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Review

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

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Abstract: Because the application of antibiotic growth promoters (AGP) causes accelerated adverse effects on the animal diet, the scientific community has taken progressive steps to enhance sustainable animal productivity without using AGP in animal nutrition. Organic acids (OAs) are non-antibiotic feed additives and a promising feeding strategy in the swine and broiler industry. Mechanistically, OAs improve productivity through multiple and diverse pathways: (a) reduction of pathogenic bacteria in the gastrointestinal tract (GIT) by reducing the gut pH; (b) boosting the digestibility of nutrients by facilitating digestive enzyme secretion and increasing feed retention time in the gut system; (c) having a positive impact and preventing meat quality deterioration without leaving any chemical residues. Recent studies have reported the effectiveness of using encapsulated OAs and synergistic mechanisms of OAs combinations in swine and broiler productivity. On the other hand, the synergistic mechanisms of OAs and the optimal combination of OAs in the animal diet are not completely understood, and further intensive scientific explorations are needed. Moreover, the ultimate production parameters are not similar owing to the type of OAs, concentration level, growth phase, health status of animals, hygienic standards, and environmental factors. Thus, those factors need to be considered before implementing OAs in feeding practices. In conclusion, the current review evaluated the basics of OAs, mode of action, novel strategies to enhance utilization, influence on growth performances, nutrient digestibility, quality traits, and meat preservation of swine and broilers and their potential concerns regarding utilization.

Keywords: organic acids; swine; broilers; digestibility; meat quality; meat preservation

1. Introduction

The ultimate goal in the global livestock sector is to achieve enhanced quantitative and qualitative productive parameters. A few decades ago, enhanced production was gained by incorporating various antibiotic growth promoters (AGP), which resulted in improved feed efficacy, growth rate, and lower mortality and disease. On the other hand, the emergence of antimicrobial resistance bacteria has led to a discussion regarding the global health problem. Consequently, the utilization of AGP was banned by the European Union. Thus, scientists and researchers have focused on sustainable potential antibiotic-free production systems in the poultry sector [1]and swine industry [2].

Researches have highlighted the effective utilization of organic acids (OAs), phytobiotics, probiotics, prebiotics, bacteriophages, and other numerous alternatives instead of antibiotics to establish appropriate health and production parameters of animals. OAs

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produced effective responses owing to their antimicrobial properties, which can enhance the pH reduction rate in the GI tract [3]. Consequently, the intestinal digestibility and mineral utilization were improved [4,5]. Acidifiers were incorporated into animal diets a few years earlier owing to the presence of preservatives and nutritional characteristics [6,7]. Despite controlling the desirable growth rate of molds, fungi, bacteria in animal feed, several studies have reported the potential ability of improving nutrition digestion and retention, intestinal health, ultimate growth development of non-ruminant animals, including feed sanitizing characteristics [8,9,10]. Enhanced meat quality characteristics and growth performances were observed in broilers fed a diet supplemented with OAs, including 30% lactic, 25.5% benzoic, 7% formic, 8% citric, and 6.5% acetic acid [11]. Partanen and Morz [6] reported that incorporating OAs into the pig diet modulates the beneficial gut microbiota and improves the growth performance. A reduced gastric pH and retarded enterotoxigenic *E.coli* proliferation in the gut system occurred due to the inclusion of lactic acid into the pig diet. Thus, developed gut health led to optimal feed intake and weight gain of the animal [12]. Furthermore, supplementation of OAs with feedstuff will increase the stimulation rate of the nutrient digestion process [13]. Effective production parameters and health-promoting evidence have been discovered for numerous OAs, such as citric, fumaric, and formic acids and their salts [14]. The application of OAs in the livestock sector has produced numerous benefits in both economic and quality product perspectives in the livestock sector (Figure 1).

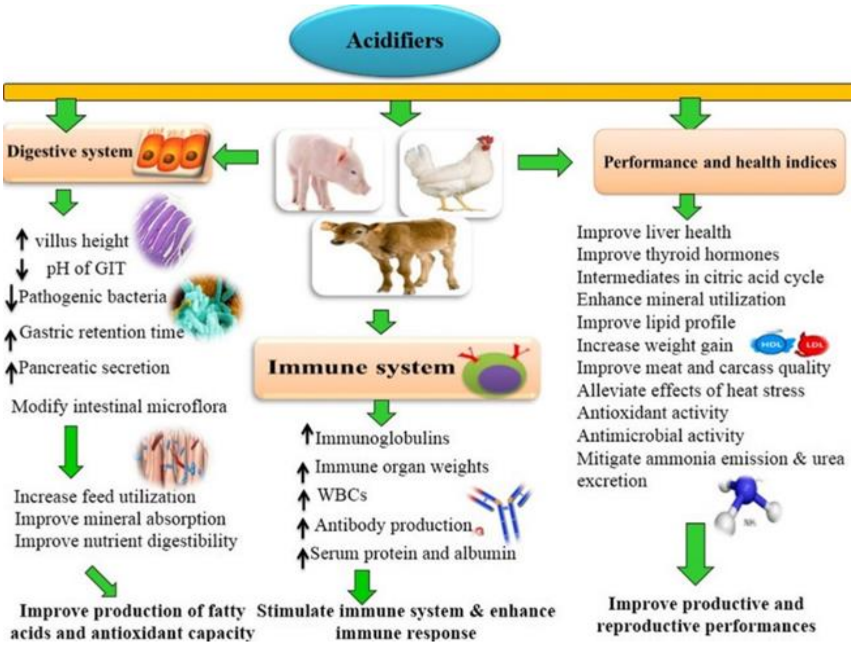

Figure 1. Various application and benefits of OAs in the livestock sector [15].

