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Chapter

Acidifiers as Alternatives for Antibiotics Reduction and Gut Health Improvement for Poultry and Swine

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Abstract

Using antibiotics of low doses as feed additives could support to improve poultry and swine performances. However, these applications have caused resistance of bacteria and antibiotic residues in foods of animal origins. Therefore, efforts were focused on solutions to replace antibiotics as growth promoters (AGPs). There are many alternatives for AGPs, in which organic acids are one of the important alternatives. The aim of this chapter is to review publications on these acids and their other forms namely as acidifiers using as feed additives including their names and forms, mode of actions, spectrum against bacteria, combinations among them, and latest updates on their effects on swine and poultry production. The scientific findings show that acidifiers can inhibit pathogenic bacteria growth, improve nutrient digestibility, enhance immunity and overall gut health, consequently increase performances of poultry and swine. Several acids and their salts in both liquid and solid forms have been studied and applied as poultry and swine feed additives; however, the efficacy levels and the mode of actions are dependent on the single acidifiers, their salts, and combinations among them. The uses of acidifiers in their salts and derivative forms and mixtures of different acidifiers seem to be more favorable.

Keywords: acidifiers, antibiotics, organic acids, poultry production, swine production

1. Introduction

Antibiotics, since their discovery in the 1920s, have been widely used as antimicrobial growth promoters in animal production to enhance productivity and prevent diseases [1, 2]. However, due to the emerging resistance against microbes and their residues in meat, milk, and egg, the World Health Organization (WHO) published guidance and recommendations to reduce the use of antibiotics in 1997. About a decade later, the European Union imposed a complete ban on the use of prophylactic antibiotics in the animal feedstuff [3, 4]. A withdrawal of growth-promoting antibiotics in livestock production has led to problems like an increase in the incidence of animal diseases and a reduction in productivity [5]. Consequently, various alternatives were sought and explored to replace the use of antibiotics in animal production to maintain performance and their health. The potential substitutes to antibiotics include probiotics and prebiotics, plant extracts, essential oils, antimicrobial peptides, functional amino acids, hyperimmune antibodies, clays, metals, and/or organic acids [6–16]. Among these alternatives, dietary organic acids, also known as acidifiers, have been applied worldwide for decades due to their strong antibacterial, anti-fungal, and anti-mold properties [17]. The organic acids with antibacterial activity are either simple monocarboxylic acid such as butyric acid, propionic acid, acetic acid, and formic acid, or carboxylic acid bearing a hydroxyl group such as tartaric acid, citric acid, malic acid, and lactic acid [18]. These are usually weak organic acids that are capable of lowering the pH of the stomach and in the gastrointestinal tract (GIT), thus inhibiting the growth of pathogenic bacteria, promoting proteolytic enzyme activity and nutrient digestibility, creating stability of the microbial population, and stimulating the growth of beneficial bacteria [19]. Single organic acids have been reported to own a wide range of microbial activities such as physiology, pH range, and membrane structure. Thus, the inclusion of organic acids mixtures in diets is not always consistent, and the response to dietary organic acids could be affected by the type of organic acids, dosage, feed formula, and the age of animals [20]. Therefore, the purpose of this review is to summarize recent studies about responses of swine and poultry to both single and a blend of organic acids aiming to support the overall insight about the effective utilization of organic acids in swine and poultry production for enhancing the performance and gut health. In addition, modes of action of organic acids (OAs) and their classification are also discussed.

2. Classification of acidifiers

Acidifiers, or so-called organic acids, are organic compounds that possess acidic properties. In general, acidifiers are divided into three functional groups including short-chain fatty acids (SCFAs, C1 to C5), medium-chain fatty acids (MCFA; C6 to C12), and tricarboxylic acids (TCA) [21]. In which, SCFAs are most commonly used, such as formic acid (C1), acetic acid (C2), propionic acid (C3), lactic acid (C3), and butyric acids (C4) [22]. These SCFAs are produced in the lower intestine of animals by the microbial fermentation of indigestible sugars and amino acids. Their pKa values are small with a range from higher than 3 to less than 5 (**Table 1**). Since this property, they can selectively inhibit the intestinal bacteria, and thus improve intestinal morphology and decrease the intestinal inflammation [23]. MCFAs are also used in combination with SCFAs as feed additive to enhance the activity of acidifiers in GIT. MCFA can disrupt the phospholipid membrane, thus exhibit potent antibacterial activity. The MCFA commonly used in livestock production include caproic acid (C6), caprylic acid (C8), capric acid (C10), and lauric acid (C12). There has been an increase in recent interest in research relevant to inhibitory activity of MCFA against a wide range of pathogens in the swine industry. For example, lauric acid and a mixture of caprylic and capric acids were reported to exhibit antibacterial activity against pathogenic bacteria such as *Escherichia coli*, *Streptococcus suis*, *Salmonella poona,* and *Clostridium perfringens* [24]. TCA is an organic carboxylic acid whose chemical structure contains three carboxyl functional groups (-COOH). They are metabolic intermediates of Krebs cycle or citric acid cycle, thus are involved in the major energy-yielding metabolic

