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Posted Date: 26 August 2024

doi: 10.20944/preprints202408.1770.v1

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Review

Organic Acids as Antibiotics Alternatives in Poultry Field: Recent Advances

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Abstract: Feed additive antibiotics have been used for many decades as growth promotors or antibacterial substances world-wide. However, the adverse impacts of using antibiotics in animal or poultry feeds were informed. Therefore, searching for alternatives such as probiotics, prebiotics, phytobiotics, post-biotics, bacteriophages, enzymes, essential oils, or organic acids (OAs) became urgent. The OAs are produced by beneficial intestinal bacteria through the fermentation process of carbohydrates. The OAs and their salts are still used as feed preservatives. They have been long added to feed in order to minimize contamination and growth of harmful bacteria and fungi, reduce the deterioration, as well as prolong the shelf life of feed commodities. Moreover, they have been mostly added to poultry feed as a blend to obtain a maximum beneficial effects. The supplementation of poultry with OAs could improve the growth performance parameters and carcass traits, promote utilization of nutrients, boost the immune response, and inhibit the growth of pathogenic bacteria. Therefore, this review article provides valuable insights into the potential benefits of using OAs-antibiotics alternative in reducing the microbial load, enhancing the performance parameters in broilers and layers, improving the gut heath, as well as boosting of the immune response.

Keywords: organic acids; carcass traits; chickens performance; gut health; immunity

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1. Introduction

Antibiotic growth promoters have been used in the livestock production systems since several years [1]. However, in 2006, the European Union prohibited the administration of these growth promoters due to the continuous development of antibiotic resistance. The hazardous use of antibiotics leads to destruction of beneficial intestinal flora and emergence of resistant bacteria which transmitted to humans through the food chains [2,3]. Therefore, the search for suitable alternatives becomes an urgent issue, especially for the poultry production system [4–6]. The European Union permitted the use of acidifiers or organic acids (OAs) and their salts in poultry production due to their safety [7]. They have also many advantages such as absence of pollution, drug resistance, and residues, as well as their beneficial effects on the health [8,9]. Dietary OAs promote the production of prebiotics and probiotic lactic acid bacteria [10]. The OAs could potentially replace antibiotic growth promoters with positive effects on performance and gut health of livestock [11] and poultry production [12–15].

There are two types of acids; organic and inorganic (Figure 1). The majority of feed additive OAs could be termed as volatile short chain fatty acids (e.g., propionic, acetic, fumaric, lactic, or butyric acids), medium chain fatty acids, and long-chain fatty acids [8]. Propionic acid, acetic acid, and butyric acid are produced by beneficial intestinal bacteria through the fermentation process of carbohydrates [16]. The organic carboxylic acid contains a generic structure of carboxyl "R-COOH" is regarded as an organic acid (including fatty acids and amino acids) [17]. Also, formic acid, propionic acid, citric acid, acetic acid, etc. are partially dissociated weak acids that are composed of saturated straight-chain monocarboxylic acids such as amino acids and fatty acids with R-COOH constituent [18]. They are present in the form of salts such as sodium, potassium, and calcium with variable physical and chemical properties. The solubility and acid-binding capacity of water [19] and

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feed ingredients [20,21] can affect the efficacy of OAs. The beneficial effects of OAs could be enhanced by using blends rather than a single acid treatment [22].

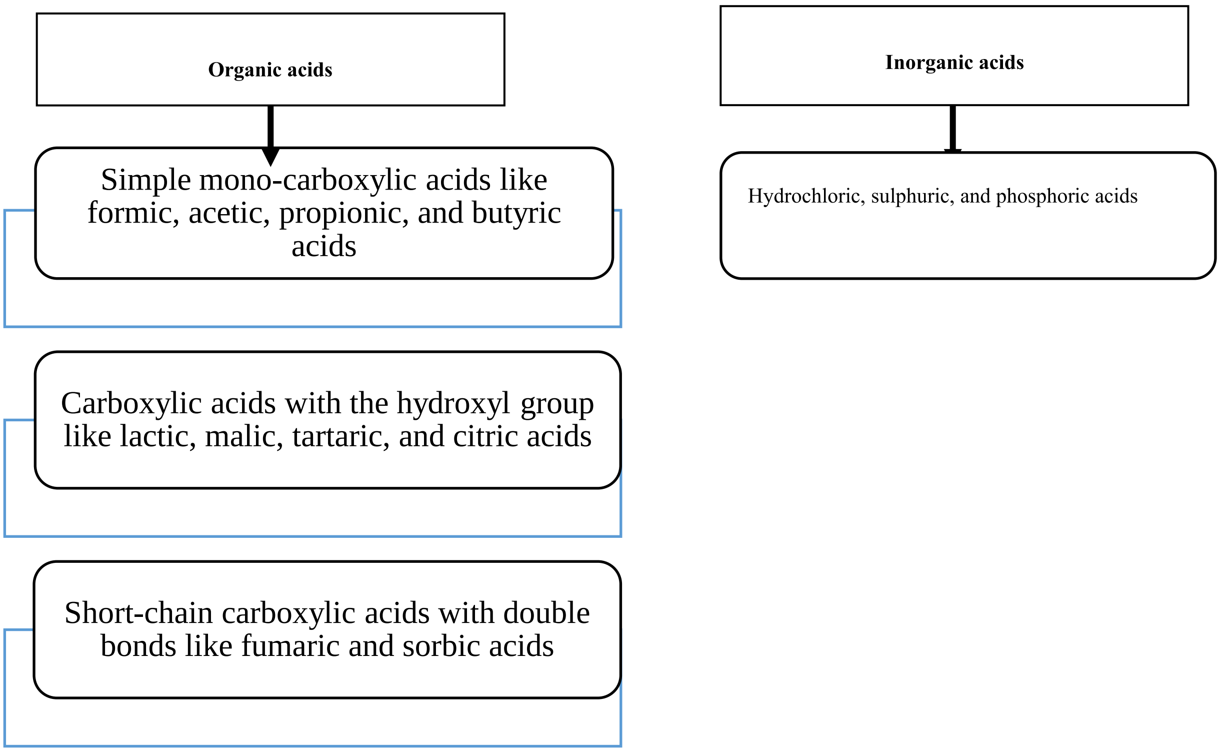

Figure 1. Types of acids used in the field of poultry industry.

OAs have been added to minimize contamination, growth of harmful bacteria and fungi, and deterioration, as well as prolong the shelf life of feed commodities [23]. Therefore, they are known to be used as good feed preservatives. Acetic acid or benzoic acid as well as their sodium salts are represented as safe feed preservatives [11]. They could act similar functions as antibiotics [7]. For instance, OAs were added to poultry feed in rates of 0.5 kg/ ton and 2.5-3.0 kg/ton to reduce mold and *Salmonella* growths, respectively [24]. In addition, dietary formic acid and propionic acid could reduce the bacterial load with *Salmonella* spp. in the contaminated feed [18].

The bad hygienic conditions in livestock farms such as increasing litter moisture and worm temperature variables can enhance the microbial growth and consequently reduce the nutritional content of proteins and carbohydrates. So, the supplementation with OAs could improve the growth performance, parameters and carcass traits [25–28], reduce the guts' pH, enhance pepsin production, promote nutrients digestibility and utilization [29,30], boost the immune response [31], and suppress the growth of pathogenic bacteria [14,32–36]. Besides, Ma et al. [26] proved the antioxidant capacity of OAs as supplementing diets mixed OAs increased the amount of serum superoxide dismutase and catalase of 3 and 6 week old broilers.

Accordingly, this review article provides a comprehensive insights into the role of using OAs-antibiotics alternative in reducing the microbial load, enhancing the performance parameters in broilers and layers, improving the gut heath, as well as boosting of the immune response.

2. The Different Effects of OAs Supplementation for Poultry

The different effects of OAs inoculation in the feed of poultry are illustrated in Table 1 and Figure 2.

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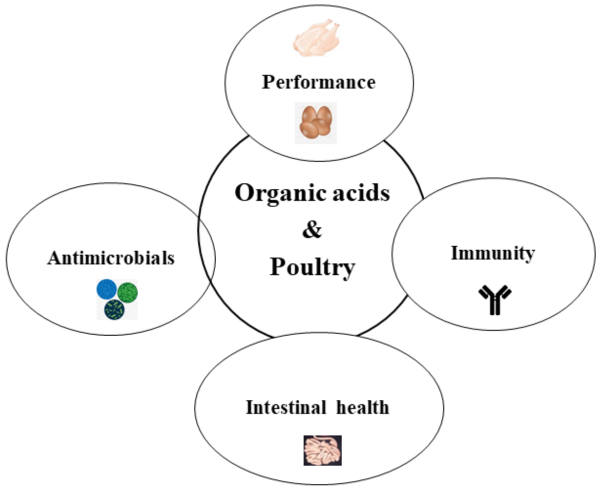

Figure 2. The different uses of OAs in poultry production system.

2.1. Antimicrobials

The different forms of OAs include solid in feed, spray on the litter, or added to the water (Figure 3). The antimicrobial efficacy of OAs is still not fully investigated. The different mechanisms of actions of OAs as antimicrobials are illustrated in Figure 4. The positive influences of their antibacterial capacity are associated with the physical chemistry of the used acid, special characteristics of dissociation, composition and pH of media, animal species, type of organism, growth conditions, exact location in the intestines, and buffering capacity [18,29]. Additionally, the efficiency of OAs relies on the acid molecular weight, dissociation constant, and antimicrobial activity [37].

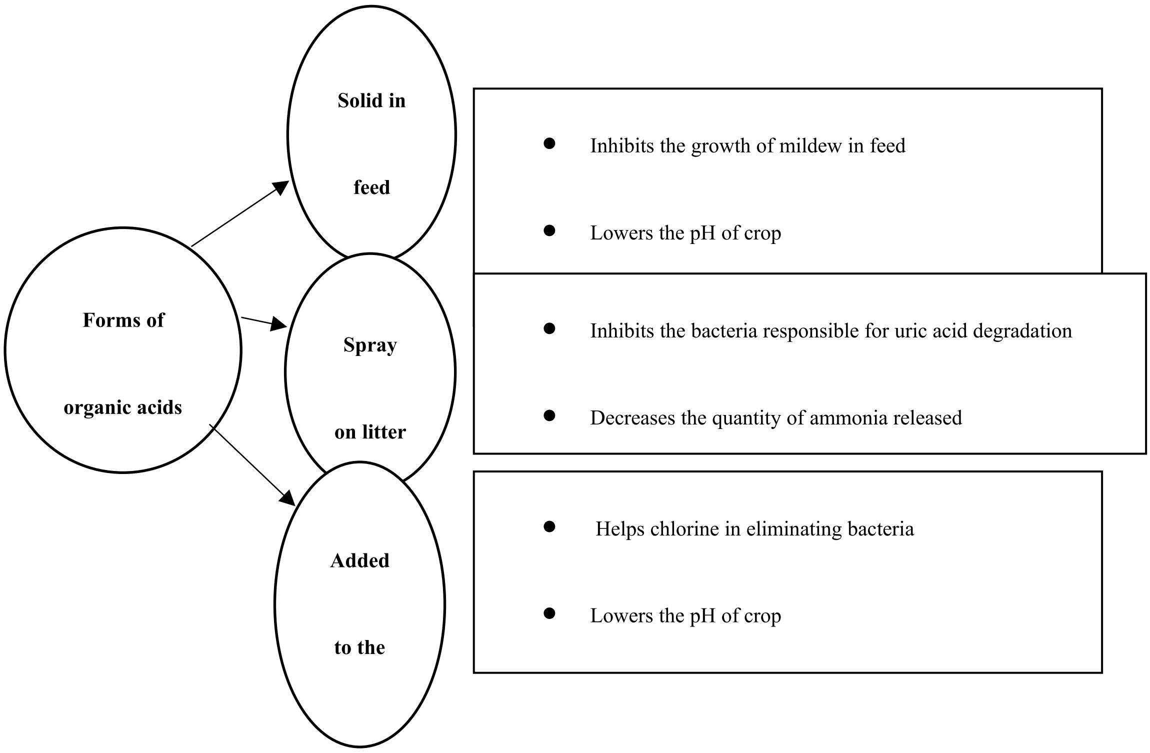

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Figure 3. The different forms of OAs in poultry production.