Chemically, organic acid consists of an organic carboxylic acid group (R-COOH) with fatty acids and amino acids. Moreover, short-chain acids (C1-C7) are involved in antimicrobial activities. Most of them are either simple carboxylic acids, such as acetic, formic, butyric, and propionic acids with a hydroxyl group, such as tartaric, malic, citric, and lactic acids or short-chain carboxylic acids with double bonds, such as sorbic and fumaric acids [16]. On the other hand, Ravindran and Kornegay [17] reported that each organic acid has a distinguished range of pH, antimicrobial potential, pKa values, and membrane structure. A combination of OAs has various pKa values, directly influencing the intestine pH due to the developed synergistic effect. The most common OAs involved in animal nutrition are listed below (Table 1)

Table 1. Common OAs and their properties involved in animal nutrition [15,18]

Acid	Chemical Name	Registration Number	Molecular weight/GE (MJ/Kg)	Odor	pKa
Butyric	Butanoic Acid	-	88.12/24.8	rancid	4.82
Citric	2-Hydroxy-1,2,3-Propanetricarboxylic Acid	E 330	192.1/10.2	odorless	3.13
Propionic	2-Propanoic Acid	1a297	74.08/20.6	pungent	4.88
Sorbic	2,4-Hexandienoic Acid	E 200	112.1/27.85	mildly acrid	4.76
Formic	Formic Acid	E 236	46.03/5.7	pungent	3.75
Acetic	Acetic Acid	E 260	60.05/14.6	pungent	4.76
Lactic	2-Hydroxypropanoic Acid	E 260	90.08/15.1	sour milk	3.83
Malic	Hydroxybutanedioic Acid	E 296	134.1/10.0	apple	3.40
Fumaric	2-Butenedioic Acid	2b08025	116.1/11.5	odorless	3.02
Benzoic	Benzenecarboxylic acid	-	-	-	4.20

This review evaluates the response of swine and broilers to OAs supplementation of previous studies in terms of the growth production parameters, including feed intake, weight gain, feed conversion ratio (FCR), nutrient digestibility, and meat quality traits. The possible modes of action, causes of various responses due to OAs, and potential concerns regarding OAs are also assessed.

2. Potential modes of action of OAs

OAs have numerous benefits on the health and development of the gut system. Nevertheless, the mode of action is not completely understood. Their modes of action may be attributed partially to different factors, such as (A) mineral chelation and stimulation on intermediary metabolism; (B) inhibition of the development of pathogenic microbes; (C) facilitate proper digestion due to lower gastric pH and enhanced pepsin secretion; (D) reduction of gastric emptying rate and maintenance of endogenous enzymes secretion [19,3].

2.1 Effect of OAs on mineral utilization and nutrient digestibility

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Mineral utilization is increased by adding OAs to the diet through the reduction of gut pH. Bolling et al. [20] reported that citric acid facilitates the removal of attached minerals to phytate molecules, such as Ca, P, and Zn. In contrast, OA anions form complexes with Mg, P, Ca, and Zn, improving digestion and minimizing the excretion of beneficial minerals from the body. Phytate phosphorous utilization occurs through OAs administration by providing favorable pH conditions to convert phytase into hydrolyze phytate. In particular, lower gastrointestinal pH has the potential to enhance P solubility [21]. It has found that fumaric acid can enhance the apparent absorption and retention of Ca, P, and Zn in the GIT [22].

The lower metabolizable energy (ME) in soya bean meal occurs due to retarded digestibility in the carbohydrate portion. Galacto-oligosaccharides in soya bean meal cannot be digested properly without the presence of endogenous α-(1,6)-galactosidase in the intestines. Ao [23] reported that the inclusion of 2% citric acid decreased the crop pH by enhancing the activity of the α-galactosidase enzyme, which increased the digestion process. Moreover, by reducing the chime pH, OAs supplementation improved protein digestion owing to microbial phytase activity and induced pepsin secretion [24]. A further protein digestion process improves through the secretion of a greater level of chymotrypsinogen A, chymotrypsinogen B, procarboxy peptidase A, procarboxy peptidase B, and trypsinogen enzymes [25]. OAs inclusion also increased the proper absorption rate of nutrients in the GI tract by increasing the digesta retention time [26]. The increased ME and crude protein (CP) was observed due to the reduced microbial competition with the host, ammonia emission, and endogenous nitrogen elimination [27].

2.2 Effect of OAs on antimicrobial activity and pathogenic bacteria

Both animals and plants have symbiotic relationships with various microbes to survive in the environment through an active defense system against pathogens and to regulate the metabolism associated with hormones. On the other hand, an excessive microflora content produces unnecessary competition between the host and nutrition. Hence, maintenance of the optimal microbe composition in the GI tract should be investigated. OAs can be divided into two groups based on the microbial ameliorate capacity in the GI tract (figure 2).

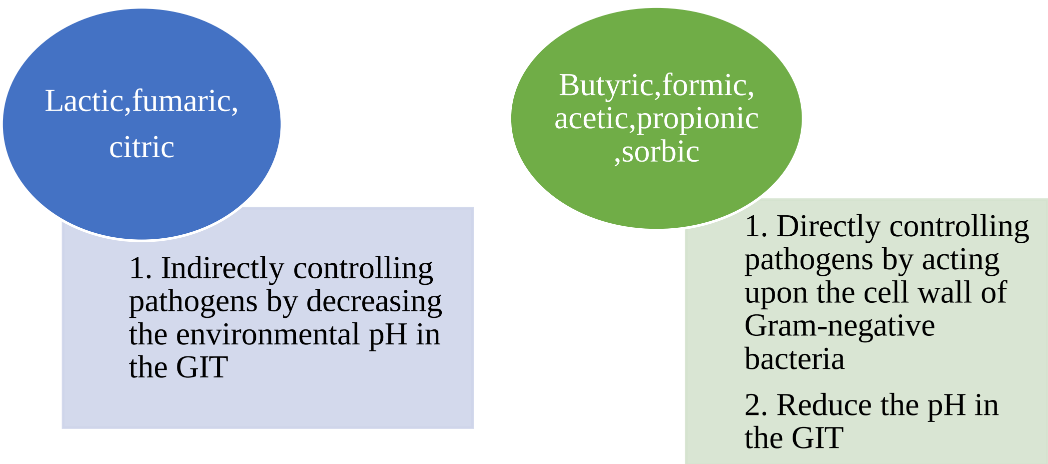

Figure 2. Two different mechanisms of OAs on altering the pH of the GI tract and their impact on pathogens [28].