Classification	Name	Used salts and derivates
Short-chain fatty acid (SCFA)	Formic acid	Ammonium formate Sodium di-formate
	Acetic acid	Sodium acetate
	Propionic acid	Ammonium propionate; Sodium propionate
	Lactic acid	Sodium lactate
	Butyric acid	Sodium butyrate mono, di-, tri-butyrin
	Valeric acid	Glyceride esters
	Benzoic acid	Benzoate
	Malic acid	Sodium, calcium-malate
Medium-chain fatty acid (MDFA)	Caproic acid	Caproates, hexanoates, caproate esters
	Lauric acid	Calcium laurate
	Caprylic acid	—
	Capric acid	—
	Sorbic acid	Calcium sorbate Potassium sorbate Sorbic chloride
Tricarboxylic acid (TCA)	Citric acid	Sodium citrate

Table 1.
Common acidifiers used as additives in swine and poultry production.

pathway in cells. These acids improve gut morphology and barrier function with positive influences on intestinal bacteria community. The best-known TCA is citric acid which has been reported that it can be a potential alternative to antibiotics in animal production [25–27].

Moreover, due to difficulties of using organic acids in practice including offensive odor and their inability to affect the lower part of GIT, different forms of organic acids such as their salts and derivatives have been developed and investigated for their effects on growth performances and gut health [28]. For examples, sodium butyrate and butyrate glycerides (mono-, di-, and tri-butyrin) were reported to have positive influences on animal production including enhancement of gut health, control of pathogens, reduction of inflammation, and improvement of performances [29]. The inclusion of valeric acid glyceride ester in the broiler dietary can improve the feed conversion ratio, positively impact to the intestinal morphology, increase the density of glucagon-like peptide-2 immunoreactive cells, and significantly reduce the number of birds infected necrotic enteritis [30]. Besides, owing to the advantages of today's modern technologies, especially encapsulation technology, which has been widely employed across various scientific fields, including animal nutrition, it effectively overcomes the limitations of conventional feeding methods [31, 32]. Coated organic acids with encapsulated nano/micro materials led to an increase in the stability, bioavailability, and their activity. For example, Feye et al. (2020) and Muniyappan et al. (2021) recently reported that the dietary inclusion of microencapsulated blend of organic acids enhanced the GIT microbiota and may be a viable antibiotic alternative for the swine and poultry industry [33, 34].

3. Mode of action

The use of acidifiers and their salts in the diet of swine and poultry with a reasonable dose can increase the body weight (ADG), improve feed conversion ratio (FCR), and reduce the pathogenic bacteria [35, 36]. Thus, it is necessary to explore the activity of acidifiers. Generally, the mechanisms of action of organic acids include: (i) Lowering of intestinal pH; (ii) Improving nutrient digestibility via the reduction of pH value by release of hydrogen ions in the stomach, thereby activating pepsinogen to form pepsin; (iii) Inhibition of Gram-negative bacteria in the gastrointestinal tract (GIT); (iv) Improved energetic utilization in the intermediate metabolism to enhance endogenous enzyme secretion and chelate minerals; (v) intestinal anti-inflammation and immunity response.

