigs. *Antioxidants*, 9: 1024.
- Li A., Ni W., Zhang Q., Li Y., Zhang X., Wu H., Du P., Hou J., Zhang Y. (2020). Effect of cinnamon essential oil on gut microbiota in the mouse model of dextran sodium sulfate-induced colitis. *Microbiol. Immunol.*, 64: 23–32.
- Li Y., Cao H., Zhang S., Guo P., Zhao J., Zhang D., Zhang S. (2023). Effects of the supplementation of essential oil mixtures on growth performance, nutrient digestibility, immune status, and microbial community in weaned piglets. *Animals*, 13: 3697.
- Liao P., Li Y., Li M., Chen X., Yuan D., Tang M., Xu K. (2020). Baicalin alleviates deoxynivalenol-induced intestinal inflammation and oxidative stress damage by inhibiting NF- κ B and increasing mTOR signaling pathways in piglets. *Food Chem. Toxicol.*, 140: 111326.
- Lin Z., Ye L., Li Z., Huang X., Lu Z., Yang Y., Xing H., Bai J., Ying Z. (2020). Chinese herb feed additives improved the growth performance, meat quality, and nutrient digestibility parameters of pigs. *Anim. Models Exp. Med.*, 3: 47–54.
- Liu Y., Song M., Che T.M., Bravo D., Pettigrew J.E. (2012). Anti-inflammatory effects of several plant extracts on porcine alveolar macrophages *in vitro*. *J. Anim. Sci.*, 90: 2774–2783.
- Lopez-Romero J.C., González-Ríos H., Borges A., Simões M. (2015). Antibacterial effects and mode of action of selected essential oils components against *Escherichia coli* and *Staphylococcus aureus*. *Evid Based Complement Altern. Med.*, 2015: 795435.
- Lukashchuk B.O., Slivinska L.G., Shcherbaty A.R., Zinko H.O., Gutty B.V. (2020). Influence of modern treatment regimens on serum biochemical parameters in piglets with gastroenteritis. *Regul. Mech. Biosyst.*, 11: 67–73.
- Martel J., Ojcius D.M., Ko Y.F., Young J.D. (2020). Phytochemicals as prebiotics and biological stress inducers. *Trends Biochem. Sci.*, 45: 462–471.
- Martínez-Miró S., Tecles F., Ramón M., Escribano D., Hernández F., Madrid J., Orengo J., Martínez-Subiela S., Manteca X., Cerón J.J. (2016). Causes, consequences, and biomarkers of stress in swine: an update. *BMC Vet. Res.*, 12: 171.
- Miguel M.G. (2010). Antioxidant and anti-inflammatory activities of essential oils: a short review. *Molecules*, 15: 9252–9287.
- Mohammadi Gheisar M., Kim I.H. (2018). Phytobiotics in poultry and swine nutrition – a review. *Ital. J. Anim. Sci.*, 17: 92–99.
- Moita V.H.C., Duarte M.E., da Silva S.N., Kim S.W. (2021). Supplemental effects of functional oils on the modulation of mucosa-associated microbiota, intestinal health, and growth performance of nursery pigs. *Animals*, 11: 1591.
- Monger X.C., Gilbert A.A., Saucier L., Vincent A.T. (2021). Antibiotic resistance: From pig to meat. *Antibiotics*, 10: 1209.
- Moniruzzaman M., Kim D., Kim H., Kim N., Chin S., Karthikeyan A., Han K., Min T. (2023). Evaluation of dietary curcumin nanospheres as phytobiotics on growth performance, serum biochemistry, nutritional composition, meat quality, gastrointestinal health, and fecal condition of finishing pigs. *Front. Vet. Sci.*, 10: 1127309.
- Morsi D.S., El-Nabi S.H., Elmaghraby M.A., Abu Ali O.A., Fayad E., Khalifa S.A.M., El-Seedi H.R., El-Garawani I.M. (2022). Antiproliferative and immunomodulatory potencies of cinnamon oil on Ehrlich ascites carcinoma bearing mice. *Sci. Rep.*, 12: 11839.
- Nowak P., Kasprówska-Potocka M., Zaworska A., Nowak W., Stefanska B., Sip A., Grajek W., Juzwa W., Taciak M., Barszcz M., Tusnio A., Grajek K., Foksowicz-Flaczyk J., Frankiewicz A. (2017). The effect of eubiotic feed additives on the performance of growing pigs and the activity of intestinal microflora. *Arch. Anim. Nutr.*, 71: 455–469.
- 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 phytobiotics and their proposed modes of action in swine. *Front. Vet. Sci.*, 10: 1265689.