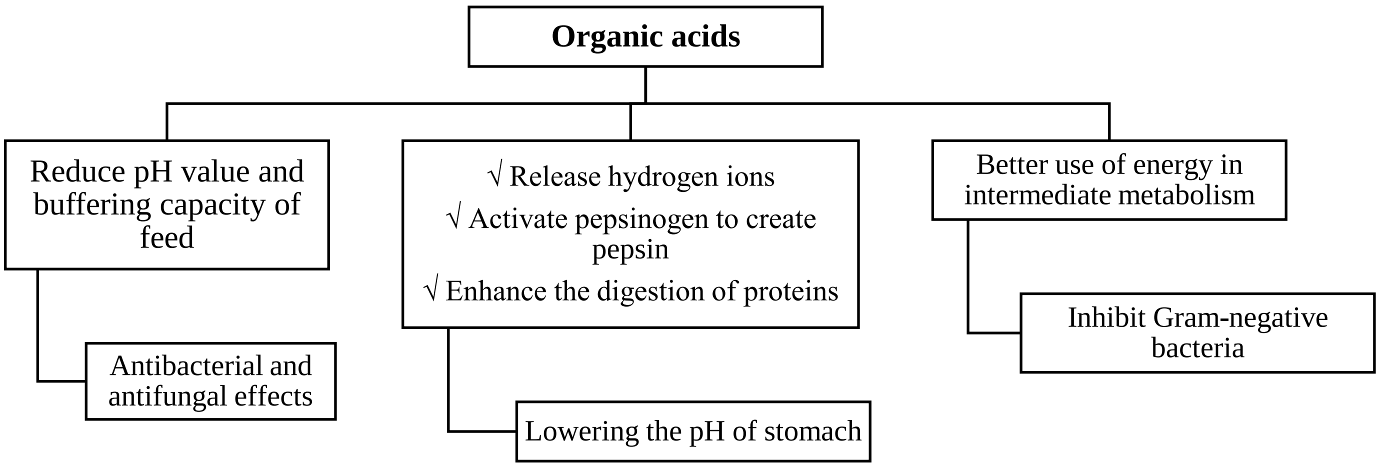

Figure 4. The different antimicrobial mechanisms of actions of OAs.

Dibner and Buttin [29] demonstrated that some OAs are of narrow spectrum which affect bacteria (lactic acid) or fungi (sorbic acid), while others are of broad spectrum against bacteria and fungi (formic acid and propionic acid). As short-chain fatty acids, both butyric acid and valeric acid have antibacterial effects against Gram-negative or Gram-positive bacteria [38]. However, formic acid and acetic acid can directly control pathogens by acting upon the cell wall of Gram-negative bacteria [9].

The concentrations and the pH of OAs affect their antimicrobial power [39]. Under low pH condition, the OAs become more available in a lipophilic dissociated form, easily diffuse into the bacterial and fungal cell membranes, and consequently cause disruption of the enzymatic reaction and transport system [6]. Moreover, the low pH condition can disturb the generation of energy and inhibit the bacterial cell proliferation and growth (bacteriostasis) [6,40]. In the upper digestive tract, the low pH enhances the antimicrobial effects of the OAs and helps their absorption by diffusion in the epithelia [6], while in the lower part of the intestine, the OAs decrease the hosts competition with the natural microflora resulting in improved digestion [40]. However, there is a discrepancy regarding the role of OAs in reducing the pH of the intestinal tract [41,42] and this may be due to the differences in acidifiers types and concentrations, experimental animals, acidifiers formulations and test sites, diets type and compositions, and other factors.

The cytoplasm of the bacterial cells contains both positive charged protons and the negatively charged anions. The accumulation of proton in the cells leads to an increase in its acidity to un-bearable limit. Therefore, the bacterial cell depletes from most of energies to adjust its internal pH. This depletion may cause inhibition of growth and multiplication and even death. Besides, the accumulation of anions in the bacterial cells disturbs the DNA copying and cells multiplication, increases the level of the internal osmotic pressure, and consequently causing cells deaths [43]. On the other hand, OAs could release proton irons in the cytoplasm.

OAs have bactericidal and bacteriostatic characteristics [44]. They diffuse into the bacterial cell membrane and dissolve in anions and protons of the cytoplasm [45] with a subsequent expulsion of protons outside the bacterial cells [46]. This process reduces the energy supply and ends by cell death [47]. The un-dissociated forms of OAs can enter the bacterial cell membrane where they are dissociated, produce H^+ ions, and rise the pH acidity of the cytoplasm [48]. Then, pH-sensitive bacteria are forced to discard the redundant proton irons via the H^+-adenosin triphosphatase pump which causes impeding of bacterial cells proliferation [9]. However, the bacterial cell use energy to restore the basic nature of cytoplasm. So, once the OAs enter the cell, where the pH is about 7, the acids are dissociated and suppress the bacterial cell enzymes such as decarboxylases and catalases

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and the nutrient transport systems [49]. Moreover, the dissociated OAs produce anions ($RCOO^-$) to disturb the protein synthesis and unable the bacterial cells to replicate. The OAs may also affect the microbial cell membranes integrity or may interfere with the nutrient transport and energy metabolism causing bacterial cells deaths [18]. They can penetrate the bacterial membrane, inhibit the synthesis of adenosine triphosphate, disturb the bacterial membrane, and denaturant the DNA [50]. In addition, OAs can prevent the release of toxic compounds following bacterial colonization, thus averts the damage of the intestinal epithelial cell and improves the villus height [23]. Moreover, they can enhance the beneficial microbiota populations and thus creating eubiotic intestinal environment [51,52].

The more efficient release of OAs compounds could be achieved via the microencapsulation process [53]. OAs could be metabolized and rapidly absorbed from the upper segments of digestive tract (proventriculus, gizzard, and duodenum), but not from the lower parts [54]. The reduction of gut's pH limits the pathogenic bacterial growth especially those which are less tolerant to the acidic pH [25,55]. However, others decrease the pH of the bacteria after dissociation causing death [13]. The orthophosphoric acid can lower the pH of the digesta resulting in more levels of the un-dissociated form of acids [29]. Moreover, carboxylic acid in citric acid, lactic acid, tartaric acid, and malic acid, as well as monocarboxylic acid in propionic acid, acetic acid, butyric acid, and formic acid have a pKa value in between 3 and 5 and consequently antimicrobial properties [56]. It has been demonstrated that acids are able to reduce the total intestinal microbial load and the subsequent infection rate leading to an enhancement of digestibility and reduction of the energy demand by the gut-associated tissue [57].

Some pathogenic intestinal pathogens such as *Salmonella* spp. [56,58–60], *Campylobacter jejuni* (*C. jejuni*) [29,61], pathogenic *Escherichia coli* (*E. coli*) [62–64], and *Clostridium perfringens* (*C. perfringens*) [65] or coccidia spp. [31,66] could be drastically affected by using OAs. However, the growth of beneficial gut microflora such as *Lactobacillus* spp. could be improved following the OAs treatment [14]. So, the reduction of intestinal bacterial load along with the enhancement of natural flora resulting in an improvement of the nutrients utilization and consequently the growth performance [3,17,67]. The drinking water acidification could diminish the clinical signs of *Campylobacter* infection in the gut [39]. Moreover, citric acid lowered the growth of *Listeria monocytogenes* on chicken's thighs at 4°C for 8 days [68]. On the other side, different OAs can flourish the growth of beneficial bacteria such as *Lactobacillus* spp. [69–71]. For instance, the dietary citric acid/and or avilamycin enhanced the development of *Lactobacillus* spp., but inhibited the growth and proliferation of pathogenic *Salmonella* spp. and *E. coli* via activation of proteolytic enzymes, absorption of minerals, decreasing ammonia, depressing microbial metabolites, and stimulation of feed intake (FI) [72]. In addition, the by-product of wheat milling ''wheat bran" showed efficacy against *Salmonella* spp. in terms of percent and particle size. It has been proven that the rapid fermentation of butyric acid downregulated *Salmonella* spp. gene expression [6,73] and inhibited the bacterial cecal colonization due improvement of intestinal barrier function [74].

2.2. Performance Parameters

The blends of OAs could improve the FI and nutrient utilization, so they able to enhance the body weight gain (BWG) and the feed conversion ratio (FCR) of poultry [7,15,65,69–71,75–78]. The OAs treatment also showed reduced intestinal lesion scores and improved the gut health of broiler chickens with necrotic enteritis [14,15]. Moreover, under *Eimeria* challenge, a blend of benzoic acid and essential oils enhanced the growth performance in broilers [79].

The supplementation of OAs could improve the performance parameters [12,15,55,80–82] which is probably due to the enhancement of digestible energy and protein contents of the feed, reducing the intestinal bacterial colonization [8], increasing the proliferation of beneficial flora, modulation of the anti-inflammatory immune response [47], and lowering the ammonia and other harmful metabolites [57]. The OAs work to improve the digestion of proteins, calcium, phosphorus, magnesium, zinc, and other nutrients which present in the feed material of the small intestine [7]. In addition, the un-dissociated forms of OAs are able to penetrate the lipid layer of the bacterial and

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fungal cell membranes causing release of proton, accumulation of intracellular anion, reduction of the intestinal pH, and then boosting the secretion of endogenous digestible enzymes [9,83]. Moreover, OAs could enhance the release of digestive enzymes, pancreatic secretion, activity of microbial phytase, and proliferation of intestinal cells [29]. Reducing in the pH of the crop, gizzard, and duodenum leads to increasing the secretion of digestible enzymes, pepsin, trypsin, chymotrypsin, proteinase, amylase, lipase, protein hydrolysate, and non-protease concentrations in the intestinal segment [84–86]. Besides, the treatments with OAs could enhance the secretion of pepsin and chyme which reach the intestine to stimulate the decomposition and absorption of nutrients. This process plays a role in stimulating the digestive system development, increasing amylase and lipase secretion, and consequently increasing the intestinal absorption capacity. The OAs slower the rate of digesta passage and thus enhance the absorption of the feed contents from the intestines [87].

The usage of OAs is also associated with the improvement in minerals digestibility [88]. The digestibility of minerals, particularly calcium and phosphorous, has been improved possibly due to the enhancing of digestible enzymes [89] or the effective role of *Lactobacillus* spp. in the gut [72,90]. Mixing of OAs with essential oils could reduce the populations of pathogenic enteric bacteria, while improve the growth of beneficial gut microbiome, and so, enhance the intestinal health [14,15].

2.3. Carcass Traits

The treatments with different OAs could improve the meat quality of chickens' carcasses [91]. Lee et al. [92] demonstrated that the pH of broiler thigh meat was increased by gallic acid and linoleic acid supplementations. Moreover, Fortuoso et al. [93] showed that a dose of 300 mg/kg glycerol monolaurate improved the nutritional quality of meat. The decrease in the muscle pH of broilers supplied by OAs may be related to the increase in the antioxidant activity in meat [94] or the affection of the gut microbiota and their metabolites [86]. The dietary supplementation with benzoic acid or amylase improved the antioxidant capacity, nutrient digestion, and the meat quality [94]. The improved meat tenderness after dietary treatments with OAs may be due to the improving nutrients metabolism, reducing anaerobic digestion, and enhancing antioxidant capacity. During the carcass's processing, the anaerobic conditions with the protein breakdown may result in accumulation of lactic acid which affects the water holding capacity of meat [86].

2.4. Intestinal Health

The addition of OAs to the drinking water of birds resulted in increasing the number of jejunal goblet cells which lead to stimulation and production of the mucus layer [95] and improving the gut epithelial cells [12,39,96–98] and the duodenal villus height [99].

Decreasing in the crypt depth and increasing in the villus height: crypt depth ratio were also found [31]. Likewise, the results of García et al. [100], Kum et al. [101], and Islam et al. [15] showed increasing the villus height and villus: crypt depth ratio, reducing the lesion scores, and thus improving in intestinal integrity following the dietary supplementation with OAs.

The treatments with OAs may reduce the pH of digesta and raise the gastric proteolytic activity [67]. The increase in the secreted pancreatic juice containing trypsin, amylase, protease, lipase, procarboxy peptidases, and chymotrypsinogen [7,55,102] as well as the enhancement of pepsin protein proteolysis activity, broken down of proteins to simple peptides, and releasing of gastrin and cholecystokinin hormones have been also noticed following addition of OAs to feed. Similarly, Ma et al. [26] reported that supplementation of chickens diets with a mixture of OAs improved the pancreatic secretions and enhanced the expression of tight junction proteins, resulting in a healthier broiler production. The acidic intestinal environment can reduce the bacterial metabolites such as ammonia and amines [103] which consequently may improve the digestion process.