3.1 Lowering of intestinal pH

Organic acids are weak acids in the sense that a certain proportion of the molecules do not fully dissociate. These undissociated, uncharged molecules diffuse easily across the bacterial cell membrane to reach the interior of the cell. After the entry of organic acids into the microbial cell, these acids release the proton (H+) in the more alkaline environment of the cytoplasm, causing a drop of bacterial intracellular pH. This impacts on bacterial metabolism, inhibiting the action of important microbial enzymes. The bacterial cell is forced to use energy to expel the protons, leading to an intracellular accumulation of acid anions. The anions within the bacterial cell are thought to disrupt the metabolic processes in the cell, consequently affecting cell multiplication and limiting growth [4, 17, 18, 36]. There are two major types of organic acids that have different modes of action in decreasing pH. The first group including lactic, fumaric, and citric acid lowers the pH of the stomach leading to indirect reduction of the population of acid sensitive bacteria. The second group including butyric, formic, acetic, propionic, and sorbic has ability to lower the pH of the GIT by penetrating the Gram-negative bacteria cell wall and directly controlling the pathogens [28].

3.2 Improving nutrient digestibility and gut morphology

Since organic acids can reduce the pH value in the GIT, thus, pepsinogen is activated to form pepsin, which causes proteolysis of protein. The protein contents are then broken down into simple peptides and amino acids that can be easily absorbed in the small intestine. In addition, in the presence of an acidic environment, bacterial metabolites such as ammonia and amines are reduced, thereby enhancing digestibility. Therefore, organic acid used as an acidifier in swine and poultry production has been considered to be a potential alternative to antibiotics for improving nutrient digestibility. Previous trials have reported that including 0,5% fumaric acid, 0,5% formic acid, 0,75% acetic acid, or 2% citric acid in broiler diets improved ME, crude protein, ether extract, crude fiber, and nitrogen-free extract [37–39]. Similarly, in swine production, the supplementation of 0,1 or 0,2% of coated organic acid including 17% fumaric acid, 13% citric acid, 10% malic acid, and 1.2% MCFA (capric and caprylic acid) in basal diets linearly increased the dry matter, nitrogen, and energy digestibility [40]. Moreover, low pH also increases the digestibility of nutrients via the changes in the villus height and depth in the small intestines, thus improving the gut morphology and is one of the reasons for the improvement of the feed to gain ratio. For example, in a study by Garciá et al. (2007), broilers fed diets containing 0.5 and

1.0% formic acid exhibited longer villi (1273 and 1250 μm, respectively) compared to the control group (1088 μm) [39]. Panda et al. (2009) reported that the addition of 0.2, 0.4, or 0.6% butyrate in the broiler's diet improved the villus length and crypt depth in the duodenum [41], in which, 0,4% of butyric acid supplementation improved performances. Similarly, Galfi and Bokori (1990) showed an increase in the length of microvilli in the ileum and the depths of the crypts in caecum in growing pigs when fed with 0.17% of sodium butyrate. This dietary increased the average daily body mass gain of pigs by 23.5% [42].

3.3 Inhibition of pathogenic bacteria

It is reported that most common bacteria that affect the intestinal health of both poultry and swine are Gram-negative bacteria such as *Escherichia coli, Salmonella,* and *Campylobacter* which can be controlled by supplementation of organic acids in diets [43–45]. The study in mode of action of organic acids showed that most of pathogenic bacteria reside at a pH close to 7, while useful bacteria survive better at a pH between 5.8 and 6.2. Therefore, owing to the intestinal pH lowering capable of organic acids, the population of the pathogenic microbes is reduced that do not affect to beneficial bacteria. In addition, the efficacy of an acid in inhibition of the pathogenic bacterial growth is dependent on its pKa value—the pH at which the acid is half dissociated. Organic acids, most of them, with antimicrobial activity, have a pKa between 3 and 5 (**Table 2**).

Organic acids with higher pKa values are commonly used as preservatives for animal feed. Their antimicrobial efficacy depends on the increasing number of carbon chains and unsaturation properties [48]. Peh et al. (2020) recently reported in-vitro susceptibility of *Campylobacter spp* to 10 organic acids including caprylic acid, sorbic acid, caproic acid, benzoic acid, ascorbic acid, propionic acid, acetic acid, formic acid, fumaric acid, and tartaric acid. In which, the antimicrobial activity of caprylic acid and sorbic acid against *Campylobacter spp* at the lowest minimum inhibitory concentration values measured at pH 7.3 ranged from 0 to 2 nmol/L and 1 to 4 nmol/L, respectively [47].