Non-disassociated OAs enter the cytoplasm through the semipermeable membrane of the microorganism. Thereafter, OAs release their protons (H^+), and the cytoplasm pH

decreases gradually. The enzymes involving reactions, such as nutrient transportation and glycolysis signal transductions of the microbes, are curtailed. Consequently, an energy deficiency occurs to maintain the normal pH [29]. Owing to the acidic conditions in the stomach, the efficacy of OAs is greater than under neutral pH conditions, as in the intestines. On the other hand, most bacteria species require optimal environmental pH conditions and pH <4.5 (extreme lower) conditions which adversely affect their survival. By releasing H^+ ions, OAs aid in the dysfunctions, retardation, or inhibition of the multiplication of pH-sensitive bacteria [30].

Moreover, some bacteria in the GI tract secrete various harmful compounds that reduce fat digestibility, rapid turnover of absorptive epithelial cells, stimulate mucus secretion, and induce an immune response due to the developed immune system. These factors help retard the growth performance, and approximately 6% net energy losses in pigs can be attributed to microflora [31]. OAs have the potential to eliminate specific species, such as coliforms, while generating eubiosis. Thus, they can provide the optimal microbial atmosphere in the GI tract that can benefit the host by accumulating lower toxic compounds, amines, and ammonia. On the other hand, gram-negative (G^-) bacteria resist OAs that consist of more than eight carbon bonds to some extent, gram-positive (G^+) bacteria are susceptible to long-chained OAs [32,33]. Stronger effects of OAs affect G^+ bacteria due to cell structural differences. In contrast, the cytoplasmic membrane of bacteria is surrounded by a thick peptidoglycan layer. Generally, this peptidoglycan layer is thicker in G^+ bacteria than G^- bacteria. Nevertheless, G^- bacteria have an extra lipopolysaccharide layer that is more resistant to hydrophobic antibiotics and chemical compounds.

Because OAs have both bactericidal and bacteriostatic properties, Luckstadt and Mellor [34] sketched out the mode of action of OAs on G^- bacteria as follows. (1) Lipophilic undissociated OAs penetrate the G^- bacteria cytoplasm (Salmonella). (2) OAs release H^+ ions, which reduces the cellular pH, and the enzyme-based microbial metabolism tends to decrease (3). To restore the normal cytoplasmic pH, the cell is forced to discard H^+ ions through the cell membrane via the H^+- ATPase pump. (4) Ultimately, G^- bacteria proliferation is gradually impeded when exposed to OAs for some time (Figure 3).

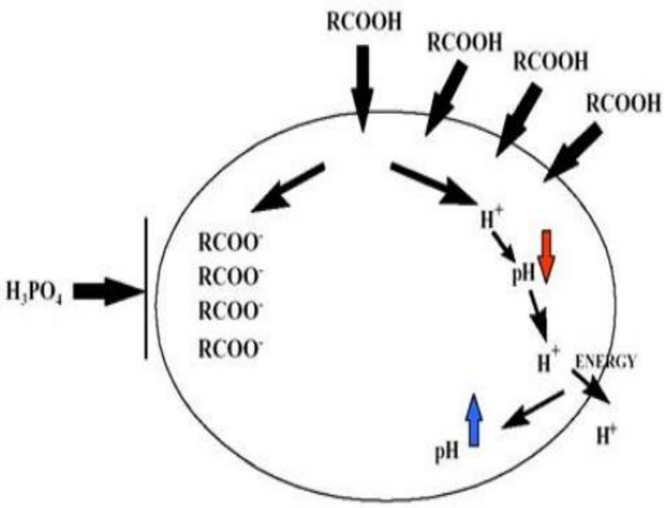

Figure 3. Mode of action of OAs on pH-sensitive bacteria (*Clostridia, Salmonella, Coliforms, listeria* spp.) [35].

This anion model of OAs can vary upon two factors: (1) The lipophilic nature of the OAs, which can transmit through the microbes cell wall; (2) various anion complexes involves with different inhibitory actions within the cell [36,37]. Some OAs can alter the GI tract by eradicating foodborne pathogens, such as salmonella and *E.coli* species [38]. Owing to pH reduction and their influence on the buffering capacity of the diet, OAs can improve gut health by providing the optimal environment to beneficial microbes while preventing the proliferation of pathogens [6,39,40].

3. Novel strategies for enhancing efficacy OAs availability in the gastrointestinal tract (GIT)

The supplementation of feed and water with OAs did not show better efficacy in the latter part of the GI tract. It occurs due to the high proportion of short-chain fatty acids (SCFA) that are metabolized and absorbed rapidly in the upper segments of the GI tract [41]. Thus, the OAs concentration tends to decrease and exert negative feedback on modifying the host microflora content in the GI tract. New studies have shown that microencapsulated lipid shells facilitate the transportation of SCFA further down the GI tract while increasing the retention time [41,42]. Furthermore, microencapsulated feed improves palatability, removes unpleasant odors/ flavors, and delivers the necessary compounds to the specific target place inside the animal body while acting as a "biological agent" (2). Further studies have demonstrated that the efficiency of OAs can be improved by incorporating phytogenic feed additives. Owing to the synergistic effects of both OAs and botanicals, food-safety bacteria, such as *C. jejuni* and *S. typhimurium* counts, tend to decrease. In particular, pore-forming agents derived from numerous aromatic compounds caused changes in the bacterial cell membrane by providing a pathway for OAs entrance [43,44]. Grilli et al. [45] indicated that a combination of microencapsulated OAs (citric and sorbic acid) and pure botanicals in weaning pigs' diet improved the maturation of the intestinal mucosa by exerting a positive impact on the barrier integrity in the jejunum and ileum while performing better growth performance. Gheisar et al. [46] observed a higher lactobacillus content in the feces of broilers fed a diet supplemented with 0.075% microencapsulated OAs. Gheisari et al. [47] also reported that 0.2% OAs inclusion enhanced the lactobacillus content while reducing the *Clostridium perfringens*, *E. coli*, and *Salmonella* spp content. Moreover, a 0.5% microencapsulated blend of OAs reduced the oxidative status, microbial loads, and improved the shelf life of broiler meat [48]. The protected OAs could be delivered to specific sites in the body and had a positive effect by eliminating the coliforms counts in both the distal jejunum and cecum. In contrast, freely available OAs had little influence [49].