The fermentation process of some OAs such as acetate, propionate, and butyrate could enhance the intestinal morphology, tight junctions, and immunological status of birds [104]. Japanese quails received a product contains acetic acid, formic acid, and butyric acid, as well as thymol, β-cymene, carvacrol, and borneol showed an improvement of the intestinal morphology including crypt depth, villus length and width, villus/crypt ratio, thickness of the intestinal wall, goblet cell percentage, and

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appearance of the intestinal surface area [105]. Adil et al. [106] demonstrated that a dietary 3% fumaric acid increased the villus height in all the segments of small intestines. Several studies showed that chickens received butyrate have increased intestinal villus height, decreased crypt depth, and thereby increased intestinal absorption surface [107–109]. It has been found that butyrate can regulate the gut barrier and plays an important role as anti-inflammatory and immuno-regulatory substance to maintain the gut homeostasis [38]. Butyric acid can promote the development of epithelial cells [110], preserve the intestinal cells viability, and enhance the turnover of enterocytes which may improve intestinal recovery. Similar results were obtained by Gao et al. [86] and Pham et al. [14]. Improved intestinal villi length and depth as well as increasing the number of goblet cells containing acidic mucins have been also reported in broilers fed on diets containing butyrate [111].

It has been known that the infection with *Eimeria* (*E*) spp. is usually associated with the gut health. The supplementation with OAs could be a suitable alternative for anticoccidial due to their ability to improve the intestinal integrity that is damaged by such infection [31]. Acetic acid could decrease the caecal pH and consequently reduces the impact of oocysts that eventually lower the intestinal lesions. In broiler chickens, Abbas et al. [112] reported that acetic acid was effective against *E. tenella* infection and Ali et al. [113] showed that the dietary inclusion of butyric acid glycerides reduced the intestinal lesion score produced by *E. maxima*.

2.5. Immune Response

The modulation of immune response in hosts fed on OAs may be due to different speculations as the main causes are unknown. However, several studies have proven the immuno-potentiating effects of OAs for poultry [6,72,76,114]. The weights of immune organs of broiler chicks have been increased in response to OAs supplementations [30]. Moreover, the levels of serum immunoglobulin (Ig) were elevated following dietary feeding of layer chickens on OAs mixture and yeast culture [115]. For instance, chickens supplemented OAs showed an improvement in immune response and enhancement of antibody titer against Newcastle disease (ND) virus infection [116,117]. Moreover, Lee et al. [118] demonstrated that the percentages of cluster of differentiation (CD4+), CD25+, and T-cells were higher in broiler chickens received avian influenza (AI) (H9N2) virus vaccine along with a diet containing OAs. The influence of three OAs on the immunity and intestinal morphology of *E. coli* (K88) challenged broiler chickens was investigated and the results revealed an improvement of the ileal morphology and immunity [63]. Also, OAs showed the ability to reverse the detrimental effects of *S*. typhimurium and boost the immunological response in the challenged chickens [87]. Emami et al. [88] reported that broiler chickens received a diet containing phytase and OAs showed high levels of IgG. It has been found that OAs supplementation may increase trypsin and chymotrypsin production and consequently activate the digestive tract to secrete IgA in the ileal mucosa [73]. Butyric acid has a positive impact on the birds' immunity through the improvement of gut eubiosis and pH, increasing the number of beneficial bacteria and limiting the colonization of pathogens [111]. The inclusion of butyric acid in the ration of broiler chickens was associated with a good cell-mediated immunity after inoculation of phytohemagglutinin-P, improved humoral antibody production after vaccination with ND virus vaccine and injection of sheep red blood cells, and increased the thymus and spleen weights [111].

Increasing *Lactobacillus* spp. count in the gut [88], inhibiting nuclear factor kappa B activation [119], increasing tumor necrotizing factor [31], improving immunological features of blood and small intestine, and modulating bacterial population of caecum [26] are possible causes of OAs immuno-potentiation effect. In the study of Rodríguez-Lecompte et al. [120], the treatment of broiler chickens with OAs blend up-regulated the interferon-γ in the caecal tonsils and the interleukin (IL-6) and IL-10 in the ileum. Similarly, Lee et al. [121] reported that the dietary addition of OAs activated the regulatory T cells and reduced the inflammatory response signal (α 1-acid glycoprotein) in broilers following vaccination with AI (H9N2) virus vaccine. Moreover, the gut associated immunity produced by the lymphoid tissues was linked with the gut bacteria following the treatment with OAs [63]. The immuno-protective effects of OAs against broilers coccidiosis were also reported [31,66]. However, Hedayati et al. [44] found no significant difference among the dietary treatments with blends of different OAs and the antibody titers against ND, infectious bursal disease, and AI viruses in broilers.

Table 1. The effects of different OAs inoculation in the feed of poultry.

Organic acid (s)	Effects	Reference
Dietary ascorbic acid, malic acid, and tartaric acid	↑ BWG and feed efficiency	[122]
0.5, 1, 2, 4, and 6% of acetic acid, citric acid, lactic acid, malic acid, mandelic acid, propionic acid, or tartaric acid, respectively	↓ *S. typhimurium* colonization count	[123]
0.5-1% fumeric acid	Improved metabolizable energy	[124]
0.16% butyric acid	↓ *Salmonella* count in caecum	[125]
0.2% butyric acid	↑ Carcass weight, breast muscles yield, and dressing % ↑ FCR ↓ Abdominal fat	[91]
Dietary citric acid	↑ FI	[126]
5 and 10 g/kg formic acid	Improved ileal nutrient digestibility	[83]
5000 and 10,000 ppm formic acid	↑ Growth ↑Apparent ileal digestibility	[100]
0.05% sodium butyrate	↓ *Lactobacilli* and *E. coli*	[127]
Butyric acid 285 mg/kg of feed	↑ Eggshell strength ↓ Mal-formed eggs	[128]
A combination of acetic acid, citric acid, and lactic acid	↑ BW	[129]
A dietary mixture of formic (70%) and propionic acid (30%)	Improved FI in a quadratic form	[130]
Dietary citric acid and phytase	↑ Specific gravity and eggshell thickness ↓ Egg weight	[90]
0.5% citric acid or avilamycin, and their combination	↑ FI, growth, carcass yield, and bone ash ↑ *Lactobacillus* spp. development ↓ Growth and proliferation of *Salmonella* and *E. coli* ↑ Phosphorus utilization in intestine	[72]
0.09% free or protected sodium butyrate	↓ *S.* enteritidis in crop, cecum, and liver	[131]
Dietary citric acid	↑ Lymphocyte number in lymphoid organs	[132]
0.45% of potassium diformate	↓ Reduced necrotic enteritis-related mortality and the amount of *C. perfringens* in the jejunum	[133]
Dietary 0.4% butyric acid	↑ BWG and FCR	[134]
Dietary 3% citric acid	↓ Ileal coliform contents	[135]
Formic acid in the drinking water	No effect on the counts of total organisms and *E. coli* in intestine	[136]
3% butyric acid	↓ Crop pH and caecal coliform count ↑ Intestinal length	[137]
0.50% formic acid, 0.50% fumaric acid, 0.25% acetic acid, and 2.0% citric acid	↑ Villus height in duodenum	[30]

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250–7,000mg/kg N-butyric acid	↓ *S. Typhimurium* or *C. perfringens* colonization	[138]
Dietary 0.15% blend of OAs for broilers	↑ Antibody titers against ND at 21 days old	[116]
1% a mixture of formic acid (32%), acetic acid (7%), ammonium format (20%), mono- and diglyceride of unsaturated fatty acids, and copper acetate in the drinking water of *C. jejuni* infected broilers	↑ FI No effect on the BWG and FCR	[61]
1% formic acid in feed for 5 days	↓ *Salmonella* count	[139]
3% butyric acid, 3% fumaric acid, and 3% lactic acid in the drinking water of broilers	↑ BW Improved FCR No effect on the cumulative FI	[140]
0.1% butyric acid	↓ *Salmonella* count in caecum	[141]
Soft Acid S includes 60% formic acid, 20% propionic acid and 20% soft acid and Soft Acid P consists of 70% propionic acid, 5% citric acid and 25% soft acid (2.5 kg/ton of feed of layer chickens)	↑ Small intestinal villi ↓ The total bacteria, total yeast-fungi account, and sheep red blood cells levels No effect on the FI, egg production, egg weight, and FCR No effect on the shell stiffness, shape index, shell thickness, albumen index, yolk index, and Haugh Unit	[142]
0.075% a blend of formic acid, acetic acid, propionic acid, and sorbic acid; medium-chain fatty acids combined with ammonium formate; and coconut/palm kernel fatty acid distillate in their water	No growth-promoting effects	[143]
0.4% formic acid, propionic acid	Improved villus height: crypt depth ratio	[144]
1% fumaric acid in diets	↑ BWG	[145]
1-3 g/kg (0.1–0.3%) of a blend of formic acid, lactic acid, malic acid, tartaric acid, citric acid, and orthophosphoric acid in the drinking water	↑ The apparent metabolizable energies and total phosphorous ileal digestibility ↑ BW, average daily gain, and average daily FI Negative impact on FCR	[146]
0.05% encapsulated butyrate	↑ Intestinal weight and epithelial cell area	[74]
2 g/kg organic oil blend	Villus height in ileum	[147]
0.02%, 0.03% and 0.04% protected calcium butyrate	↑ BWG ↑ Mucosa thickness, villus length, and crypt depth	[148]
2% citric acid	↑ Epithelial cell proliferation and villi height of gastrointestinal tract	[149]
5g/kg formic acid	↑ BWG, dressing % ↓ FCR	[150]
3 kg/ton a commercial acidifier	↑ Average daily gain ↓ FCR	[151]
0.1, 0.02, and 0.04% of formic and propionic acids	↑ Beneficial intestinal bacterial flora load ↓ *E. coli* (K:88) ↑ Growth performance parameters	[88]

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	↑ IgG titer to sheep red blood cells and vaccination with infectious bursal disease and infectious bronchitis viruses	
0.1% and 0.3% formic acid and citric acid for ducklings	↑ BW, BWG, and FCR	[152]
0.05 or 0.1% Encapsulated sodium butyrate	↑ Ileal energy digestible coefficient	[72]
2 g/kg OAs combined with 2 g/kg probiotics	↑ Villus height and crypt depth	[153]
800mg/kg micro encapsulated sodium butyrate	↑ BW, daily gain, and FCR	[154]
0.1% fermented fatty acids of wheat bran	↓ *Salmonella* count	[58]
1% formic acid in water of *S. typhimurium* infected broilers	↓ Decreased BW	[155]
0.05 % encapsulated butyric acid	↑ *Lactobacilli* and *Bifidobacterium* ↓ *Salmonella* and coliform No effect on amylase, protease, and lipase	[156]
Protected or unprotected 0.1% butyrate	No effect on gut weight, retention time, dry matter, organic matter, Nitrogen, and non-protein nitrogen	[157]
0.2% mixture of 32% fumaric acid, 3% formic acid, 13% lactic acid, 3% propionic acid, and 1% citric acid	↑ The expression of tight junction proteins and performance	[69]
0.1%, 0.15%, and 2% a blend of ortho phosphoric acid, formic acid, and propionic acid in the drinking water	↓ Growth performance parameters	[158]
Dietary 0.30 g/ kg sorbic acid and fumaric acid	↑ Secretion of trypsin, lipase, and chymotrypsin in the intestine ↑ Spleen index ↑ Ig A in duodenal and ileal mucosa	[75]
0.06% sodium butyrate	↑ *Lactobacilli* ↓ *E. coli* in Ileum	[159]
A combination of sodium butyrate, citric acid, phosphoric acid, acetic acid, propionic acid, formic acid, and lactic acid	↑ Growth performance parameters	[160]
3 g/kg organic acid blend in Japanese quails	↑ Villus height and width in jejunum and dudenum	[161]
A blend of OAs (0.1%) in the drinking water of broiler chickens orally challenged with (10^9 CFU/mL) *C. jejuni*	↓ *C. jejuni* counts	[162]
0.9% formic acid and sodium format	↓ *S. typhimurium* colonization ↑ Growth performance parameters	[163]
Dietary fumaric acid	↑Erythrocyte counts, hemoglobin concentration, and the serum total protein, albumin, globulin, total cholesterol, high-density lipoprotein cholesterol	[164]