Organic acids	pKa value	Minimum inhibitory concentration (nmol/l)	
		E. coli	*Campylobacter jejuni*
Acetic	4.75	1.55	64.00
Benzoic	4.19	0.316	8.0
Butyric	4.81	1.41	nd
Citric	3.13	38.2	nd
Formic	3.75	64.0	128.0
Lactic	3.86	3.72	nd
Malic	3.40	50	nd
Propionic	4.87	64.0	32.0
Sorbic	4.76	4.0	4.0

nd: not detected.

Table 2.
The pKa values of common organic acids and the minimum inhibitory concentration (MIC) of these organic acids against pathogenic bacteria [46, 47].

3.4 Provision of energy source in the GIT

Organic acids act as an energy source in the GIT as they are metabolic intermediates from Krebs cycle, thus directly influencing intestinal metabolic status. For example, Kirchgessner and Roth found that fumaric acid, a product of metabolic pathway in the Kreb cycle, can be used as an energy source with an efficiency close to that of glucose in pigs [49]. In addition, the beneficial effects of organic acids on the growth performance were considered due to their energy contribution. Blank et al. reported that fumaric acid as an available energy source can influence the intestinal mucosa and thus increasing the absorptive surface and capacity of the small intestines due to the rapid recovery of the gut epithelial cells of pigs after weaning [50]. Besides, the intestinal microbiota can ferment fibers and oligosaccharides to produce SCFAs including acetate, propionate, and butyrate. These metabolites play a significant role in maintaining the intestinal homeostasis [51]. SCFAs were reported to contribute 5–15% and 60–70% of the total energy requirements of colonic epithelial cells in humans, respectively. Among SCFAs, butyrate is the major energy source for colonocytes, which have beneficial effects on both cellular energy metabolism and intestinal homeostasis [52]. Donohoe et al. also showed that butyrate maintains energy homeostasis and prevents autophagy by acting as an energy source rather than a histone deacetylase inhibitor in mammalian colon [53].

3.5 Preventing the intestinal inflammation status and supporting immunity homeostasis

There is mechanistic evidence for the effects of SCFA on mucosal immune and inflammatory status, based on studies involving cell lines and small animal models [51]. SCFAs, particularly butyrate, have been shown to exert their effects through

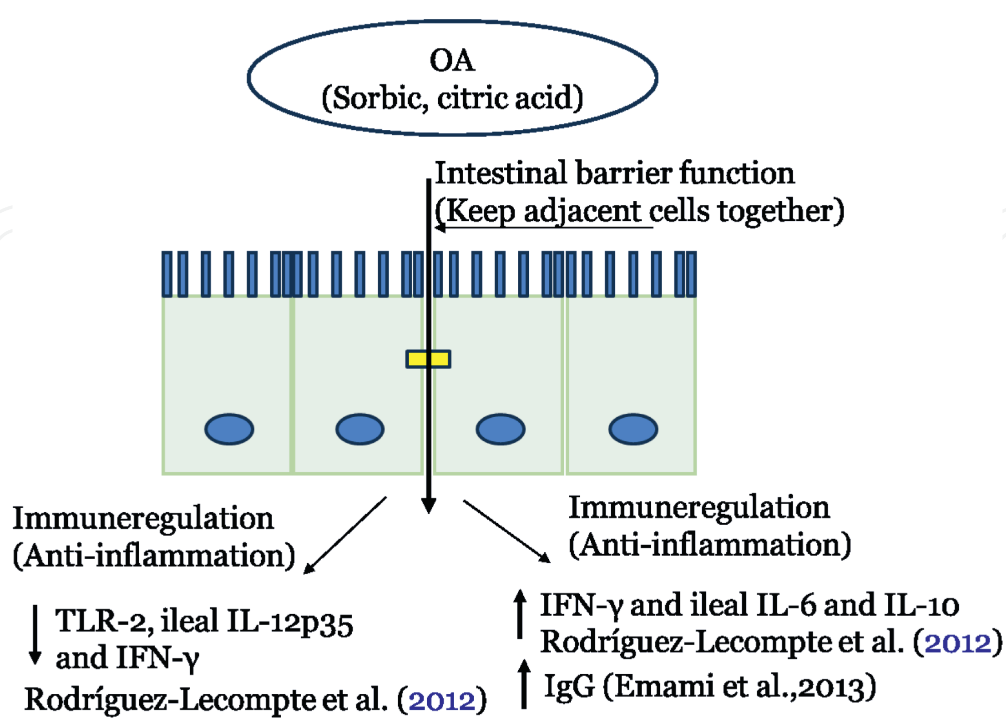

Figure 1.
The role of organic acids (sorbic and acid citric) in the intestinal anti-inflammation and immune response in broiler chickens.

several mechanisms, including the reduction of pro-inflammatory cytokines (INF-γ, TNF-α, IL-1β, IL-6, and IL-8), while also including IL-10 and TGF- β (**Figure 1**).