Since the form of OAs (SCFA) is naturally produced by the GI tract, some studies reported that introducing both prebiotics and probiotics could stimulate the synthesis of SCFAs in the GI tract [50,51]. This could be implemented in two ways: (1) direct administration of lactic acid-producing bacteria in the diet; (2) the addition of prebiotic substances that enhance the proliferation of lactic acid bacteria and increase SCFA production [52,53].

Streptococcus, Saccharomyces, Enterococcus, Lactobacillus, Bacillus, Bifidobacterium, and *Pediococcus* are the probiotic strains mainly used in nutritional studies. These microbes protect the GI tract through barrier effects, competitive exclusion, bacterial interference process, prevention of colonization, and bacterial antagonism [54,55]. These probiotic supplementations develop the cell structure, have immunological effects, and are resistant to pathogens. Ultimately, they enhance the production rate of SCFAs, intermediary products, and H_2O_2. *Lactobacillus* spp. can generate lactic acid, which can facilitate the synthesis of butyric acids with the collaboration of *Clostridial* clusters that reinforce the animal cross-feeding process [56]. Oligosaccharides and polysaccharides (Non- digestible carbohydrates (NDC)), proteins, and particular lipids are used as prebiotics to provide a proper

substrate for beneficial host microbes. Previous studies have stated that the administration of prebiotics has a positive effect on the natural production of OAs in the GI tract. The supplementation of the diet with NDC enhances the *lactobacillus* and *bifidobacterium* population. In contrast, these microbes promote the synthesis of SCFA, such as propionate, acetate, and butyrate acids [57]. Rehman et al. [58] reported that 1% inulin inclusion increased the jejunum acetate concentration and n-valerate in the cecal digesta in broilers compared to the control diet. Overall, the dietary supplementation of prebiotics and probiotics will lead to optimal OAs production in the animal body.

4. Effect of OAs in swine and broiler

4.1 Supplementation of OAs on the growth performance of swine and broilers

Studies have found that the optimal dosage of OAs can enhance the productivity of pigs compared to AGPs. Increased growth performance, gain to feed (G: F), and feed intake (FI) was observed in piglets supplemented with an OAs mixture (benzoic, fumaric, lactic, propionic, and citric) [59]. Because benzoic acid in the diet can increase the butyric acid concentration in the GI tract, the gut microflora ameliorating process occurs by acting as an energy source agent in gut epithelial cells [60]. The feed conversion ratio (FCR) was increased by 10%, and the average daily gain (ADG) was increased by 3% when pigs were administered fumaric and citric acids at four weeks of age [61]. Kuang et al. [62] reported that the inclusion of an OAs blend (calcium formate, calcium lactate, and citric acid) and medium-chain fatty acids (MCFAs - lauric, capric, and myristic) enhanced the FI, ADG, and FCR in weaning pigs compared to pigs fed with dietary zinc oxide inclusion. Feeding weaning pigs with 0.8% fumaric acids reduced the *E.coli* and *coliforms* population in the cecum [63]. On the other hand, Risley et al. [64] reported that 1.5 % fumaric acid addition did not affect the microflora composition in the GI tract. According to the study conducted by Htto et al. [65], the ADG, FCR, and BW during 0-14 days (piglets) were not significantly different from those fed OAs. In the same study, however, the ADG and FCR were enhanced during 15-35 days and overall 35 days of periods due to potassium diformate and potassium formate supplementation. Furthermore, a trend of developed growth performance in response to the inclusion of OAs combined with salts combination was more reliable in growing-finishing pigs than in weaning pigs [6]. Canibe et al. [66] and Partanen et al. [67] reported increased ADG and G: F ratios in pigs fed a diet containing formic acid-ammonium formate and formic acids. A combination of phytogenic feed additives with organic acids (10% citric,10% sorbic, 6.5% malic, and 13.5% fumaric acid) also improved the BW and ADG of weaning pigs. Moreover, Yang et al. [68] reported that the high abundance of *Lactobaillus mucosae* also occurred compared to the control treatment. Nevertheless, 1.8% formic acid inclusion did not have a positive response on the ADG and ADFI of weaning pigs, but it enhanced the G: F [66]. The above dissimilarities among the different studies might be related to the inclusion dosage of OAs, diet complexity, growth phase, and animals' health conditions. Therefore, further studies will be needed to identify the best OAs concentration for different growth stages.

In the broiler growth performance, the utilization of OAs has not gained as much attention as in the swine industry. The rapid metabolization process in crops to the gizzard (foregut) causes a deficiency of OAs availability and retards the growth performance [34]. On the other hand, Fascina et al. [11] reported that the administration of OAs combination (30% lactic, 25.5% benzoic, 7% formic, 8% citric, and 6.5% acetic acid) improved the BW, WG, and FCR compared to the control group at 42-day-old broilers. The supplementation of 3% fumaric acid could increase the WG and FCR in broilers compared to the diet comprised of 3% lactic acid. OAs-included diets resulted in a lower voluntary feed intake (VFI) because of the presence of strong flavor compounds. The improved FCR might have occurred due to lower VFI, which resulted in enhanced BWG because of the efficient nutrients utilization in the body [69]. Hassan et al. [70] reported that microencapsulated galliacid OAs mixture (fumaric acid, calcium formate, calcium propionate, potassium sorbate,

and hydrogenated vegetable oil) enhanced the WG by 16% compared to the control groups. Kamal and Ragaa [71] also indicated that in 42 days old broilers, the BWG and FCR were enhanced in those fed 3% organic acids (butyric, fumaric, and lactic acid). Hence, the higher BWG was achieved through direct antimicrobial effect, reducing the digesta pH level in the GI tract while acting as a barrier to pathogens, and buffering reactivity in conjunction with the enhanced nutrient digestibility [72]. Interestingly, the synergistic effects of combined 0.3g/kg essential oils with OAs (200g/kg sorbic, 200g/kg fumaric, and 100g/kg thymol) increased the FCR significantly while minimizing the *E.coli* population through a lower gut pH value [73].