0.1% (formic acid, acetic acid, and ammonium formate) in drinking water of broilers	↑ Growth performances ↑ *Actinobacteria* count ↓ *Proteobacteria*, *Verrucomicrobia*, and *Cyanobacteria* count The relative abundance of the *Bacteroidetes*, *Firmicutes*, and the Firmicutes/Bacteroidetes ratio were not affected	[165]
0.6 and 1.2g/kg Sodium butyrate	↑ Average daily gain and FCR	[166]
3% fumaric acid in a diet	↓ Cholesterol and total lipids	[167]
Encapsulated organic acids of formic acid, acetic acid, and butyric acid, besides, essential oils thymol, carvacrol,β-cymene, borneol and myrcene coated with a matrix of triglyceride	↑ Epithelium thickness and surface area	[105]
0.5 kg/ton feed formic acid with cinnamaldehyde	↓ Proliferation of *C. coli* No effect on the cecal and carcass surface loads	[168]
0.2% butyric acid	No significant effect on dry matter, crude protein, ether extract, calcium, phosphorus, and apparent metabolized energy	[169]
0.2% a mixture of 32% fumaric acid, 3% formic acid, 13% lactic acid, 3% propionic acid, and 1% citric acid	↓ *E. coli* population ↑ *Lactobacillus* spp. and *E. coli* ratio in the ileum and caecum	[64]
0.3% a blend of acetic acid, propionic acid, formic acid, and ammonium formate	↑ Villus height	[4]
Dietary supplementation of phosphoric acid (0.1, 0.2, and 0.3/kg) and lactic acid (0.3 g/kg).	↑ Feed-to-gain ratio ↑ Trypsin, chymotrypsin, and lipase secretion in the duodenum ↑ Breast and thigh muscle pH value ↓ Cooking loss and meat tenderness ↓ Abundance of *E. coli* and *Salmonella* ↑ Villus height of the duodenum	[86]
1 g/kg of diet a mixture of formic acid 40%, formate 40%, and sodium 20%	↑ Serum glucose level	[170]
0.5-2.5 g/kg feed short and medium chain fatty acids	↓ *C. perfringens* shedding in the caecum	[171]
A blend of formic acid, acetic acid, and ammonium formate (1.5 ml/L drinking water) + a blend of encapsulated butyrate, encapsulated multi-chain fatty acids, OAs mainly sorbic acid, and phenolic compound) was added to the basal diets at 0.15% and 0.1% in *Eimeria* spp. challenged broilers	↑ Average BW, average BWG, and FCR ↑ TNF-γ ↓ Intestinal crypt depth ↑ Villus-height: crypt depth ratio ↑ Intestinal goblet cells ↑ *Lactobacillus reuteri*, *Cyanobacteria*	[31]

0.3% a mixture of 11% formic acid, 13% ammonium formate, 5.1% acetic acid, 10% propionic acid, 4.2% lactic acid, and 2% of other lower levels of OAs (sorbic acid and citric acid) (3000 mg/kg diet)	↑ Formic acid in cecal contents on day 21 and acetic acid, propionic acid, butyric acid, and the total volatile fatty acids in the cecal content on day 42. ↑ IgA, D-lactate, and IL-10 ↓ pH value in duodenum ↑Amylase activity of the pancreas and the tight junction protein (mainly Claudin-1, Claudin-2, and ZO-1) in duodenum ↑ Villus: crypt ratio in ileum Modulate s microbiota structure ↓ Abundance of *E. coli*	[26]
Dietary fumaric acid (15 g/kg feed) in Japanese quails	↑ BW, BWG, and FCR	[27]
0.1% organic acid	↑ villus height of jejunum	[70]
A blend of formic acid (32%), acetic acid (7%), and ammonium formate (20%)	Formic acid improved the physical growth, digestibility, immunity, and antimicrobial activity Acetic acid showed anti-bacteria effect	[3]
0, 1, 1.5 g/kg feed formic acid	↑ BW, BWG, and the amount of feed ingested ↓ Glucose, triglycerides, and cholesterol	[28]
A mixture of formic acid (32%), acetic acid (7%), ammonium format (20%), mono- and diglyceride of unsaturated fatty acids, and copper acetate (Under high stocking density)	↓ Chyme pH value in the proventriculus, gizzard, and duodenum ↑ acetic acid, butyric acid, and isovaleric acid in cecal chyme ↓ Valeric acid in cecal chyme	[54]
A combination of both OAs blend (formic acid, propionic acid, ammonium formate, and ammonium propionate) (200 mg/kg) and essential oils mixture (150mg/kg)	Improve BWG and FCR ↑ Villus height ↓ Growth of *C. perfringens*, *E. coli*, and *Salmonella* ↓ Intestinal lesion score ↓ Serum level of calprotectin and liver enzymes	[15]

↓= Decrease ↑= Increase.

3. Conclusion

The supplementation of poultry feed with OAs could improve performance of broilers and layers, carcass traits, gut health, colonization of beneficial bacteria, and the immune response, but reduced the intestinal load of pathogenic bacteria. Therefore, they were highly valuable that might have contributed to improve the birds' performance and health and improved performance and they could be used as an alternative to antibiotics in the poultry feed.

Author Contributions: WAA collected the date: wrote, prepared, and submitted the original article draft, as well as revised and edited the article. The author has read and agreed to the published version of the manuscript.

Funding: This article received no external funding.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflicts of Interest: The author declares no conflicts of interest.

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References

1. Haulisah, N.A.; Hassan, L.;Bejo, S.K.; Jajere, S.M.; Ahmad, N.I. High levels of antibiotic resistance in isolates from diseased livestock. *Front. Vet. Sci*. **2021**, *8*, 652351. https://doi.org/10.3389/fvets.2021.652351
2. Robinson, K.; Becker, S.; Xiao, Y.; Lyu, W.; Yang, Q.; Zhu, H.; Yang, H.; Zhao, J.; Zhang, G. Differential impact of sub therapeutic antibiotics and ionophores on intestinal microbiota of broilers. *Microorganisms*. **2019**, *7*, 282. https://doi.org/10.3390/microorganisms7090282
3. Khan, R.U.; Naz, S.; Raziq, F.; Qudratullah, Q.; Khan, N.A.; Laudadio, V.; Tufarelli, V.; Ragni, M. Prospects of organic acids as safe alternative to antibiotics in broiler chickens diet. *Environ. Sci. Pollut. Res. Int*. **2022**, *29*, 32594–32604. https://doi.org/10.1007%2Fs11356-022-19241-8
4. Dai, D.; Qiu, K.; Zhang, H.J.; Wu, S.G.; Han, Y.M.; Wu, Y.Y.; Qi, G.; Wang, J. Organic acids as alternatives for antibiotic growth promoters alter the intestinal structure and microbiota and improve the growth performance in broilers. *Front. Microbiol*. **2021**, *11*, 618144. https://doi.org/10.3389/fmicb.2020.618144
5. Hafeez, A.; Iqbal, S.; Sikandar, A.; Din, S.; Khan, I.; Ashraf, S.; Khan, R.U.; Laudadio, V.; Tufarelli, V. Feeding of phytobiotics and exogenous protease in broilers: comparative effect on nutrient digestibility, bone strength and gut morphology. *Agriculture*. **2021**, *11*, 228. https://doi.org/10.3390/agriculture11030228
6. Scicutella, F.; Mannelli, F.; Daghio, M.; Viti, C.; Buccioni, A. Polyphenols and organic acids as alternatives to antimicrobials in poultry rearing: a review. *Antibiotics (Basel)*. **2021**, *10*, 1010. https:// doi.org/ 10.3390/antibiotics10081010
7. Adil, S.; Banday, M.T.; Bhat, G.A., Mir, M.S.; Rehman, M. Effect of dietary supplementation of organic acids on performance, intestinal, histomorphology, and serum biochemistry of broiler chicken. *Vet. Med. Int*. **2010**, *2010*, 479485. https://doi.org/10.4061%2F2010%2F479485
8. Dittoe, D.K.; Ricke, S.C.; Kiess, A.S. Organic acids and potential for modifying the avian gastrointestinal tract and reducing pathogens and disease. *Front. Vet. Sci*. **2018**, *5*, 216. https://doi.org/10.3389/fvets.2018.00216
9. Rathnayake, D.; Mun, H.S.; Dilawar, M.A.; Baek, K.S.; Yang, C.J. Time for a paradigm shift in animal nutrition metabolic pathway: Dietary inclusion of organic acids on the production parameters, nutrient digestibility, and meat quality traits of swine and broilers. *Life (Basel)*. **2021**, *11*, 476. https://doi.org/10.3390/life11060476
10. Brzóska, F.; Śliwiński, B.; Michalik-Rutkowska, O. Effect of dietary acidifier on growth, mortality, post-slaughter parameters and meat composition of broiler chickens. *Ann. Anim. Sci*. **2013**, *13*, 85–96. https://doi.org/10.2478/v10220-012-0061-z
11. Pearlin, B.V.; Muthuvel, S.; Govidasamy, P.; Villavan, M.; Alagawany, M., Ragab Farag, M., Dhama, K., Gopi, M. Role of acidifiers in livestock nutrition and health: a review. *J. Anim. Physiol. Anim. Nutr. (Ber)*. **2020**, *104*, 558–569. https://doi.org/10.1111/jpn.13282
12. Vinolya, R.E.; Balakrishnan U.; Yasi, B.; Chandrasekar, S. Effect of dietary supplementation of acidifiers and essential oils on growth performance and intestinal health of broiler. *J. Appl. Poult. Res*. **2021**, *30*, 100179. https://doi.org/10.1016/j.japr.2021.100179
13. AbdEl-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.. Alternatives to antibiotics for organic poultry production: Types, modes of action and impacts on bird's health and production. *Poult. Sci*. **2022**, *101*, 101696. https://doi.org/10.1016/j.psj.2022.101696
14. Pham, V.H.; Abbas, W.; Huang, J.; He, Q.; Zhen, W.; Guo, Y.; Wang, Z. Effect of blending encapsulated essential oils and organic acids as an antibiotic growth promoter alternative on growth performance and intestinal health in broilers with necrotic enteritis. *Poult. Sci*. **2022**, *101*, 101563. https://doi.org/10.1016%2Fj.psj.2021.101563
15. Islam, Z.; Sultan, A.; Khan, S.; Khan, K.; Jan, A.U.; Aziz, T.; Alharbi, M.; Alshammari, A.; Alasmari, A.F. Effects of an organic acids blend and coated essential oils on broiler growth performance, blood biochemical profile, gut health, and nutrient digestibility. *Ital. J. Anim. Sci*. **2024**, *23*, 152–163. https://doi.org/10.1080/1828051X.2023.2297562
16. Rawi, M.H.; Abdullah, A.; Ismail, A.; Sarbini, S.R. Manipulation of gut micro biota using acacia gum polysaccharide. *ACS Omega*. **2021**, *6*, 17782–17797. https://doi.org/10.1021/acsomega.1c00302
17. Ebeid, T.A.; Al-Homidan, I.H. Organic acids and their potential role for modulating the gastrointestinal tract, antioxidative status, immune response, and performance in poultry: a review. *Worlds Poult. Sci. J*. **2022**, *78*, 83–101. https://doi.org/10.1080/00439339.2022.1988803
18. Ricke, S.C. Perspectives on the use of organic acids and short chain fatty acids as antimicrobials. *Poult. Sci*. **2003**, *82*, 632–639. https://doi.org/10.1093/ps/82.4.632
19. Coban, H.B. Organic acids as antimicrobial food agents: applications and microbial productions. Bioprocess Biosyst. Eng. **2020**, *43*, 569–591. https://doi. org/10.1007/s00449-019-02256-w
20. Mohammadpour, A.A.; Kermanshahi, H.; Golian, A.; Gholizadeh, M.; Gilani, A. Evaluation of varying levels of acid-binding capacity of diets formulated with various acidifiers on physical and histological