With this property, butyrate enhances intestinal barrier function and mucosal immunity leading to the enhanced protection against luminal pathogens [52]. For example, feeding the ApoE knockout mice with butyrate decreased the pro-inflammatory cytokines, leading to a reduction in atherosclerotic lesions and a decrease in macrophage migration [54]. Kim et al. (2013) found that SCFAs activate GPR41 and GPR43 in mice intestinal epithelial cells, leading to the production of chemokines and cytokines, which are required for an inflammatory response to bacterial infection [55]. Rodríguez-Lecompte et al. (2012) indicated that broiler chicks fed with probiotics (*Lactobacillus casei*, *Lactobacillus acidophillus*, *Streptococcus faecium*, and *Saccharomyces cerevisiae*) and organic acids (sorbic and citric acid) positively responded to anti-inflammatory via pathways involving cytokines by decreasing TLR-2 and ileal IL-12p35 and increasing IFN-γ and ileal IL-6 and IL-10 [56]. In addition, IgA (SIgA) is the most prominent antibody produced in the intestinal mucosa that protects the intestines against bacterial and viral infections [51]. Schilderink et al. reported that acetate increased fecal IgA and IgA-positive B-cells in the lamina propria of wild-type mice indicating that the process was mediated through specific SCFA receptor interaction [57]. Emami et al. found that broilers fed with phytase and organic acids showed higher IgG in the primary and secondary response compared to the control group [58]. Park et al. noticed that the supplementation of 0.2% organic acid to layer diet aged 75 weeks significantly increased IgY level [59].

4. Effect of acidifiers on swine and poultry production

4.1 Effect of acidifiers on swine production

Previous research showed positive effects of supplementing dietary acidifiers at optimal levels on the performance and gut health of swine at different growth stages (**Table 3**). For example, Li et al. (2008) reported that weanling piglets fed a diet supplemented with 0.5% of a mixture of acidifiers, including calcium salt of 2-hydrozy-4(methylthio) butanoic acid, fumaric acid, and benzoic acid) exhibited better weight gain and feed efficiency ($p < 0,05$), higher levels of lactobacilli in the duodenum, and lower levels of ileal *E. coli* [71]. Kuang et al. (2015) also noted that 21-day-old crossbred pigs, when fed a diet supplemented with 0.3% blends of acidifiers containing citric acid, calcium formate, calcium lactate, and MCFAs (capric, lauric, and myristic acids), experienced improvements in ADG, average daily feed intake (ADFI), increased AA digestibility, and enhanced immunity [72].

It is reported that supplementation of 0.4% acidifier mixture (fumaric, lactic, propionic acids, citric, benzoic) in the dietary of weaning piglets improved the growth performance, feed intake (FI) and gain-to-feed ratio (G: F) compared to the diet without acidifiers supplementation [73]. Regarding the growing pigs and finishing pigs, it is also demonstrated that the supplementation of 0.2% of coated organic acids in the dietary including 10% malic, 13% citric, 17% fumaric acids, and 1.2% MCFA (capric and caprylic acid) has a positive influence on the growth performance. Feces from pigs fed a diet supplemented with this organic acid blend showed a linear reduction ($p < 0.001$) in *E. coli* counts and a tendency for a linear increase ($p = 0.06$) in *Lactobacillus* counts [74]. Zhai et al. (2017) reported that the nursery