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Dosage and Organic acid/acids	Growth phase	Growth performances			Intestinal/fecal microbial counts (CFU)	Other parameters	References
		BWG/FBW	ADFI	G:F			
Swine							
0.1% & 0.2% fumaric, citric, malic, MCFA (capric and caprylic)	Weaning	S	NS	S	*E.coli*; S *Lactobacillus*; S *Clostridium*; S *Salmonella*; S	a. Reduced diarrhea score, fecal ammonia, and acetic acid emission	Yang et al., 2018 [74]
0.1% & 0.2% fumaric, citric, malic, MCFA (capric & acrylic)	Growing	S	NS	S	*Lactobacillus*; S *E.coli*; NS	-	Upadhya et al., 2016 [75]
0.15% benzoic, fumaric, calcium formate	Weaning	S	NS	NS	*E.coli*; NS *Lactobacilli*; NS	a. Increased villus height in duodenum and jejunum b. Increased butyric acid level in the cecum and valeric acid level in the colon	Xu et al., 2017 [76]
1.1% acetic, propionic, phosphoric, citric acid	Weaning	NS	NS	NS	*Lactobacilli*; NS *E.coli*; NS	a. Reduced pH level in colon	Namkung et al., 2004

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					Coliforms; NS	b. Retardation of coliform proliferation	[77]
0.4% & 0.2% fumaric, lactate, citric, propionic, benzoic acid	Weaning	NS	NS	NS	*E. coli*; NS	-	Walsh et al., 2007 [59]
0.5% benzoic acid	Weaning	S	S	S	*Lactobacilli*; S	-	Wei et al., 2021 [78]
0.5, 1% benzoic acid	Weaning	S	NS	NS	NE	a. Reduced the number of aerobic, total anaerobic, lactic acid-forming, and gram-negative bacteria in the stomach b. Reduced gram-negative bacteria and acetic acid in the duodenum c. Reduced gram-negative bacteria in ileum	Kluge et al., 2005 [79]
0.5% butanoic, fumaric , benzoic acid	piglets	S	NS	S	*Lactobacilli*; NS *E.coli*; NS	a. Decreased ileal *E.coli* bacteria level b. Did not exert negative impacts on GI tract pH level and immunity	Li et al., 2008 [80]

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0.1% fumaric , citric, malic, MCFA (capric & caprylic)	Finishing	S	NS	S	*Lactobacilli*; NS *E. coli*; NS	a. Reduced feces H_2S gas emission	Upadhya et al., 2014 [81]
0.85% formic, benzoic, sorbic, Ca- butyrate	Growing male pigs	NS	NS	NS	*E. coli*; S *Lactobacilli*; S	a. Lower level of *coliforms*, *enterococci* and lactic acid bacteria in jejunum and colon descendens	Øverland et al., 2007 [82]
0.5% benzoic acid	Weaning	S	S	S	*E.coli*; NS *Lactobacilli*; NS	a. Reduced diarrhea in weaning pigs	Papatsiros et al., 2011 [83]
0.14% & 0.64% formic acid	Weaning	S	S	NS	*Lactobacilli*; S	a. Higher microbiota diversity in 0.64% dosage	Luise et al., 2017 [84]
Broilers							
0.3% & 0.4% calcium formate, calcium propionate 0.3, 0.4% ammonium formate, ammonium propionate	Finishing	S	NS	S	NE	a. Reduced the illeal total bacterial count b. Improved villi length	Saleem et al., 2020 [85]
1% formic, lactic, propionic, citric acid	Finishing	S	NS	NS	NE	a. Enhanced V:C in GI tract b. Increased water consumption	Ali et al., 2020 [86]

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						during 15-22 days	
0.5% citric, sorbic, synthetic essential oil	Finishing	NS	NS	NS	*E.coli*; NS *Enterococci*; S *Clostridium*; NS *Enterobattericeae*; NS	a. Increased villi height, crypt depth, number of villi, mucosa thickness, and villi area	Stamilla et al., 2020 [87]
0.15% formic, lactic, citric, malic, tartaric, phosphoric acids	Finishing	S	S	S	*Lactobacilli*; S *E.coli*; S	a. Enhanced inhibitory action owing to organic acid	Goh et al., 2020 [88]
0.3% formic, acetic, propionic, ammonium formate	Finishing	S	NS	NS	NE	a. Increased SCFAs level in the cecum b. Increased jejunal goblet cell density and ileal villus height	Dai et al., 2021 [89]
0.1% lactic, citric, acetic, formic, propionic, phosphoric, and sodium butyrate	Finishing	S	NS	S	*Lactobacilli*; S *Coliforms*; NS	a. Increased jejunum villus height b. Enhanced humoral immune response	Sabour et al., 2018 [90]
0.3, 0.5% formic, propionic acid	Finishing	S	NS	S	*Lactobacilli*; S *E.coli*; S	a. Lower duodenal pH b. High immune response against Newcastle disease, infectious bronchitis	Fathi et al., 2016 [91]

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0.6% fumaric, calcium format, calcium propionate, potassium sorbate, hydrogenated vegetable oil 0.1% citric acid, calcium formate, calcium butyrate, calcium lactate	Finishing	S	S	S	*Lactobacilli*; S *Salmonella*; S	a. Increased dressing percentage and bursa weight	Hassan et al., 2010 [70]
0.2, 0.4 & 0.6% butyric acid	Finishing	S	NS	S	*E.coli*; S	a. pH reduction of upper GI tract b. Increased villus length and crypt depth in the duodenum	Panda et al., 2009 [92]
0.5, 1, 1.5 & 2% citric , lactic, phosphoric acid	Finishing	S	NS	S	*E.coli*; S *Salmonella*; S	a. 2% OAs blend enhanced the carcass yield b. 1.5%, 2% OAs blend increased the liver weight	Sultan et al., 2015 [93]
0.6% formic acid	Finishing	S	NS	S	*E.coli*; S (in crop)	a. Higher digestibility of crude protein, high dressed yield, and lower fat content in carcass	Panda et al., 2009 [94]
2% butyric, fumaric, lactic & 3% butyric, fumaric, lactic acid	Finishing	S	NS	S	NE	a. Increased villus height in the small intestines b. Enhanced serum calcium and	Adil et al., 2010 [95]