- Pannee C., Chandhane I., Wacharee L. (2014). Anti-inflammatory effects of essential oil from the leaves of *Cinnamomum cassia* and cinnamaldehyde on lipopolysaccharide-stimulated J774A.1 cells. *J. Adv. Pharm. Technol. Res.*, 5: 164–170.
- Park I., Lee J.K., Wang J., Kim S.W. (2016 a). Effects of dietary supplementation of phytobiotics on intestinal health and growth performance of nursery pigs. *J. Anim. Sci.*, 94: 456.
- Park I., Parnsen W., Kim S.W. (2016 b). Effects of dietary supplementation of phytobiotics on growth performance and health status of growing-finishing pigs. *J. Anim. Sci.*, 94: 127–128.
- Patra A.K., Amasheh S., Aschenbach J.R. (2019). Modulation of gastrointestinal barrier and nutrient transport function in farm animals by natural plant bioactive compounds – a comprehensive review. *Crit. Rev. Food Sci. Nutr.*, 59: 3237–3266.
- Pei R., Zhou F., Ji B., Xu J. (2009). Evaluation of combined antibacterial effects of eugenol, cinnamaldehyde, thymol, and carvacrol against *E. coli* with an improved method. *J. Food Sci.*, 74: 379–383.
- Poltorak A., He X., Smirnova I., Liu M.Y., Van Huffel C., Du X., Birdwell D., Alejos E., Silva M., Galanos C., Freudenberg M., Ricciardi-Castagnoli P., Layton B., Beutler B. (1998). Defective LPS signaling in C3H/HeJ and C57BL/10ScCr mice: mutations in Tlr4 gene. *Science*, 282: 2085–2088.
- Rabelo-Ruiz M., Teso-Pérez C., Peralta-Sánchez J.M., Ariza J.J., Martín-Platero A.M., Casabuena-Rincón O., Vázquez-Chas P., Guillamón E., Aguinaga-Casañas M.A., Maqueda M., Valdivia E., Baños A., Martínez-Bueno M. (2021). *Allium* extract implements weaned piglet's productive parameters by modulating distal gut microbiota. *Antibiotics*, 10: 269.
- Rahimi N. (2017). Defenders and challengers of endothelial barrier function. *Front. Immunol.*, 8: 1847.
- Reuben R.S., Onimisi P.A., Sekoni A.A., Salihu E.A. (2022). Growth performance, carcass characteristics and villi morphometry of broiler chickens fed diets containing *Mentha piperita* and *Adansonia digitata* leaves meals as phytobiotics. *Niger. J. Anim. Prod.*, 48: 217–228.
- Rossi B., Toschi A., Piva A., Grilli E. (2020). Single components of botanicals and nature-identical compounds as a non-antibiotic strategy to ameliorate health status and improve performance in poultry and pigs. *Nutr. Res. Rev.*, 33: 218–234.
- Samanta A.K., Gali J.M., Dutta T.K., Rajkhowa T.K., Mandal G.P., Patra A.K. (2021). Effect of dietary phytobiotic mixture on growth performance, nutrient utilization, and immunity in weaned piglets. *Trop. Anim. Health Prod.*, 53: 1–13.
- Samolińska W., Grela E.R., Kowalczyk-Vasilev E., Kiczorowska B., Klebaniuk R., Hanczakowska E. (2020). Evaluation of garlic and dandelion supplementation on the growth performance, carcass traits, and fatty acid composition of growing-finishing pigs. *Anim. Feed Sci. Technol.*, 259: 114316.
- Shaikh J., Bhosale R., Singhal R. (2006). Microencapsulation of black pepper oleoresin. *Food Chem.*, 94: 105–110.

- Shen J., Liu T., Qian Y., Yan S., Liu Z., Jia F. (2024). Therapeutic effect of probiotic-fermented herbal blend as antibiotic alternative on salmonellosis by multi-drug-resistant *Salmonella pullorum*. *Food Biosci.*, 57: 103585.
- Shen Y.B., Voilqué G., Odle J., Kim S.W. (2012). Dietary L-tryptophan supplementation with reduced large neutral amino acids enhances feed efficiency and decreases stress hormone secretion in nursery pigs under social-mixing stress. *J. Nutr.*, 142: 1540–1546.
- Singh I. (2017). Antimicrobials in higher plants: Classification, mode of action, and bioactivities. *Chem. Biol. Lett.*, 4: 48–62.
- Srinivasan K. (2007). Black pepper and its pungent principle-piperine: A review of diverse physiological effects. *Crit. Rev. Food Sci. Nutr.*, 47: 735–754.
- Strycharz-Dudziak M., Foltyn S., Dworżański J., Kielczykowska M., Malm M., Drop B., Polz-Dacewicz M. (2020). Glutathione peroxidase (GPx) and superoxide dismutase (SOD) in oropharyngeal cancer associated with EBV and HPV coinfection. *Viruses*, 12: 1008.