Composition of acidifiers	Dose	Age	Growth performance			Gut health	Ref
			ADG	ADF1	G:F		
Single acidifiers							
Fumaric	0,15%, 0,3%	Weaned	*	*	*	NA	[60]
Benzoic	0,3%; 0,5%	Nursery, Grower, Finisher	*	*	*	NA	[61]
Lactic	2,8%	Weaned	NA	NA	NA	Control clinical and subclinical infections of *S. Typhimurium*	[62]
	1,6%		*	*	*	Reduced incidence and severity of diarrhea	[63]
Formic	1,2%	Weaned	*	*	*	Reduced incidence and severity of diarrhea	[63]
Propionic	1,0%	Weaned	*	*	*	Reduced incidence and severity of diarrhea	[63]
Citric acid	1,0%	Weaned	NS	NS	*	Improved intestinal morphology	[26]
Mixture of acidifier							
Formic acid, acetic acid, propionic acid, and butyric acid	1,5 g/kg	Weaned	*	*	*	Increased *lactobacillus*,	[64]
Formic acid, acetic acid, and propionic acid, medium-chain fatty acids (MCFA)		Weaned	*	*	*	Improved intestinal structure	[65]
Formic acid (31.0%), ammonium formate (23.0%), and acetic acid (8.3%)	2 L/ton in drinking water	Weaned	NS	*	NS	Decreased diarrhea rate, regulate gut microbiota	[66]
Formic acid (11%), ammonium formate (13%), propionic acid (10%), acetic acid (5.1%), and citric acid (3.7%)	3 g/kg 5 g/kg	Weaned	*	NS	*	Improved intestinal morphology	[67]
Salts of acidifier							
Encapsulated sodium butyrate	30.00%	Growing-finishing	*	NS	NS	NA	[68]
Sodium butyrate	0.8 g/kg	Weaned	*	*	*	NA	[69]

Composition of acidifiers	Dose	Age	Growth performance			Gut health	Ref
			ADG	ADF1	G:F		
Coated sodium butyrate	300 mg/kg 450 mg/kg	Weaned	*	*	*	*Increased lactobacillus*, decreased *E. coli* counts	[70]

*NA: not available, NS: not significant difference in p-value, ADFI: average daily feed intake, ADG: average daily gain, G:F: gain: feed, *: significant effect of OAs on growth performance (p < 0,05).*

Table 3.
Effects of acidifiers on growth performance and gut health of swine.

and grower-finisher pigs fed with the supplementation levels of 0.3 and 0.5% benzoic acid showed a significant improvement in growth performance. In which, the supplementation of 0.5% benzoic acid promoted better performance in nursery pigs, while grower-finisher pigs fed with 0.36% gained optimal ADG [61].

Moreover, evidence also showed the importance of organic acids on gut health and livestock environment. For example, addition of benzoic acid (1 or 2%) in the dietary for grower-finisher pigs reduced urinary pH and NH3 emissions [75, 76]. Diao et al. (2014) also reported that benzoic acid supplementation (5 g/kg) in the dietary decreased the GIT pH values. The number of *Bifidobacterium* and *Bacillus* in pigs fed the benzoic acid diet was greater than in pigs fed the control diet, while the number of *Escherichia coli* decreased in pigs fed the benzoic acid diet. In addition, benzoic acid increased the content of propionic acid and total volatile fatty acids and decreased the concentrations of NH_3–N in cecum ($P < 0.05$). The gut morphology was also improved in pigs fed the benzoic acid diet ($P < 0.05$), with observed increases in villus height in the ileum and decreased crypt depth in the duodenum [77]. Lynch et al. (2017) indicated a significant decrease in *Salmonella* levels in the feces of grower pigs fed with sodium butyrate (p = 0.001) and a blend of formic and citric acids (p < 0.001) [78]. Zhang et al. (2018) showed that dietary supplementation with chlorogenic acid improved intestinal health and regulated the composition of selected intestinal microbiota in weaned piglets. To put it more specific, an increase in the population of *Lactobacillus* (p < 0.05) and a decrease in the population of *E. coli* were observed in the colon of pigs fed chlorogenic acid diets. Dietary supplementation with chlorogenic acid also resulted in an increase (p < 0.05) in duodenal villus height and villus height: crypt depth compared to the control group. This positive influence on intestinal morphology in weaned piglets ultimately improved their growth performance [79].