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						phosphorus concentrations	
0.2% propionic 0.3% butyric acid	Finishing	S	NE	S	NE	a. Increased tibia weight, tibia length,	Lakshmi and Sunder., 2015 [96]

BWG: body weight gain; FBW: final body weight; ADFI; average daily feed intake; G: F; gain to feed ratio; S: Significant; NS: Non-significant; NE: Not-evaluated

4.2 Supplementation of OAs on nutrient digestibility of swine and broilers

Microencapsulated OAs, including 10% malic, 13% citric, and 17% fumaric acids, enhanced the digestion of N, DM, and energy in finishing pigs and lactating sows [81,97,98] and significantly increased DM, CP, fat, and energy digestibility in growing pigs [99]. The supplementation of 1.5% citric acid increased the coefficient of the total tract digestibility (CTTAD) of crude protein (CP), calcium (Ca), and phosphorous (P) of sows during the late gestation and lactation period [100]. Moreover, Yang et al. [101] stated that protected OAs incorporation has positive effects on the apparent total tract digestibility (ATTD) of dry matter (DM) in weaning pigs. The inclusion of benzoic acid resulted in improved apparent digestibility of Ca and P in growing pigs [102,103]; CP content in weaning pigs [104]; and the DM, CP, ether extract (EE), and crude fiber (CF) of sows [105]. Nevertheless, Upadhya et al. [75] reported inconsistent results in that dietary supplementation of 0.1%, 0.2%, and 0.4% OAs blends did not influence the digestibility DM, nitrogen (N), and energy favorably in growing pigs.

Since OAs were used as an alternative feed additive, they help improve the growth performance and productivity parameters in broilers. The addition of 0.5% and 1% formic acid into the finisher diet was enhanced apparent ileal digestibility (AID) of DM and CP compared to the control treatment [106,107]. Ao et al. [108] reported that 2% citric acid incorporation improved the retention of DM, CP, and neutral detergent fiber content in the GI tract. Another study revealed that at nine days of age, the gross energy, CP, and EE digestibility were 78.01, 76.07, and 72.85%, respectively, in diets supplemented with 200 ppm ascorbic acid [109]. The supplementation of 0.2% OAs with a phytase combination significantly enhanced the CP (0.8858) and EE (0.8561) digestibility in chicks than the CP (0.7751) and EE (0.7949) values in the control treatment [110]. The reason for the higher N retention might have been the improved epithelial cell proliferation in the GI tract, while non-protected OAs tended to be metabolized rapidly [111].

In contrast, Hu and Guo [112] explained that the disassociation of fat-coated OAs and their bioactive compounds in the GI tract would help modulate the gut microflora content and mucosal morphology of chickens. Smulikowska et al. [113] reported that fat-coated OAs inclusion improved the N retention, OM, and AMEN values. Owing to the synergistic effect, combined OAs and essential oil (EO) administration into the broiler diet enhanced the AID of DM and energy at 21 days of rearing [114]. Nevertheless, the expected synergism effect was not observed from the combination of citric acid with microbial phytase. The non-significant impact on the AID of CP and amino acids (AA) might be associated with the formation of complexes among citric acids with Ca and the subsequent decrease in binding ability with phytate allowing easy hydrolyzation by the enzymes [115].

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Dosage and Organic acid/acids	Growth phase	Digestibility				Reference
		DM	N	E	CP	
Swine						
0.2% fumaric, citric, malic, capric, and caprylic acid	Growing	S	S	S	S	Hossain et al., 2011 [99]
0.05% citric, sorbic acid	Growing	S	NS	S	NC	Cho et al., 2014 [116]
2% benzoic acid	lactating sows	S (OM)	NE	NE	S	Kluge et al., 2010 [117]
0.1% & 0.2% fumaric, citric, MCFA	finishing	S	S	S	NE	Upadhaya et al., 2014 [97]
0.5% phenyllactic acid	Weaning	S	S	NE	NE	Wang et al., 2009 [118]
0.3% formic, acetic, propionic, MCFA	Weaning	S (DM) NS (OM)	NS	NS	NS	Long et al., 2018 [119]
0.5% formic, propionic, lactic, citric, sorbic acid	post-weaning	NS	NS	NS	NS	Gerritsen et al., 2010 [120]
300 mEq acid/kg formic, n-butyric acid	Growing	S	S	S	S	Mroz et al., 2000 [121]
0.15% citric acid	Lactating sows	NE	NE	NE	S	Liu et al., 2014a [122]
0.2% fumaric , citric , malic , capric , caprylic acid	Lactating sows	S	S	S	NE	Devi et al., 2016 [123]

Broilers						
0.2% formic, propionic acid	Finishing	NS	NE	NE	S	Emami et al., 2013 [124]
0.5% formic acid	Finishing	NS	NE	NE	NS	Hernández et al., 2006 [106]
0.25, 0.5 & 0.75% formic acid	Finishing	NS	NE	NE	S	Ndelekwute et al., 2015 [125]
5000ppm and 10,000ppm formic acid	Finishing	S	NE	NE	S	Garcia et al., 2007 [107]
0.25% acetic, butyric, citric, formic acid	Finishing	S	NE	NS	S	Ndelekwute et al., 2019 [145]
1,2 & 3% citric acid	Finishing	NE	NE	S	S	Ghazalah et al., 2011 [127]
0.5,1 & 1.5% fumaric acid	Finishing	NE	NE	S	S	Ghazalah et al., 2011 [127]
0.25, 0.5% formic acid	Finishing	NE	NE	NS	S	Ghazalah et al., 2011 [127]
0.25, 0.5 & 0.75% acetic acid	Finishing	NE	NE	S	NS	Ghazalah et al., 2011 [127]

N: nitrogen; E: energy; CP: crude protein; S: significant; NS: non-significant; NE: not-evaluated; OM: organic matter; DM: dry matter