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

characteristics of leg bones in broiler chickens. *Comp. Clin. Pathol*. **2014**, *23*, 1409–1420. https://doi.org/10.1007/s00580-013-1798-1
21. Hogan, K.; Page, G. Validation of an alternative growth promoter, Presan FY, under research and commercial broiler production conditions in North America. In: Metabolism and Nutrition: Feed Additives I. Poultry Science, United State, 2017; pp. 118.
22. Polycarpo, G.V.; Andretta, I.; Kipper, M,; Cruz-Polycarpo, V.C.; Dadalt, J.C.; Rodrigues, P.H.M.; Albuquerque, R. Meta-analytic study of organic acids as an alternative performance-enhancing feed additive to antibiotics for broiler chickens. *Poult. Sci*., **2017**, *96*, 3645–3653. https://doi.org/10.3382/ps/pex178
23. Adewole, D.I.; Oladokun, S.; Santin, E. Effect of organic acids–essential oils blend and oat fiber combination on broiler chicken growth performance, blood parameters, and intestinal health. *Anim. Nutr*. **2021**, *7*, 1039–1051. https://doi.org/10.1016/j.aninu.2021.02.001
24. Banupriya, S.; Kathirvelan, C.; Patric Joshua, P. Significance of feed acidification in poultry feed. *Int. J. Sci. Environ. Technol*. **2016**, *5*, 1596–1599.
25. Hamid, H.; Shi, H.Q.; Ma, G.Y.; Fan, Y.; Li, W.X.; Zhao, L.H.; Zhang, J.Y.; Ji, C.; Ma, Q.G. Influence of acidified drinking water on growth performance and gastrointestinal function of broilers. *Poult Sci.* **2018**, *97*, 3601–3609. https://doi.org/10.3382/ps/pey212
26. Ma, J.; Mahfuz, S.; Wang, J.; Piao, X. Effect of dietary supplementation with mixed organic acids on immune function, antioxidative characteristics, digestive enzymes activity, and intestinal health in broiler chickens. *Front. Nutr*. **2021**, *8*, 673316. https://doi.org/10.3389/fnut.2021.673316
27. Reda, F.M.; Ismail, I.E.; Attia, A.I.; Fikry, A.M.; Khalifa, E.; Alagawany, M. Use of fumaric acid as a feed additive in quail's nutrition: its effect on growth rate, carcass, nutrient digestibility, digestive enzymes, blood metabolites, and intestinal microbiota. *Poult. Sci.* **2021**, *100*, 101493. https://doi.org/10.1016/j.psj.2021.101493
28. Allaw, A.A.; Hatem, Q.Z.; Kamil, Y.M. Effect of dietary fumaric acid on growth performance and some biochemical parameters in broiler. *IOP Conf. Ser.: Earth Environ. Sci.* **2023**, *1252*, 012120. https://doi.org/10.1088/1755-1315/1252/1/012120
29. Dibner, J.J.; Buttin, P. Use of organic acids as a model to study the digestibility, immune response and intestinal morphology of male broilers fed phosphorus deficient diets supplemented with microbial phytase and organic acids. *Livest. Sci*. **2002**, *157*, 506–513.
30. Ghazalah, A.A.; Atta, A.M.; Elkloub, K.; Mustafa, M.E.L.; Shata, R.F.H. Effect of dietary supplementation of organic acids on performance, nutrients digestibility and health of broiler chicks. *Int. J. Poult. Sci*. **2011**, *10*, 176–184. https://doi.org/10.3923/ijps.2011.176.184
31. Mustafa, A.; Bai, S.P.; Zeng, Q.F.; Ding, X.M.; Wang, J.P.; Xuan, Y.; Su, Z.W.; Zhang, K.Y. Effect of organic acids on growth performance, intestinal morphology, and immunity of broiler chickens with and without coccidial challenge. *AMB Express*. **2021**, *11*, 140. https://doi.org/10.1186/s13568-021-01299-1
32. Dauksiene, A.; Ruzauskas, M.; Gruzauskas, R.; Zavistanaviciute, P.; Starkute, V.; Lele, V.; Klupsaite, D.; Klementaviciute, J.; Bartkiene, E. A comparison study of the caecum microbial profiles, productivity and production quality of broiler chickens fed supplements based on medium chain fatty and organic acids. *Animals (Basel)*. **2021**, 11, 610. https://doi.org/10.3390/ani11030610
33. Melaku, M.; Zhong, R.; Han, H.; Wan, F.; Yi, B.; Zhang, H. Butyric and citric acids and their salts in poultry nutrition: Effects on gut health and intestinal microbiota. *Int. J. Mol. Sci.* **2021**, *22*, 10392. https://doi.org/10.3390%2Fijms221910392
34. Guo, Y.J.; Wang, Z.Y.; Wang, Y.S.; Chen, B.; Huang, Y.Q.; Li, P.; Tan, Q.; Zhang, H.Y.; Chen, W. Impact of drinking water supplemented 2-hydroxy-4-methylthiobutyric acid in combination with acidifier on performance, intestinal development, and microflora in broilers. *Poult. Sci*. **2022**, *101*, 101661. https://doi.org/10.1016/j.psj.2021.101661
35. Hamidifard, M.; Khalaji, S.; Hedayati, M.; Rajaei sharifabadi, H. Use of condensed fermented corn extractives (liquid steep liquor) as a potential alternative for organic acids and probiotics in broiler ration. *Ital. J. Anim. Sci*. **2023**, *22*, 418–429. https://doi.org/10.1080/1828051X.2023.2206420
36. Okey, S.N. Alternative feed additives to antibiotics in improving health and performance in poultry and for the prevention of antimicrobials: A review. *Niger. J. Anim. Sci. Technol*. **2023**, *6*, 65–76.
37. Hermans, D.; Martel, A.; Van Deun, K.; Verlinden, M.; Van Immerseel, F.; Garmyn, A.; Messens, W.; Heyndrickx, M.; Haesebrouck, F.; Pasmans, F. Intestinal mucus protects *Campylobacter jejuni* in the ceca of colonized broiler chickens against the bactericidal effects of medium-chain fatty acids. *Poult. Sci*. **2010**, *89*, 1144–1155. https://doi.org/10.3382/ps.2010-00717
38. Liu, L.; Li, Q.; Yang, Y.; Guo, A. Biological function of short-chain fatty acids and its regulation on intestinal health of poultry. *Front. Vet. Sci*. **2021**, *8*, 736739. https://doi.org/10.3389%2Ffvets.2021.736739
39. Chaveerach, P.; Lipman, L.J.A.; van Knapen, F. Antagonistic activities of several bacteria on in vitro growth of 10 strains of *campylobacter jejuni/coli*. *Int. J. Food Microbiol*. **2004**, *90*, 43–50. https://doi.org/10.1016/s0168-1605(03)00170-3

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

40. Khan, S.H.; Iqbal, J. Recent advances in the role of organic acids in poultry nutrition. *J. Appl. Anim. Res.* **2016**, *44*, 359–369. https://doi.org/10.1080/09712119.2015.1079527
41. Giannenas, I.A.; Papaneophytou, C.P.; Tsalie, E.; Triantafillou, E.; Tontis, D.; Kontopidis, G. A. The effects of benzoic acid and essential oil compounds in combination with protease on the performance of chickens. *J. Anim. Feed Sci*. **2014**, *23*, 73–81. https://doi.org/10.22358/jafs/65719/2014
42. Palamidi, I.; Paraskeuas, V.; Theodorou, G.; Breitsma, R.; Schatzmayr, G.; Theodoropoulos, G.; Kostas, F.; Mountzouris, K.C. Effects of dietary acidifier supplementation on broiler growth performance, digestive and immune function indices. *Anim. Prod. Sci*. **2016**, *57*, 271–281. https://doi.org/10.1071/AN15061
43. Biggs, P.; Parsons, C.M. The effects of several organic acids on growth performance, nutrient digestibilities, and cecal microbial populations in young chicks. *Poult. Sci.* **2008**, *87*, 2581–2589. https://doi.org/10.3382/ps.2008-00080
44. Hedayati, M.; Manafi, M.; Yari, M.; Avara, A. The influence of an acidifier feed additive on biochemical parameters and immune response of broilers. *Annu. Res. Rev. Biol.* **2014**, *4*, 1637–1645. https://doi.org/10.9734/ARRB/2014/8210
45. Eklund T. The antimicrobial effect of dissociated and un-dissociated sorbic acid at different pH levels. *J. Appl. Bacteriol*. **1983**, *54*, 383–389. https://doi.org/10.1111/j.1365-2672.1983.tb02632.x
46. Hajati H. Application of organic acids in poultry nutrition. *Int. J. Avian Wildlife Biol*. **2018**, 3, 324–329. https://doi.org/10.15406/ijawb.2018.03.00114
47. Markazi, A.D.; Luoma, A.; Shanmugasundaram, R.; Muruge san, R.; Mohnl, M.; Selvaraj, R. Effect of acidifier product supplementation in laying hens challenged with Salmonella. *J. Appl. Poult. Res*. **2019**, *28*, 919–929. https://doi.org/10.3382/japr/pfz053
48. Stefanello, C.; Vieira, S.L.; Rios, H.V.; Simoes, C.T.; Ferzola, P.H.; Sorbara, J.O.B.; Cowieson, A.J. Effects of energy, α-amylase, and β-xylanase on growth performance of broiler chickens. *Anim. Feed Sci. Tech*. **2017**, *225*, 205–212. https://doi.org/10.1016/j.anifeedsci.2017.01.019
49. Huyghebaert, G.; Richard, D.; Van Immerseel, F. An update on alternatives to antimicrobial growth promoters for broilers. *Vet. J*. **2011**, *187*, 182–188. https://doi.org/10.1016/j.tvjl.2010.03.003
50. Nguyen, D.H.; Seok, W.J.; Kim, I.H. Organic acids mixture as a dietary additive for pigs—A review. *Animals (Basel)*. **2020**, *10*, 952. https://doi.org/10.3390%2Fani10060952
51. Carrasco, J.M.D.; Casanova, N.A.; Miyakawa, M.E.F. Microbiota, gut health and chicken productivity: what is the connection? *Microorganisms*. **2019**, *7*, 374. https://doi.org/10.3390/microorganisms7100374
52. Jackman, J.A.; Boy, R.D.; Elrod, C.C. Medium-chain fatty acids and monoglycerides as feed additives for pig production: towards gut health improvement and feed pathogen mitigation. *J. Anim. Sci. Bio*. **2020**, *11*, 44. https://doi.org/10.1186/s40104-020-00446-1
53. Galli, G.M.; Aniecevski, E.; Petrolli, T.G.; Da Rosa, G.; Boiago, M.M.; Simões, C.A.; Wagner, R.; Copetti, P.M.; Morsch, V.M.; Araujo, D.N.; Marcon, H.; Pagnussatt, H.; Santos, H.V.; Mendes, R.E.; Loregian, K.E.; Da Silva, A.S. Growth performance and meat quality of broilers fed with micro encapsulated organic acids. *Anim. Feed Sci. Technol*. **2021**, *271*, 114706. https://doi.org/10.1016/j.anifeedsci.2020.114706
54. Hirshfield, I.N.; Terzulli, S.; O'Byrne, C. Weak organic acids: A panoply of effects on bacteria. *Sci. Prog*. **2003**, *86*, 245–270. https://doi.org/10.3184/003685003783238626
55. Han, M.; Chen, B.; Dong, Y.; Miao, Z.; Su, Y.; Liu, C.; Li, J. Evaluation of liquid organic acids on the performance, chyme ph, nutrient utilization, and gut microbiota in broilers under high stocking density. *Animals (Basel)*. **2023**, *13*, 257. https://doi.org/10.3390/ ani13020257
56. Aljumaah, M.R.; Alkhulaifi, M.M.; Abudabos, A.M.; Alabdullatifb, A.; El Mubarak, A.H.; Al Suliman, A.R.; Stanley, D. Organic acid blend supplementation increases butyrate and acetate production in Salmonella enterica serovar Typhimurium challenged broilers. *PLoS One*. **2020**, *15*, 0232831–0232831. https:// doi.org/ 10. 1371/ journal.pone.0232831
57. Khan, R.U.; Chand, N.; Ali, A. Effect of organic acids on the performance of Japanese quails. Pak. J. Zool. **2016**, *48*, 1799–1803.
58. Vermeulen, K.; Verspreet, J.; Courtin, C.; Haesebrouck, F.; Ducatelle, R.; Van Immerseel, F. Reduced particle size wheat bran is butyrogenic and lowers *Salmonella* colonization, when added to poultry feed. *Vet. Microbiol*. **2017**, *198*, 64–71. https://doi.org/10.1016/j.vetmic.2016.12.009
59. Wang, J.; Dai, D.; Zhang, H.J.; Wu, S.G.; Han, Y.M.; Wu, Y.Y.; Qi, G.H. Organic acids modulate systemic metabolic perturbation caused by *Salmonella pullorum* challenge in early-stage broilers. *Front. Physiol*. **2019**, *10*, 1418. https://doi.org/10.3389/fphys.2019.01418
60. El-Saadony, M.T.; Salem, H.M.; El-Tahan, A.M.; Abd El-Mageed, T.A.; Soliman, S.M.; Khafaga, A.F.; Swelum, A.A.; Ahmed, A.E.; Alshammari, F.A.; Abd El-Hack, M.E. The control of poultry salmonellosis using organic agents: An updated overview. *Poult. Sci.* **2022**, *101*, 101716. https://doi.org/10.1016/j.psj.2022.101716
61. Naseri, K.G.; Rahimi, S.; Khaki, P. Comparison of the effects of probiotic, organic acid and medicinal plant on *Campylobacter jejuni* challenged broiler chickens. *J. Agric. Sci. Technol*. **2012**, *14*, 1485–1496. http://dorl.net/dor/20.1001.1.16807073.2012.14.7.15.7