In addition, the recent study showed the effect of a microencapsulated mixture of organic acids (MOAs) supplementation on the growth performance and meat-carcass grade quality in growing-finishing pigs. The supplementation of MOAs (0,05 and 0,1%) in the basal diet resulted in a significant ($P < 0.05$) linear improvement in ADG, a linear decrease in fecal *E. coli* counts, a linear ($P < 0.05$) increase in backfat thickness and lean meat percentage, and a decrease in drip loss [33]. Similarly, the previous trial showed that piglets received a basal diet with the addition of MOAs at 3 kg/ton had higher ADFI (+ 4.6%; $P = 0.08$), ADG (+ 8%; $P < 0.01$), and final body weight (+ 6.5%, $P < 0.01$) [80]. Nguyen et al. indicated that the administration of MOAs (0,1 and 0,2% in the diets) *increased Lactobacillus* counts and decreased *E. coli* counts compared to the control diet (p < 0.05) [62]. These findings suggest that organic acids have growth-promoting properties and can be used as alternatives to antibiotics in swine production.

4.2 Effect of acidifiers on poultry production

Acidifiers and their salts have also been used in poultry dietary and drinking water for the past decades. Literature showed that the broilers/layers fed with acidifiers in the diet improved growth performance, reduced toxic bacterial mass, and enhanced nutrient digestibility and GIT immunity (**Table 4**).

When it comes to broiler growth performance, previous trials have demonstrated the efficiency of supplementing diets with butyric acid and its salt (sodium butyrate) in improving body weight, feed intake, and FCR. For instance, Leeson et al. (2005) and Anton Giovanni et al. (2007) showed that the carcass weight and breast meat yield significantly increased ($p < 0.05$) in birds fed 0.2% butyric acid [91, 92]. Besides, Adil et al. (2011) found that birds fed 3% fumaric acid exhibited significantly ($p < 0.05$) higher body weight gains and better feed conversion ratio [93].

For the combination of organic acids, Nguyen et al. (2018) reported that broilers fed with various levels of mixed acidifiers (0.02, 0.03, 0.04, 0.05, and 0.06%) and MCFAs showed positive growth performance, nutrient digestibility, and excreta microflora. In detail, broilers exhibited a linear increase ($P < 0.05$) in body weight gain and an improvement in feed conversion ratio ($P < 0.0001$). Additionally, there was a linear increase ($P < 0.05$) in the *Lactobacillus*: *E. coli* ratio. An increase in the levels of organic acids and MCFAs also significantly improved the IgG concentration ($P = 0.011$) [86]. However, Youshelf et al. (2017) reported that supplements of single lactic acid (0,2%) in broiler diets seem to obtain better performances than the organic acid mixture (0,4%). It was also found that the inclusion of single lactic acid in broiler diets declined the serum cholesterol level, the pH of small intestine, the counts of fecal coliforms and *E. coli*, but did not affect the carcass yield, breast, or organ weights [94].

In addition, salts of organic acids, such as potassium diformate and sodium diformate have been shown to have positive effects on performance and GIT health. To put it more specific, Paul et al. (2007) reported that ammonium formate or calcium propionate (0.3%) increased the live weight gain and FCR at day 21 in broiler chickens [95]. Mikkelsen et al. (2009) showed that inclusion of 0.45% potassium diformate reduced mortality caused by necrotic enteritis (*Clostridium perfringens*) [96]. Raaga et al. (2016) reported that broilers fed basal diet supplemented with formic acid (5 g/kg diet), or potassium diformate (5 g/kg diet) exhibited significantly increased body weight gain and improved feed conversion ratio ($P < 0.05$). An improvement in villus height was also observed in both of these groups. [97]. Besides, different organic acids have been used in drinking water. Formic, propionic acids, and their salts have exceptionally good solubility in water. Their supplementation in drinking water with 0,3 L/1000 L significantly improved the intestinal structure [98].

In the laying hen industry, the efficiency of dietary acidifiers on egg production and quality have been well-documented. Yesilbag and Çolpan (2006) reported that the laying hens fed with a mixture of acidifiers at levels of 0,5%, 1,0%, and 1,5% exhibited a slight increase in average egg production (91.03, 90.94, and 91.30%, respectively) compared to the control group (85.76%) [99]. Grashorn et al. (2013) showed that the supplementation of organic acids mixture (SALMO-NIL dry) at 2 kg/ton of feed increased average egg weight and egg production capacity [100]. Recently,