4.3 Effect of OAs supplementation on meat quality on pigs and broilers

Few studies have investigated the meat quality parameters based on the incorporation of OAs in animal diets. On the other hand, an examination of the meat quality traits of pork and broilers is important because the consumption of qualitative meat has gained an important place in the food industry. Upadhya et al. [97] reported that supplementation of an OAs blend (consisting of fumaric, citric, malic, and MCFA) did not have adverse effects or improve the meat color. Furthermore, other analyzed parameters, including pH, cooking loss, drip loss, and water holding capacity (WHC), were not influenced by the inclusion of OAs. Similarly, Cho et al. [128] reported that the administration of a microencapsulated OAs combination, including citric and sorbic acids, did not affect the meat color, pH, sensory attributes (color, firmness, marbling), cooking loss, and WHC. In contrast, the inclusion of 0.05 and 0.1% fumaric, citric, malic, and MCFAs resulted in lower drip loss in pork, except for any differences in meat color, sensory evaluation, cooking loss, pH, and WHC. Further investigations will be needed to determine the possible mode of actions associated with the meat quality characteristics by introducing OAs to the animal diet. Jansons et al. [129] reported a higher protein content in muscle tissues and lower cholesterol content in pork after the addition of formic, acetic, citric, phosphoric acid along with phytogenic feed additives to the diet. This might be attributed to the synergistic effect and the presence of antioxidant compounds in the feed.

Brzóska et al. [130] reported that the supplementation of OAs to a broiler diet resulted in an increased breast muscle content and decreased leg muscle weight. The chemical constitutes of the leg meat, including DM, protein, and fat content, did not vary due to OAs application. Supplementation at the recommended dosage of an acetic, butyric, formic, phosphoric, lactic acid blend did not have significantly favorable results on carcass pH, shear force, WHC, cooking loss, and meat color values, but the TBARS value was enhanced significantly in birds fed with an OAs mixed diet. The suggests that a higher fat content facilitated a higher lipid oxidation process in meat [131]. Lower meat pH resulted in the metabolism of the glycogen reserves and subsequent H+ emission through the ATP hydrolysis process. Thus, meat pH has a significant impact on determining the meat quality traits [132]. In contrast, at a lower pH range (pH < 5.8), broiler meat exhibited a pale, soft, and exudative (PSE) condition, which is considered a degraded meat quality parameter compared to meat exposed to higher pH levels (pH > 5.8). Sugiharto et al. [133] found that a higher meat pH in broilers occurred in a diet administered with 0.1% formic and 0.3% butyric acid compared to the control group. El-Senousey et al. [134] presented a possible reason for the OAs and higher meat pH occurrence; the decline in post-mortem muscle glycolysis inhibited the decrease in muscle pH after slaughter. Furthermore, lower drip loss and a lightness value were reported in the diet combined with both formic and butyric acid but decreased due to the single administration of butyric acid. This might be due to the distinctive characteristics of each OA and their metabolic activities associated with their specific pKa. Menconi et al. [135] and Shin et al. [133] reported less drip loss in broiler meat with feeding blends of lactic, tannic, caprylic, propionic, acetic acids, and butyric acid. Nevertheless, inconsistent results were obtained by Attia et al. [136], who reported a decrease in WHC in broiler meat owing to the supplementation of citric and fumaric acids. These results were attributed to differences in the OAs type, dosage, and experimental environment. Göksoy et al. [137] reported a numerical reduction of meat lightness owing to the combination of lactic, formic, and propionic acids. Similarly, Sughirto et al. [133] and Jha et al. [138] reported lower meat lightness in broiler meat along with OAs administration. The possible cause might be the destruction of the myoglobin content and subsequent reduction of the meat redness.

Moreover, Jha et al. [138] reported that the inclusion of OAs (formic + propionic acid, formic + citric acid, formic + sorbic, and formic+ lactic acid) enhanced the meat thigh weight, back weight, wings weight, and breast weight compared to the control group. On

the other hand, they did not evaluate any other meat quality parameters regarding OAs inclusion. Lower saturated fatty acid (SFA) and higher polyunsaturated fatty acid (PUFA) contents of meat reduce the risks on human health. Because promising feeding strategies directly influence the meat quality parameters, it is important to discover effective feeding techniques to ensure the safety and quality of the meat. Akbar et al. [139] observed a significantly higher PUFA content and lower SFA proportion than the birds fed a basal diet. Furthermore, a lower cholesterol content was also reported in the diet containing dietary OAs. Heat stress is considered one of the significant issues that have adversely affected the global poultry sector. Previous studies found that acute heating conditions led to a decrease in meat pH, lightness of major muscle tissues, and increased cooking losses [140]. On the other hand, He et al. [141] stated that a diet supplemented with fumaric acid for birds under heat stress helped alleviate the poorer meat quality traits, including excessive pH, drip loss, and cooking loss.

4.4 Effects of the incorporation of OAs on meat preservation

Meat preservation and protecting its organoleptic properties contribute to the consumer's nutritional trends, food safety, and qualitative characteristics of meat. Consumers' demand for natural food consumption has increased gradually, resulting in increased interest in the modern "biopreservation" process in the meat industry. Thus, OAs administration acts as a bio-preservation agent in animal source-based food products [142]. The most widely used OAs in meat product preservation are acetic, lactic, propionic, sorbic, benzoic, citric acids, and sulfites, which can disrupt the proliferation and colonization of pathogenic microbes [143]. Despite ameliorating the microbial activities, OAs influenced the development of sensory attributes, physical properties, such as stabilization, color, and regulation of acidity [144,145]. Nair et al. [146] reported that incorporating sorbic acid in meat products could inhibit mold growth while not affecting the lactic acid bacteria population, thereby ensuring the beneficial preservative characteristics of fermented meat products.