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

62. Hassan, H.M.A.; Mohamed, M.A.; Youssef, A.W.; Hassan, E.R. Effect of using organic acids to substitute antibiotic growth promoters on performance and intestinal microflora of broilers. *Asian-Australas J. Anim. Sci.* **2010**, *23*, 1348–1353. https://doi.org/10.5713/ajas.2010.10085
63. Emami, N.K.; Daneshmand, A.; Naeini, S.Z.; Graystone, E.N.; Broom, L.J. Effects of commercial organic acid blends on male broilers challenged with *E. coli* K88: performance, microbiology, intestinal morphology, and immune response. *Poult. Sci*. **2017**, *96*, 3254–3263. https://doi.org/10.3382/ps/pex106
64. Amer, S.A.; A-Nasser, A.; Al-Khalaifah, H.S.; AlSadek, D.M.M.; Abdel fattah, D.M.; Roushdy, E.M.; Sherief, W.R.I.A.; Farag, M.F.M.; Altohamy, D.E.; Abdel-Wareth, A.A.A.; Metwally, A.E. Effect of dietary medium-chain-monoglycerides on the growth performance, intestinal histomorphology, amino acid digestibility, and broiler chickens' blood biochemical parameters. *Animals (Basel)*. **2021**, *11*, 57. https://doi.org/10.3390/ani11010057
65. Abdelli, N.; Pérez, J.F.; Vilarrasa, E.; Cabeza Luna, I.; Melo-Duran, D.; D'Angelo, M.; Solà-Oriol, D. Targeted-release organic acids and essential oils improve performance and digestive function in broilers under a necrotic enteritis challenge. *Animals (Basel)*. **2020**, 10, 259. https://doi.org/10.3390%2Fani10020259
66. Abdullahi, A.Y.; Yu, X.G.; Fu, Y.Q.; Wang, M.W.; Qi, N.S.; Xia, M.H.; Kallon, S.; Pan, W.D.; Shi, X.L.; Fang, Y. Effects of dietary supplement of organic acids induced protective immunity against coccidiosis. *Iran. J. Appl. Anim. Sci*. **2020**, *10*, 119–129.
67. Khan, R.U.; Naz, S.; Dhama, K.; Kathrik, K.; Tiwari, R.; Abdelrahman, M.M.; Alhidary, I.A.; Zahoor, A. Direct-fed microbial: beneficial applications, modes of action and prospects as a safe tool for enhancing ruminant production and safeguarding health. *Int. J. Pharmacol*. **2016**, *12*, 220–231. https://doi.org/10.3923/ijp.2016.220.231
68. Gonzalez-Fandos, E.; Martinez-Laorden, A.; Perez-Arnedo, I. Combined effect of organic acids and modified atmosphere packaging on listeria monocytogenes in chicken legs. *Animals (Basel).* **2020**, *10*, 1818. https://doi.org/10.3390/ani10101818
69. Rodjan, P.; Soisuwan, K.; Thongprajukaew, K.; Theapparat, Y.; Khongthong, S.; Jeenkeawpieam, J., Salaeharae, T. Effect of organic acids or probiotics alone or in combination on growth performance, nutrient digestibility, enzyme activities, intestinal morphology and gut microflora in broiler chickens. *J. Anim. Physiol. Anim. Nutr. (Berl)*. **2018**, *102*, 931–940. https://doi.org/10.1111/jpn.12858
70. Nguyen, D.H.; Kim, I.H. Protected organic acids improved growth performance, nutrient digestibility, and decreased gas emission in broilers. *Animals (Basel)*. **2020**, *10*, 416. https:// doi.org/ 10. 3390/ ani10 030416
71. Sureshkumar, S.; Park, J.H.; Kim, I.H. Effects of the inclusion of dietary organic acid supplementation with anti-coccidium vaccine on growth performance, digestibility, fecal microbial, and chicken fecal noxious gas emissions. *Braz. J. Poultry Sci*. **2021**, *23*, eRBCA-2020-1425. https://doi.org/10.1590/1806-9061-2020-1425
72. Chowdhury, R.; Islam, K.M.S.; Khan, M.J.; Karim, M.R.; Haque, M.N.; Khatun, M.; Pesti, G.M. Effect of citric acid, avilamycin, and their combination on the performance, tibia ash, and immune status of broilers. *Poult, Sci*. **2009**, *88*, 1616–1622. https://doi.org/10.3382/ps. 2009-00119
73. Liu, J.D.; Bayir, H.O.; Cosby, D.E.; Cox, N.A.; Williams, S.M.; Fowler, J. Evaluation of encapsulated sodium butyrate on growth performance, energy digestibility, gut development, and *Salmonella* colonization in broilers. *Poult. Sci*. **2017**, *96*, 3638–3644. https://doi.org/10.3382/ps/pex174
74. Abdelqader, A.; Al-Fataftah, A.R. Effect of dietary butyric acid on performance, intestinal morphology, microflora composition and intestinal recovery of heat-stressed broilers. Livest. Sci. **2016**, *183*, 78–83. https://doi.org/10.1016/j.livsci.2015.11.026
75. Hassan, R.I., Mosaad, G.M., Abd Elstar, M. Effect of feeding citric acid on performance of broiler ducks fed different protein levels. J. Adv. Vet. Res. **2016**, *6*, 18–26.
76. Yang, X.; Xin, H.; Yang, C.; Yang, X. Impact of essential oils and organic acids on the growth performance, digestive functions and immunity of broiler chickens. *Anim. Nutr*. **2018**, *4*, 388–393. https://doi.org/10.1016/j.aninu.2018.04.005
77. Araujo, R.; Polycarpo, G.; Barbieri, A.; Silva, K.; Ventura, G.; Polycarpo, V.C.C. Performance and economic viability of broiler chickens fed with probiotic and organic acids in an attempt to replace growth-promoting antibiotics. *Braz. J. Poult. Sci*. **2019**, *21*, eRBCA-2018-0912. https://doi.org/10.1590/1806-9061-2018-0912
78. Stefanello, C.; Rosa, D.P.; Dalmoro, Y.K.; Segatto, A.L.; Vieira, M.S.; Moraes, M.L.; Santin, E. Protected blend of organic acids and essential oils improves growth performance, nutrient digestibility, and intestinal health of broiler chickens undergoing an intestinal challenge. *Front. Vet. Sci*. **2020**, *6*, 491. https://doi.org/10.3389/fvets.2019.00491
79. Aristimunha, P.C.; Rosa, A.P.; Boemo, L.S.; Garcez, D.C.; Rosa, D.P.; Londero, A.; Scher, A.; Forgiarini, J. A blend of benzoic acid and essential oil compounds as an alternative to antibiotic growth promoters in broiler diets. *J. Appl. Poult. Res*. **2016**, *25*, 455–463. https://doi.org/10.3382/japr/pfw015
80. Yegani, M.; Korver, D.R. Factors affecting intestinal health in poultry. *Poult. Sci*. **2008**, 87, 2052–2063. https://doi.org/10.3382/ps.2008-00091
81. Mourya, P.S. Nutrient utilization and growth performance of broilers on dietary supplementation of acidifiers. *Ind. J. Anim. Nutr*. **2011**, *28*, 98–101.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

82. Hashemi, S.R.; Zulkifli, I.; Davoodi, H.; Zunita, Z.; Ebrahimi, M. Growth performance, intestinal microflora, plasma fatty acid profile in broiler chickens fed herbal plant (*Euphorbia hirta*) and mix of acidifiers. *Anim. Feed Sci. Technol*. **2012**, *178*, 167–1674. https://doi.org/10.1016/J.ANIFEEDSCI.2012.09.006
83. Hernández, F.; García, V.; Madrid, J.; Orengo, J.; Catalá, P.; Megías, M.D. Effect of formic acid on performance, digestibility, intestinal histomorphology and plasma metabolite levels of broiler chickens. *Br. Poult. Sci*. 2006, 47, 50–56. https:// doi.org/ 10. 1080/00071660500475574
84. Kong, L.J.; Zheng, Y.W.; Lai, C.H.; Wang, X.Y.; Zeng, X. Effects of the cooperation of EM and acidifier on digestive enzyme activity, blood biochemical indes and calcium and phosphorus metabolism of broiler. *Shandong Poult*. **2003**, *6*, 10–13 [In Chinese)].
85. Luckstadt, C.; Mellor, S. The use of organic acids in animal nutrition, with special focus on dietary potassium diformate under European and austral-Asian conditions. *Recent Adv. Anim. Nutr. Aus*. **2011**, *18*, 123–130.
86. Gao, C.Q.; Shi, H.Q.; Xie, W.Y.; Zhao, L.H.; Zhang, J.Y.; Ji, C.; Ma, Q.G. Dietary supplementation with acidifiers improves the growth performance, meat quality and intestinal health of broiler chickens. *Anim. Nutr*. **2021**, *7*, 762–769. https://doi.org/10.1016/j.aninu.2021.01.005
87. Abudabos, A.M.; Alyemni A.H.; Dafalla, Y.M.; Khan, R.U. Effect of organic acid blend and *Bacillus subtilis* alone or in combination on growth traits, blood biochemical and antioxidant status in broilers exposed to *Salmonella typhimurium* challenge during the starter phase. *J. Appl. Anim. Res*. **2017**, *45*, 538–542. https://doi.org/ 10.1080/09712119.2016.1219665
88. Emami, N.K.; Naeini, S.Z.; Ruiz-Feria, C.A. Growth performance, digestibility, immune response and intestinal morphology of male broilers fed phosphorus deficient diets supplemented with microbial phytase and organic acids. *Livest. Sci*. **2013**, *157*, 506–513. https://doi.org/10.1016/j.livsci.2013.08.014
89. Dhawale, A. Better eggshell quality with a gut acidifier. *Poult. Int*. **2005**, 44, 18–21.
90. Nezhad, Y.E.; Sis, N.M.; Shahryar, H.A.; Dastouri, M.R.; Golshani, A.A.; Tahvildarzadeh, A.; Najafyan, K.A. The effects of combination of citric acid and microbial phytase on the egg quality characteristics in laying hens. Asian J. Anim. Vet. Adv. **2008**, *3*, 293–297. https://doi.org/10.3923/ajava.2008.293.297
91. Leeson, S.; Namkung, H.; Antongiovanni, M.; Lee, E.H. Effect of butyric acid on the performance and carcass yield of broiler chickens. *Poult. Sci*. **2005**, *84*, 1418–1422. https://doi.org/10.1093/ps/84.9.1418
92. Lee, K.H.; Jung, S.; Kim, H.J.; Kim, I.S.; Lee, J.H.; Jo, C. Effect of dietary supplementation of the combination of gallic and linoleic acid in thigh meat of broilers. *Asian-Australas J. Anim. Sci*. **2012**, *25*, 1641–1848. https://doi.org/10.5713%2Fajas.2012.12260
93. Fortuoso, B.F.; Dosreis, J.H.; Gebert, R.R.; Barreta, M,; Griss, L.G.; Casagrande, R.A.; De Cristo, T.G.; Santiani, F.; Campigotto, G.; Rampazzo, L.; Stefani, L.M,; Boiago, M.M,; Lopes, L.Q.; Santos, R.C.V,; Baldissera, M.D,; Zanette, R.A,; Tomasi, T.; Da Silva, A.S. Glycerol monolaurate in the diet of broiler chickens replacing conventional antimicrobials: impact on health, performance and meat quality. Microb. Pathog. **2019**, *129*, 161–167. https://doi.org/10.1016/j.micpath.2019.02.005
94. Wang, Y.B.; Wang, Y.; Lin, X.J.; Gou, Z.Y.; Fan, Q.L.; Ye, J.L.; Jiang, S,Q. Potential effect of acidifier and amylase as substitutes for antibiotic on the growth performance, nutrient digestion and gut microbiota in yellow-feathered broilers. *Animals (Basel)*. **2020**, *10*, 1858. https://doi.org/10.3390%2Fani10101858
95. Strous, G.J.; Dekker, J. Mucin-type glycoproteins. *Crit. Rev. Biochem. Mol. Biol*. **1992**, *27*, 57–92. https://doi.org/10.3109/10409239209082559
96. Khatun, M.; Islam, K.M.S.; Howleder, M.A.R.; Haque, M.N.; Chowdhury, R.; Karim, M.R. Effects of dietary citric acid, probiotic and their combination on the performance, tibia ash and non-specific immune status of broiler. *Ind. J. Anim. Sci*, **2010**, *80*, 813–816.
97. Adil, S.; Banday, T.; Bhat, G.A.; Mir, M.S.; Rehman, M. Effect of dietary supplementation of organic acids on performance, intestinal histomorphology, and serum biochemistry of broiler chicken. *Vet. Med. Int*. **2010**, *2010*, 479485. https://doi.org/10.4061%2F2010%2F479485
98. Alagawany, M.; Elnesr, S.S.; Farag, M.R.; Abd El-Hack, M.E.; Barkat, R.A.; Gabr, A.A.; Foda, M.A.; Noreldin, A.E.; Khafaga, A.F.; El-Sabrout, K.; Elwan, H.A.; Tiwari, R.; Yatoo, M.T.; Michalak, I.; Di Cerbo, A.; Dhama, K. Potential role of important nutraceuticals in poultry performance and health– a comprehensive review. *Res. Vet. Sci*. **2021**, *137*, 9–29. https://doi.org/10.1016/j.rvsc.2021.04.009
99. Cakir, S.; Midilli, M.; Erol, H.; Simsek, N.; Cinar, M.; Altintas, A.; Alp, H.; Altintas, L.; Cengiz, Ö.; Antalyali A. Use of combined pro biotic-prebiotic, organic acid and avilamycin in diets of Japanese quails. *Rev. Med. Vet*. **2008**, *159*, 565–569.
100. García, V.; Catalá-Gregori, P.; Hernández, F.; Megías, M.D.; Madrid, J. Effect of formic acid and plant extracts on growth, nutrient digestibility, intestine mucosa morphology, and meat yield of broilers. *J. Appl. Poult. Res*. **2007**, 16, 555–562. https://doi.org/10.3382/ japr.2006-00116
101. Kum, S.; Eren, U.; Önol, A.G.; Sandikci, M. Effects of organic acid supplementation on the intestinal mucosa in broilers. *Rev. Med. Vet*. **2010**, *10*, 463–468.
102. Dibner, J.J.; Richards, J.D. Antibiotic growth promoters in agriculture: History and mode of action. *Poult. Sci*. **2005**, *84*, 634–643. https://doi.org/10.1093/ps/84.4.634