Composition of acidifiers	Dose	Age	Growth performance			Gut health	Ref
			ADG	ADF1	G: F		
Single acidifiers							
Phosphoric	0.1%, 0.2%	1–42 days old	*	*	*	Decreased *E. coli, Salmonella*	[81]
Lactic	0.3%	1–42 days old	*	*	*	Decreased *E. coli, Salmonella*	[81]
Propionic	0.5%	1–42 days old	*	*	*	Increased *Lactobacillus*, decreased *E. coli*	[82]
Formic	0.5%	1–42 days old	*	*	*	Increased *Lactobacillus*, decreased *E. coli*	[82]
Formic	0.4%	1–48 days old	*	*	*	NA	[83]
Citric	0.3%	1–42 days old	*	*	*	Improved gut morphology	[84]
Encapsulated Butyric	0.03%; 0.05%	1–42 days old	*	*	*	NA	[85]
Mixture of acidifier							
17% fumaric acid, 13% citric acid, 10% malic acid, and 1.2% MCFAs	0.06%	Broiler	*	*	*	Increased IgG, increased *Lactobacillus*, decreased *E. coli*	[86]
Formic, propionic	0,2%; 0,4%	Starter, Grower, Finisher broiler	*	*	*	Increased *Lactobacillus*, decreased *E. coli*	[87]
Formic acid 31%, propionic acid 19%, ammonium format 26%, ammonium propionate 6%	0,3 L/1000 L drinking water	1–42 days old	*	*	*	Improved intestinal structure	[88]
Salts of acidifiers							
Sodium butyrate	500, 1000, 2000 mg/kg	1–42 days old	*	*	*	Improved intestinal structure, increased *Lactobacillus*	[89]

Composition of acidifiers	Dose	Age	Growth performance			Gut health	Ref
			ADG	ADF1	G: F		
Sodium butyrate	0.3 g/kg; 0.6 g/kg; 1.2 g/kg	1–21 days old	*	*	*	Improved intestinal structure, enhanced the immune response of ND vaccine.	[90]

*NA: not available, NS: not significant difference in p-value, ADFI: average daily feed intake, ADG: average daily gain, G:F: gain: feed, *: significant effect of OAs on growth performance (p < 0,05).*

Table 4.
Effects of acidifiers on growth performance and gut health of broilers.

Gong et al. (2021) reported that the dietary supplementation with 1 g/kg benzoic acid exhibited no effect on production performance, but it significantly improved egg quality, intestinal morphology, and bacterial profiles [101]. Encapsulation technology is also currently employed in laying hen industry to produce protected organic acids. Youself et al. (2013) evaluated the effect of microencapsulated organic acids including fumaric acid, calcium formate, calcium propionate, potassium sorbate on egg quality. The results showed that microencapsulated organic acids did not affect shape index, yolk index, Haugh unit or specific gravity, but showed significant increase in shell thickness and yolk color [102]. Recently, Garcia et al. (2019) showed the effects of beak trimming and the inclusion of sodium butyrate in the diet from at hatch to 6 weeks of age on the growth performance and GIT traits of brown-egg pullets. The results showed that sodium butyrate tended to improve growth and FCR from 0 to 6 weeks of age but did not affect body weight uniformity [103].

In addition, drinking water acidification is also preferred in layer industry for improving performance. Kadim et al. (2008) reported that the average egg production significantly increased by approximately 20, 15, and 10% in the trial groups where acetic acid was administered through drinking water at levels of 0.06, 0.04, and 0.02%, respectively, during the hot season (P < .01) [104]. Abbas et al. (2013) indicated that administration of formic acid through drinking water at levels of 0, 0.05, 0.10, or 0.15% increased average egg production in hens by approximately 72, 80, 86, and 88%, respectively [105].

5. Conclusions

From the scientific results presented and discussed in this chapter, the following main conclusions can be drawn: (i) OAs and their salts are among the most promising future products of the livestock industry, owing to their antimicrobial activity, which reflect in improved overall gut health, inhibition of pathogenic bacteria growth, increased apparent total tract digestibility, and enhanced growth performance (ii) Both single OAs and mixed OAs are utilized as additives in swine and poultry feeds, and have positive influences on growth performance and gut health in the different growth periods of swine and poultry. In which, the mixed OAs seem to be more favorable for recent investigations shown with the enormous number of publications (iii) the different forms of OAs such as their salts and derivates seem to be more efficacy for the growth performance and gut health of pig and poultry compared to original OA forms. (iv) OAs can be added in drinking water or in the dietary of swine and poultry. Both supplementation methods were evaluated to improve the growth performance and control pathogenic bacteria.

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