The addition of sodium lactate at 1.5 and 3% favorably enhanced the sensory attributes and shelf life of fresh ground pork. Furthermore, it enhanced the meat juiciness and flavor while reducing the aerobic plate counts significantly [147]. Higher redness value, less protein degradation, and less residual nitrite level were exhibited when pork loin was cured with ascorbic acids compared to the control treatments [148]. Furthermore, Carpenter et al. [149] reported a lower salmonella population on pork belly treated with 2% of lactic or acetic acid spray washing, which minimized the tendency of a later growth rate of pathogens. A recent study assessed the antimicrobial effect of organic acids (1,2 and 3% of acetic, lactic, and citric acids) against *L. monocytogenes*, *E. coli*, *S. Enteritidis*, *Y. enterocolitica*, and *C. jejuni* in pork meat. However, the most effective OA was lactic acid, followed by acetic and citric acid, respectively [150]. González Sánchez [151] evaluated the antimicrobial capacity of formic acid (1.5%) and peroxyacetic acid (400 ppm). They reported that acid spray treatment effectively influenced the reduction of *Salmonella enterica* counts in meat pork after 24h at a lower temperature (4°C).

Gonzalez-Fandos et al. [152] evaluated the decontaminating ability of acetic, citric, and fumaric acids, and potassium sorbate to decrease *Campylobacter jejuni* on chicken legs. The analyzed data showed the lowest *Pseudomonas* counts, lowest *Enterobacterales* counts, and highest *C. jejuni* reductions in treatments, consisting of 2% fumaric, 2% fumaric, or 2% acetic, and 2% citric acid, respectively. Interestingly, the application of 0.5% microencapsulated OAs (citric and sorbic) with essential oil resulted in less intramuscular fat, lower saturated/polyunsaturated fatty acids ratio, reduced TBARS value, zero contamination of *Listeria* spp., *Campylobacter* spp., and *Clostridium* spp. and increased meat color values than the control treatment [153]. A lower TBARS value influenced the lower lipid oxidation in meat, and prevented the degradation of unsaturated fatty acids, and converted oxymyoglobin to metmyoglobin. Otherwise, the high lipid oxidation process led

to the generation of free radicals and rapid meat quality deterioration [154]. Therefore, OA treatments for meat preservation will improve qualitative characteristics in both meat pork and broilers.

5. Potential concerns regarding OAs utilization

Pathogenic microbial activities encompass a broad range of survival mechanisms that facilitate the multiplication and survival by evading their host defense system. Although OAs supplementation has a favorable impact on pigs and broiler production through the biological defense system, bacterial resistance should be considered. Recent studies revealed the specific developed mechanisms of *Escherichia coli* [142] and *Salmonella enterica* [155,156]. Some genes, including wecA (rfe), waaG (rfaG), fcl (Fucose, FX-like), and wecB (rffE), can control the manipulation of acid tolerance response. The degradation of surface O-polysaccharide plus enterobacterial common antigen (ECA) and O-polysaccharide occur because of those mutations, which are acting as reinforcement agents in *Salmonella* spp and *E. coli* groups against the OAs. This adaption process consists of two mechanisms: (1) transient adaptation and (2) pre-challenge adaptation, which occurs specifically in lower pH ranges [157,158,159]. Despite minimizing the cost of production and the requirement of specific awareness, encapsulated OAs utilization has gained less popularity in the commercial livestock sector except for experimental studies. Hume et al. [160] reported that most unprotected propionic acid did not reach the crop, proventiculus, gizzard, and rest of the small intestines. Because the crop acts as a primary site for salmonella colonization, the movements of OAs to the lower GIT tract should be ensured by incorporating novel technological methods. Conner and Kotrola [161] reported that *E.coli* could survive under pH≥4.0 and below 4.0 °C for up to 56 days. On the other hand, the prevalence is affected by the temperature and type of the acidifier. OAs, being SCFA, have lower pH levels in the GI tract, consequently reducing the livability of pathogenic bacteria at the cellular level. Nevertheless, pH-independent tolerance is also possible. Higher resistance to *S. typhimurium* was observed when the animals were exposed to higher SCFA concentrations, which produced a lower pH environment in the GI tract [162]. Kwon et al. [163] reported that higher SCFA concentrations in the large intestines cause the cross-resistance of *S. typhimurium* 14028S to other stressors, including extreme pH level and 20 mM H_2O_2. Dickenes et al. [164] and Dickenes and Whittemore [165] reported that the appearance and texture quality of broiler meat was influenced adversely by acetic acid dipping. Although most OA combinations were favorably associated with nutrient digestibility, Garber and Sauer [166] reported lower CP and amino acid digestibility in the pig ileum. Another considerable effect of supplementation of OAs is the reduction of lactic acid synthesis and LAB population in the GI tract. Thompsan and Hinton [167] reported the interaction of formic and propionic acid inclusion on lower lactic acid production in the crop. Thus, the concentrations and interactions among each OA combination will require further molecular based studies.

6. Conclusion

The supplementation of organic acids has significant effects on the growth performance and digestion of nutrients by modulating the gut environment of both swine and broilers. In particular, some OAs significantly developed the gut physiology by increasing the villus height: width ratio and surface area of the duodenum, jejunum, and ileum of swine and broilers. Previous studies reported that protective OAs supplementation is effective and safe for monogastric animal diets because they act on the exact stimulus while delaying quick movement in the GI track. On the other hand, to benefit from the effectiveness of OAs, the inclusion dosage, rearing environment, nutrient composition, growth phase, and health status of animals need to be considered. The lack of consistency in exhibiting the benefits of dietary inclusion of OAs on meat quality parameters, sensory attributes, and storage safety should be evaluated further. The chemical mechanisms of OAs in animal diet and synergism effects are not completely understood. Therefore, it is impossible

to recommend a specific combination of OAs and concentrations that will positively affect the swine and broiler production parameters and meat quality traits. On the other hand, the application of OAs treatments on meat product preservation has positive impacts on the quality improvements. Further scientific exploration will be needed to unravel the exact modes of action in different parts of the GI tract and based on the inclusion concentration. Once more knowledge comes available, promising feeding strategies can be implemented by incorporating various organic acid formulas into the animal diet.

Funding: This research received no external funding

Institutional Review Board Statement: Not applicable

Informed Consent Statement: Not applicable

Data Availability Statement: Not Applicable

Acknowledgments: Industrial Technology Innovation Business Development and Demonstration of Renewable Energy Mixed-Use System for the Livestock Industry, Korea and the Cooperative Research Program for Agriculture Science & Technology Development Rural Development Administration, Republic of Korea.

Conflicts of Interest: The authors declare no conflict of interest.

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