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

103. Samanta, S.; Haldar, S.; Ghosh, T.K. Comparative efficacy of an organic acid blend and bacitracin methylene disalicylate as growth promoters in broiler chickens: effects on performance, gut histology, and small intestinal milieu. *Vet. Med. Int.* **2010**, *2010*, 645150. https://doi.org/10.4061/2010/645150
104. Corrêa-Oliveira, R.; Fachi, J.L.; Vieira, A.; Sato, F.T.; Vinolo, M.A.R. Regulation of immune cell function by short-chain fatty acids. *Clin. Transl. Immunol*ogy. **2016**, *5*, 73. https://doi.org/10.1038/cti.2016. 17
105. Matty, H.N.; Hassan, A.A. Effect of supplementation of encapsulated organic acid and essential oil Gallant+® on some physiological parameters of Japanese quails. *Iraqi J. Vet. Sci.* **2020**, *34*, 181–188.
106. Adil, S.; Banday, T.; Bhat, G.A.; Salahuddin, M.; Raquib, M.; Shanaz, S. Response of broiler chicken to dietary supplementation of organic acids. *J. Cent. Eur. Agric*. **2011**, *12*, 498–508. https://doi.org/10.5513/JCEA01/12.3.947
107. Qaisrani, S.N.; Van Krimpen, M.M.; Kwakkel, R.P.; Verstegen, M.W.A.; Hendriks, W.H. Diet structure, butyric acid, and fermentable carbo hydrates influence growth performance, gut morphology, and cecal fermentation characteristics in broilers. *Poult. Sci*. **2015**, *94*, 2152–2164. https://doi.org/10.3382/ps/pev003
108. Wu, W.; Xiao, Z.; An, W.; Dong, Y., Zhang, B. Dietary sodium butyrate improves intestinal development and function by modulating the microbial community in broilers. *PLoS One.* **2018**; *13*, e0197762. https://doi.org/10.1371/journal.pone.0197762
109. Elnesr, S.S.; Ropy, A.; Abdel-Razik, A.H. Effect of dietary sodium butyrate supplementation on growth, blood biochemistry, haematology and histomorphometry of intestine and immune organs of Japanese quail. *Animal*. **2019**, *13*, 1234–1244. https://doi.org/10.1017/s1751731118002732
110. Levy, A.W.; Kessler, J.W.; Fuller, L.; Williams, S.; Mathis, G.F.; Lumpkins, B.; Valdez, F. Effect of feeding an encapsulated source of butyric acid (ButiPEARL) on the performance of male Cobb broilers reared to 42 d of age. *Poult. Sci*. **2015**, *94*, 1864–1870. https://doi.org/10.3382/ps/pev130
111. Sikandar, A.; Zaneb, H.; Younus, M.; Masood, S.; Aslam, A.; Khattak, F.; Ashraf, S.; Yousaf, M.S.; Rehman, H. Effect of sodium butyrate on performance, immune status, microarchitecture of small intestinal mucosa and lymphoid organs in broiler chickens. *Asian-Australasian J. Anim. Sci*. **2017**, *30*, 690–699. https://doi.org/10.5713%2Fajas.16.0824
112. Abbas, R.Z.; Munawar, S.H.; Manzoor, Z.; Iqbal, Z.; Khan, M.N.; Saleemi, M.K,; Zia, M.A.; Yousaf, A. Anticoccidial effects of acetic acid on performance and pathogenic parameters in broiler chickens challenged with *Eimeria tenella*. *Pesqui. Vet. Bras.* **2011**, *31*, 99–103. https://doi.org/10.1590/S0100-736X2011000200001
113. Ali, A.M.; Seddiek, S.A.; Khater, H.F. Effect of butyrate, clopidol and their combination on the performance of broilers infected with *Eimeria maxima*. *Br. Poult. Sci*. **2014**, *55*, 474–482. https://doi.org/10.1080/00071668.2014.920488
114. Fascina, V.B.; Pasquali, G.A.M.; Carvalho, F.B. et al. Effects of phytogenic additives and organic acids, alone or in combination, on the performance, intestinal quality and immune responses of broiler chickens. *Rev. Bras. Cienc. Avic*. **2017**, *19*, 497–508. https://doi.org/10.1590/1806-9061-2016-0422
115. Park, J.H.; Park, G.H.; Ryu, K.S. Effect of feeding organic acid mixture and yeast culture on performance and egg quality of laying hens. *Kor. J. Poult. Sci*, **2009**, *29*, 109–115.
116. Houshmand, M.; Azhar, K.; Zulkifli, I.; Bejo, M.H.; Kamyab, A. Effects of non-antibiotic feed additives on performance, immunity and intestinal morphology of broilers fed different levels of protein. S. Afr. J. Anim. Sci. **2012**, *42*, 22–32. http://dx.doi.org/10.4314/sajas.v42i1.3
117. Abbas, G.; Khan, S.H.; Rehman, H. Effects of formic acid administration in the drinking water on production performance, egg quality and immune system in layers during hot season. *Avian Biol. Res*. **2013**, *6*, 227–232. https://doi.org/ 10. 3184/ 17581 5513X 13740 707043279
118. Lee, I.K.; Bae, S.; Gu, M.J.; You, S.J.; Kim, G.; Park, S.M.; Jeung, W.H.; Ko, K.H.; Cho, K.J.; Kang, J.S.; Yun, C.H. H9N2-specific IgG and CD4+ CD25+ T cells in broilers fed a diet supplemented with organic acids. *Poult Sci*. **2017**, *96*, 1063–1070. https://doi.org/10.3382/ps/pew382
119. Zhang, W.H.; Jiang, Y.; Zhu, Q.F.; Gao, F.; Dai, S.F.; Chen, J.; Zhou, G.H. Sodium butyrate maintains growth performance by regulating the immune response in broiler chickens. *Br. Poult. Sci*. **2011**, *52*, 292–301. https://doi.org/10.1080/00071668.2011.578121
120. Rodríguez-Lecompte, J.C.; Yitbarek, A.; Brady, J.; Sharif, S.; Cavanagh, M.D.; Crow, G.; Guenter, W.; House, J.D.; Camelo-Jaimes, G. The effect of microbial nutrient interaction on the immune system of young chicks after early probiotic and organic acid administration. *J. Anim. Sci*. **2012**, *90*, 2246–2254. https://doi.org/10.2527/jas.2011-4184
121. Lee, K.W.; Lillehoj, H.S.; Jeong, W.; Jeoung, H.Y. An Avian necrotic enteritis: experimental models, host immunity, pathogenesis, risk factors, and vaccine development *Poult. Sci*. **2011**, *90*, 1381–1390. https://doi.org/10.3382/ps.2010-01319
122. Vogt, H.; Matthes, S.; Harnisch S. The effect of organic acids in the rations on the performances of broilers and laying hens. *Arch. Geflugelkd*. **1981**, *45*, 221–232.
123. Tamblyn, K.C., Conner, D.E. Bactericidal activity of organic acids against *Salmonella typhimurium* attached to broiler chicken skin. *J. Food Prot*. **1997**, *60*, 629–633. https://doi.org/10.4315/0362-028x-60.6.629

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

124. Runho, R.C.; Sakomura, N.K.; Kuana, S.; Banzatto, D.; Junqueira, O.M.; Stringhini, J.H. Use of an organic acid (fumaric acid) in broiler rations. *Rev. Bras. Zootec*. **1997**, *26*, 1183–1191.
125. Van Immerseel, F.; Fievez, V.; De Buck, J.; Pasmans, F.; Martel, A.; Haesebrouck, F.; Ducatelle, R. Microencapsulated short-chain fatty acids in feed modify colonization and invasion early after infection with Salmonella Enteritidis in young chickens. *Poult. Sci*. **2004**, *83*, 69–74. https://doi.org/10.1093/ps/83.1.69
126. Moghadam, A.N.; Pourreza, J.; Samie, A.H. Effect of different levels of citric acid on calcium and phosphorus efficiencies in broiler chicks. *Pak. J. Biol. Sci*. **2006**, *9*, 1250–1256. https://doi.org/10.3923/pjbs.2006.1250.1256
127. Hu, Z.; Guo, Y. Effects of dietary sodium butyrate supplementation on the intestinal morphological structure, absorptive function and gut flora in chickens. *Anim. Feed Sci. Technol*. **2007**, *132*, 240–249. https://doi.org/10.1016/j.anifeedsci.2006.03.017
128. Sengor, E.; Yardimci, M.; Cetingul, S.; Bayram, I.; Sahin, H.; Dogan, I. Short communication effects of short chain fatty acid (SCFA) supplementation on performance and egg characteristics of old breeder hens. *S. Afr. J. Anim. Sci*. **2007**, *37*, 158–163.
129. Abdel-Fattah, S.A.; El-Sanhoury, M.H.; El-Medany, N.M.; Abdelazeem, F. 2008. Thyroid activity, some blood constituents, organs morphology and performance of broiler chicks fed supplemental organic acids. *Int. J. Poult. Sci*. **2008**, *7*, 215–222. https://doi.org/10. 3923/ijps. 2008.215.222
130. Martinez Do Vale, M.; Menten, J.F.M.; Daroz De Morais, S.C.; Brainer, M.M.A. Mixture of formic and propionic acid as additives in broiler feeds. *Sci. Agric. (Piracicaba, Braz.)*. **2004**, *61*, 371–375.
131. Fernández-Rubio, C.; Ordonez, C.; Abad-González, J.; Garcia-Gallego, A.; Honrubia, M.P.; Mallo, J.J.; Balana-Fouce, R. Butyric acid-based feed additives help protect broiler chickens from *Salmonella enteritidis* infection. *Poult. Sci*. **2009**, *88*, 943–948. https://doi.org/10.3382/ps.2008-00484
132. Haque, M.N.; Chowdhury, R.; Islam, M.A.; Akbar, M.A. Propionic acid is an alternative to antibiotics in poultry diet. *Bangladesh J. Anim. Sci*. **2009**, *38*, 115–122. https://doi.org/10.3329/bjas.v38i1-2.9920
133. Mikkelsen, L.L.; Vidanarachchi, J.K.; Olnood, C.G.; Bao, Y.M.; Selle, P.H.; Choct, M. Effect of potassium diformate on growth performance and gut microbiota in broiler chickens challenged with necrotic enteritis. *Br. Poult. Sci*. **2009**, *50*, 66–75. https://doi.org/10.1080/00071660802613252
134. Panda, A.; Rao, S.R.; Raju, M.; Sunder, G.S. Effect of butyric acid on performance, gastrointestinal tract health and carcass characteristics in broiler chickens. *Asian-Australs. J. Anim. Sci*. **2009**, *22*, 1026–1031. https://doi.org/10.5713/ajas.2009.80298
135. Aydin, A.; Pekel, A.Y.; Issa, G., Demirel, G.; Patterson, P.H. Effect of dietary copper, citric acid, and microbial phytase on digesta pH and ileal and carcass microbiata of broiler chickens fed a low available phosphorus diet. *J. Appl. Poult. Res*. **2010**, *19*, 422–431. https://doi.org/10.3382/japr.2009-00123
136. Açikgöz, Z.; Bayraktar, H.; Altan, Ö. Effects of formic acid administration in the drinking water on performance, intestinal microflora and carcass contamination in male broilers under high ambient temperature. *Asian-Australs. J. Anim. Sci*. **2011**, *24*, 96–102.
137. Adil, S.; Banday, M.T.; Bhat, G.A.; Qureshi, S.D.; Wani, S.A. Effect of supplemental organic acids on growth performance and gut microbial population of broiler chicken. *Livestock Res. Rural Dev*. **2011**, *23*, 241–149.
138. Namkung, H.; Yu, H.; Gong, J.; Leeson, S. Antimicrobial activity of butyrate glycerides toward *Salmonella typhimurium* and *Clostridium perfringens*. *Poult. Sci*. **2011**, *90*, 2217–2222. https://doi.org/10.3382/ps.2011-01498
139. Koyuncu, S.; Andersson, M.G.; Löfström, C.; Skandamis, P.N.; Gounadaki, A.; Zentek, J.; Häggblom P. Organic acids for control of Salmonella in different feed materials. *BMC Vet. Res*. **2013**, *9*, 81. https://doi.org/10.1186/1746-6148-9-81
140. Kamal, A.M.; Ragaa, N.M. Effect of dietary supplementation of organic acids on performance and serum biochemistry of broiler chicken. *Nat. Sci*. **2014**, *12*, 38–45.
141. Cerisuelo, A; Marín, C.; Sánchez-Vizcaino, F.; Gómez, E.A.; De La Fuente, J.M.; Durán, R.; Fernández, C. The impact of a specific blend of essential oil components and sodium butyrate in feed on growth performance and *Salmonella* counts in experimentally challenged broilers. *Poult. Sci*. **2014**, *93*, 599–606. https://doi.org/10.3382/ps.2013-03528
142. Gül, M.; Ali Tunç, M.; Seyda Cengiz; Yildiz, A. Effect of organic acids in diet on laying hens' performance, egg quality indices, intestinal microflora, and small intestinal villi height. *Europ. Poult. Sci*., **2014**, *78*, 1–9. http://dx.doi.org/10.1399/eps.2013.5
143. Jansen, W.; Reich, F.; Klein, G. Large-scale feasibility of organic acids as a permanent preharvest intervention in drinking water of broilers and their effect on foodborne Campylobacter spp. before processing. *J. Appl. Microbiol*. **2014**, *116*, 1676–1687. https://doi.org/10.1111/jam.12490
144. Agboola, A.F.; Omidiwura, B.R.O.; Odu, O.; Popoola, I.O.; Iyayi, E.A. Effects of organic acid and probiotic on performance and gut morphology in broiler chickens. *S. Afr. J. Anim. Sci*. **2015**, *45*, 494–501. https://doi.org/10.4314/sajas.v45i5.6
145. Banday, M.T.; Adil, S.; Khan, A.A.; Untoo, M. A study on efficacy of fumaric acid supplementation in diet of broiler chicken. *Int. J. Poult. Sci*. **2015**, *14*, 589–594. https://doi.org/10.3923/ijps.2015.589.594