- Sun Y., Kim S.W. (2017). Intestinal challenge with enterotoxigenic *Escherichia coli* in pigs, and nutritional intervention to prevent postweaning diarrhea. *Anim. Nutr.*, 3: 322–330.
- Surh Y.J. (2008). NF-kappa B and Nrf2 as potential chemopreventive targets of some anti-inflammatory and antioxidative phytonutrients with anti-inflammatory and antioxidative activities. *Asia Pac. J. Clin. Nutr.*, 17: 269–272.
- Tajodini M., Saeedi H.R., Moghbeli P. (2015). Use of black pepper, cinnamon and turmeric as feed additives in the poultry industry. *World's Poult. Sci. J.*, 71: 175–183.
- Tsao R., Deng Z. (2004). Separation procedures for naturally occurring antioxidant phytochemicals. *J. Chromatogr. B.*, 812: 85–99.
- Van Noten N., Van Liefferinge E., Degroote J., De Smet S., Desmet T., Michiels J. (2020). Fate of thymol and its monoglucosides in the gastrointestinal tract of piglets. *ACS Omega*, 5: 5241–5248.
- Vlaicu P.A., Untea A.E., Panaite T.D., Saracila M., Turcu R.P., Dumitru M. (2023). Effect of basil, thyme and sage essential oils as phytogetic feed additives on production performances, meat quality and intestinal microbiota in broiler chickens. *Agriculture*, 13: 874.
- Wang L., Huo B., Huang L., Che L., Feng B., Lin Y., Xu S., Wu D., Fang Z. (2022). Dietary supplementation with a mixture of herbal extracts during late gestation and lactation improves performance of sows and nursing piglets through regulation of maternal metabolism and transmission of antibodies. *Front. Vet. Sci.*, 9: 1026088.
- Williams J.M., Duckworth C.A., Burkitt M.D., Watson A.J.M., Campbell B.J., Pritchard D.M. (2015). Epithelial cell shedding and barrier function: a matter of life and death at the small intestinal villus tip. *Vet. Pathol.*, 52: 445–455.
- Windisch W., Schedle K., Plitzner C., Kroismayr A. (2008). Use of phytogetic products as feed additives for swine and poultry. *J. Anim. Sci.*, 86: 140–148.
- Xu X., Yan G., Chang J., Wang P., Yin Q., Liu C., Liu S., Zhu Q., Lu F. (2020). Astilbin ameliorates deoxynivalenol-induced oxidative stress and apoptosis in intestinal porcine epithelial cells (IPEC-J2). *J. Appl. Toxicol.*, 40: 1362–1372.
- Yang Y., Zhao L., Shao Y., Liao X., Zhang L., Lu L., Luo X. (2019). Effects of dietary graded levels of cinnamon essential oil and its combination with bamboo leaf flavonoid on immune function, antioxidative ability and intestinal microbiota of broilers. *J. Integr. Agric.*, 18: 2123–2132.
- Yeh C.H., Chen K.Y., Chou C.Y., Liao H.Y., Chen H.C. (2021). New insights on volatile components of *Vanilla planifolia* cultivated in Taiwan. *Molecules*, 26: 3608.
- Yitbarek M. (2015). Phytogetics as feed additives in poultry production: a review. *Int. J. Extensive Res.*, 3: 49–60.
- Zhang T., Zhou Y.F., Zou Y., Hu X.M., Zheng L.F., Wei H.K., Giannenas I., Jin L.Z., Peng J., Jiang S.W. (2015). Effects of dietary oregano essential oil supplementation on the stress response, antioxidative capacity, and HSPs mRNA expression of transported pigs. *Livest. Sci.*, 180: 143–149.
- Zhang J., Ye K., Zhang X., Pan D., Sun Y., Cao J. (2016). Antibacterial activity and mechanism of action of black pepper essential oil on meat-borne *Escherichia coli*. *Front. Microbiol.*, 7: 2094.
- Zhao B., Wang T., Chen J., Qiu B., Xu Y., Zhang Q., Li J., Wang C., Nie Q., Li J. (2023). Effects of dietary supplementation with a carvacrol–cinnamaldehyde–thymol blend on growth performance and intestinal health of nursery pigs. *Porcine Health Manag.*, 9: 24.
- Zheng L., Duarte M.E., Sevarolli Loftus A., Kim S.W. (2021). Intestinal health of pigs upon weaning: challenges and nutritional intervention. *Front. Vet. Sci.*, 8: 628258.

Received: 19 VIII 2024

Accepted: 4 XI 2024