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

146. Khooshechin, F.; Hosseini, S.M.; Nourmohammadi, R. Effect of dietary acidification in broiler chickens: 1. Growth performance and nutrients ileal digestibility. *Ital. J. Anim. Sci*. **2015**, *14*, 3885. https://doi.org/10.4081/ijas.2015.3885
147. Basmaciolu-Malayoglu, H.; Ozdemir, P.; Bagriyanik, H.A. Influence of an organic acid blend and essential oil blend, individually or in combination, on growth performance, carcass parameters, apparent digestibility, intestinal microflora and intestinal morphology of broilers. *Br. Poult. Sci*. **2016**, *57*, 227–234. https://doi.org/10.1080/00071668.2016.1141171
148. Kaczmarek, S.A.; Barri, A.; Hejdysz, M.; Rutkowski, A. Effect of different doses of coated butyric acid on growth performance and energy utilization in broilers. *Poult. Sci*. **2016**, *95*, 851–859. https://doi.org/10.3382/ps/pev382
149. Mohammadagheri, N.; Najafi, R.; Najafi, G. Effects of dietary supplementation of organic acids and phytase on performance and intestinal histomorphology of broilers. *Vet. Res. Forum*. **2016**, *7*, 189–195.
150. Naela, M.; Korany, R.M. Studying the effect of formic acid and potassium deformity on performance, immunity and gut health of broiler chickens. *Anim. Nutr*. **2016**, *2*, 296–302. https://doi.org/10.1016/j.aninu.2016.08.003
151. Ding, X.; Yang, C.W.; Yang, Z.B.; Yang, W.R.; Jiang, S.Z.; Yi Wen, K.E. Effects of feed acidifiers on growth performance, caecum micro flora and nutrient and energy utilisation in broilers. *Eur. Poult. Sci*. **2017**, *81*, 180. http://dx.doi.org/10.1399/eps.2017.180
152. Elnaggar, A.S.; Abo El-Maaty, H.M.A. Impact of using organic acids on growth performance, blood biochemical and hematological traits and immune response of ducks (*Cairina moschata*). *Egypt. Poult. Sci. J.* **2017**, *37*, 907–925. https://dx.doi.org/10.21608/epsj.2017.7740
153. Rodjan, P.; Soisuwan, K.; Thongprajukaew, K.; Theapparat, Y.; Khongthong, S.; Jeenkeawpieam, J.; Salaeharae T. Effect of organic acids or probiotics alone or in combination on growth performance, nutrient digestibility, enzyme activities, intestinal morphology and gut microflora in broiler chickens. *J. Anim. Physiol. Anim. Nutri (Berl)*. **2017**, *102*, 931–940. https://doi.org/10.1111/jpn.12858
154. Song, B.; Li, H.; Wu, Y.; Zhen, W.; Wang, Z.; Xia, Z.; Guo, Y. Effect of microencapsulated sodium butyrate dietary supplementation on growth performance and intestinal barrier function of broiler chickens infected with necrotic enteritis. *Anim. Feed Sci. Technol*. **2017**, *232*, 6–15. https://doi.org/10.1016/j.anifeedsci.2017.07.009
155. Bourassa, D.V.; Wilson, K.M.; Ritz, C.R.; Kiepper, B.K.; Buhr, R.J. Evaluation of the addition of organic acids in the feed and/or water for broilers and the subsequent recovery of *Salmonella typhimurium* from litter and ceca. *Poult. Sci*. **2018**, *97*, 64–73. https://doi.org/10.3382/ps/pex289
156. Jazi, V.; Foroozandeh, A.D.; Toghyani, M.; Dastar, B.; Koochaksaraie, R.R. Effects of *Pediococcus acidilactici*, mannan-oligosaccharide, butyric acid and their combination on growth performance and intestinal health in young broiler chickens challenged with *Salmonella typhimurium*. *Poult. Sci*. **2018**, *97*, 2034–2043.
157. Moquet, P.C.A.; Salami, S.A.; Onrust, L.; Hendriks, W.H.; Kwakkel, R.P. Butyrate presence in distinct gastrointestinal tract segments modifies differentially digestive processes and amino acid bioavailability in young broiler chickens. *Poult. Sci*. **2018**, *97*, 167–176. https://doi.org/10.3382/ps/pex279
158. Sultan, A.; Khan, S.; Khan, S.; Chand, N.; Khan, M.S.; Maris, H. Effect of organic acid blend on carcass yield, nutrient digestibility and tibia ash during starter phase of broiler chicks. *Pak. J. Zool*. **2018**, *50*, 1483–1488. http://dx.doi.org/10.17582/journal.pjz/2018.50.4.1483.1488
159. Makled MN, Abouelezz KFM, Gad-Elkareem AEG and Sayed AM (2019) Comparative influence of dietary probiotic, yoghurt, and sodium butyrate on growth performance, intestinal microbiota, blood hematology, and immune response of meat-type chickens. Tropical Animal Health and Production 51, 2333–2342.
160. Sabour, S.; Tabeidian, S.A.; Sadeghi, G. Dietary organic acid and fiber sources affect performance, intestinal morphology, immune responses and gut microflora in broilers. *Anim. Nutr*. 2019, 5, 156–162. https://doi.org/10.1016/j.aninu.2018.07.004
161. Ustundag, O.A.; Ozdogan, M. Effects of bacteriocin and organic acid on growth performance, small intestine histomorphology, and microbiology in Japanese quails (*Coturnix coturnix* japonica). *Trop. Anim. Health Prod*. **2019**, *51*, 2187–2192. https://doi.org/10.1007/s11250-019-01931-0
162. Wang, Z.C.; Yu, H.M.; Xie, J.J.; Cui, H.; Gao, X.H. Effect of pectin oligosaccharides and zinc chelate on growth performance, zinc status, antioxidant ability, intestinal morphology and short-chain fatty acids in broilers. *J. Anim. Physiol. Anim. Nutr. (Berl)*. **2019**, *103*, 935–946. https://doi.org/10.1111/jpn.13076
163. Adhikari, P.; Yadav, S.; Cosby, D.E.; Cox, N.A.; Jendza, J.A.; Kim, W.K. Research Note: Effect of organic acid mixture on growth performance and Salmonella typhimurium colonization in broiler chickens. *Poult. Sci*. **2020**, *99*, 2645–2649. https://doi.org/10.1016/j.psj.2019.12.037
164. Ding, J.; He, S.; Xiong, Y.; Liu, D.; Dai, S.; Hu, H. Effects of dietary supplementation of fumaric acid on growth performance, blood hematological and biochemical profile of broiler chickens exposed to chronic heat stress. *Braz. J. Poult. Sci*. **2020**, *22*, eRBCA-2019-1147. https://doi.org/10.1590/1806-9061-2019-1147
165. Hu, Y.; Wang, L.; Shao, D.; Wang, Q.; Wu, Y.; Han, Y.; Shi, S. Selectived and reshaped early dominant microbial community in the cecum with similar proportions and better homogenization and species

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 August 2024 doi:10.20944/preprints202408.1770.v1

diversity due to organic acids as AGP alternatives mediate their effects on broilers growth. *Front. Microbiol.* **2020**, *10*, 2948. https://doi.org/10.3389/fmicb.2019.02948
166. Lan, R.X.; Li, S.Q.; Zhao, Z.; An, L. Sodium butyrate as an effective feed additive to improve growth performance and gastrointestinal development in broilers. *Vet. Med. Sci.* **2020**, *6*, 491–499. https://doi.org/10.1002%2Fvms3.250
167. Mahmoud, H.; Afiffy, O.; Mahrous, M. Effect of using formic acid on growth performance and some blood parameter of broiler chicken. *Assiut Vet. Med. J.* **2020**, *66*, 140–154. https://doi.org/10.21608/avmj.2020.167272
168. Mortada, M.; Cosby, D.E.; Shanmugasundaram, R.; Selvaraj, R.K. In vivo and in vitro assessment of commercial probiotic andorganic acid feed additives in broilers challenged with *Campylobacter coli*. *J. Appl. Poult. Res.* **2020**, *29*, 435–446. https://doi.org/10.1016/j.japr.2020.02.001
169. Nari, N.; Ghasemi, H.A. Growth performance, nutrient digestibility, bone mineralization, and hormone profile in broilers fed with phosphorus deficient diets supplemented with butyric acid and *Saccharomyces boulardii*. *Poult. Sci.* **2020**, *99*, 926–935. https://doi.org/10.1016/j.psj.2019.10.046
170. Iqbal, H.; Rahman, A.; Khanum,S.; Arshad, M.; Badar, I.H.; Asif, A.R.; Hayat, Z.; Iqbal, M.A. Effect of essential oil and organic acid on performance, gut health, bacterial count and serological parameters in broiler. *Braz. J. Poult. Sci.* **2021**, *23*, eRBCA-2021-1443. https://doi.org/10.1590/1806-9061-2021-1443
171. Kumar, A.; Toghyani, M.; Kheravii, S.K.; Pineda, L.; Han, Y.; Swick, R.A., Wu, S.B. Organic acid blends improve intestinal integrity, modulate short-chain fatty acids profiles and alter microbiota of broilers under necrotic enteritis challenge. *Anim. Nutr.* **2021**, *8*, 82–90. https://doi.org/10.1016/j.aninu.2021.04.003

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