

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.

For more information visit www.intechopen.com



The Prophylactic Use of Acidifiers as Antibacterial Agents in Swine

V. G. Papatsiros and C. Billinis
*School of Veterinary Medicine,
University of Thessaly,
Greece*

1. Introduction

In recent decades, acidifiers have emerged as viable alternatives to antibiotics in swine diets, in order to stimulate optimal growth performance and prevent various enteric diseases. Antimicrobials have been used for more than 50 years to enhance growth performance and prevent various pig diseases (Gustafson & Bowen, 1997). There is growing public awareness of the relationship between the feed medication with antimicrobials as growth promoters in livestock diets and the risk of developing cross-resistance of pathogens to antibiotics, threatening animals and human health (Corpet, 1996; Mathew et al. 2007; Hunter et al. 2010). During the last few years, as the use of antibiotics in pig diets has decreased, the use of acidifiers has increased.

Acidifiers can be in organic or inorganic acids or associated salts. As a group of chemicals, organic acids are considered to be any organic carboxylic acid of the general structure R-COOH (including fatty acids and amino acids) (Partanen & Mroz, 1999). Organic acids are widely distributed in plants and animals. They are also produced by microbial fermentation of carbohydrates and other fermentable material, predominantly in the large intestine of pigs. Table 1 shows the common name, chemical name, formula and first pKa- the pH at which the acid is half dissociated - of organic acids that are commonly used as dietary acidifiers in pigs (Partanen & Mroz, 1999).

The activity of most common acids, as well as their beneficial effects is shown in Table 2. Acidifiers have received much attention in pig production due to their beneficial effects on growth performance of pigs (Mahan et al. 1996; Partanen, 2001; Papatsiros et al. 2011). Many acids are available as sodium, potassium or calcium salts and several researchers have proposed their use because of their convenient application and their better effects than those of pure state acids. Table 3 shows a list of the most common salts of acids and their properties. The advantage of salts over free acids is that they are generally odourless and easier to handle in the feed manufacturing process due to their solid and less volatile form. Salts of acids are also less corrosive and may be more soluble in water than free acids (Partanen & Mroz, 1999). Although beneficial effects have been reported from trials using supplements of salts in pig diets (Table 3), other studies have not introduced any positive effects (Biagi et al. 2007; Weber & Kerr, 2008).

Acid	Chemical name	Formula	pKa	Solubility in water	Physical form	Odour / Taste	Production
Formic	Formic Acid	HCOOH	3.75	soluble in all proportions	Liquid (in pure state) Colourless, transparent, fuming	Pungent odour Emission of strong odors	Synthetically: from methyl formate and formamide, by-product of acetic acid production and by laboratory methods Naturally: in many fruits (apples, strawberries and raspberries), honey and nettles
Acetic	Acetic Acid	CH ₃ COOH	4.76	soluble in all proportions	Liquid Colourless, Very volatile	Pungent odour Sour taste	Synthetically: by various methods Naturally: by bacterial fermentation dietary fibre in the colon
Propionic	2-Propanoic Acid	CH ₃ CH ₂ COOH	4.88	soluble in all proportions	Liquid (in pure state) Oily	Pungent odour Emission of very strong smells	Synthetically: from ethyl alcohol and carbon monoxide Naturally: by bacteria of genus Propionibacterium, as the end product of their fermentation of dietary fibre in the colon
Butyric	Butanoic Acid	CH ₃ CH ₂ CH ₂ COOH	4.82	soluble in all proportions	Liquid Oily	Rancid, unpleasant odour Acrid taste, with a sweetish after taste (similar to ether)	Synthetically: by fermentation of sugar or starch Naturally: by bacterial fermentation dietary fibre in the colon
Lactic	2-Hydroxypropanoic Acid	CH ₃ CH(OH)COOH	3.83	very soluble	Liquid (in pure state) colourless or slightly yellow	Rancid, disagreeable odour Sour milk taste	Synthetically: from chemicals or organically as a byproduct of corn fermentation. Naturally: by bacterial fermentation of carbohydrates such as glucose, sucrose, or lactose by many species (Lactobacillus, Bifidobacterium, Streptococcus) Natural constituent of some feedstuffs
Sorbic	2,4-Hexandienoic Acid	CH ₃ CH:CHCH:CHCOOH	4.76	sparingly soluble	Solid white crystalline powder or granule form	Distinctive odour Midly acrid and sour taste	Synthetically: by several different chemical pathways Naturally: in certain berries
Fumaric	2-Butenedioic Acid	COOHCH:CHCOOH	3.02	sparingly soluble	Solid white crystalline powder	Odourless Tart flavour, fruit-like taste	Synthetically: from malic acid Naturally: in fumitory (Fumaria officinalis), bolete mushrooms (specifically Boletus fomentarius var. pseudo-igniarius), lichen, and Iceland moss.
Malic	Hydroxybutanedioic Acid	COOHCH ₂ CH(OH)COOH	3.40	soluble in all proportions	Liquid / Solid white crystal or crystalline powder	Odourless Apple taste	Synthetically: from maleic anhydride Naturally: in apples and in many other fruits (mostly in unripe fruits)
Tartaric	2,3-Dihydroxy-Butanedioic Acid	COOHCH(OH)CH(OH)COOH	2.93	very soluble	Liquid	Strong acid taste	Synthetically: by chemical reactions of maleic anhydrid Naturally: in many plants (particularly grapes, bananas, tamarinds)
Citric	2-Hydroxy-1,2,3-Propanetricarboxylic Acid	COOHCH ₂ C(OH)(COOH)CH ₂ COOH	3.13	very soluble	Solid	Odourless Pleasant sour taste	Synthetically: by a fermentation process Naturally: in a variety of fruits (most notably citrus fruits- lemons, limes) and vegetables
Benzoic acid	Benzenecarboxylic acid	C ₆ H ₅ COOH	4.19		Solid colorless crystalline	Highly fragrant odour	Synthetically: by partial oxidation of toluene with oxygen Naturally: in many plants as an intermediate in the formation of other compounds

Table 1. List of acids and their properties

Inorganic acids added to the pig diets are hydrochloric, sulfuric, and phosphoric acid. Organic and inorganic acids or/and salt form combinations are often used in commercially available acidifiers. The response to mixed acids is generally better than to single acids possibly due to dissociation properties of these acids at various locations in the pig's digestive tract (Hardy 2002; Franco et al. 2005; Partanen et al. 2007; Kasproicz-Potocka et al. 2009).

Acid	Beneficial effects	
	Antimicrobial activity	Improvement of growth performance
Formic	<i>High antibacterial activity: Coliforms (E. coli - ETEC strains), Salmonella spp.</i> Creus et al. 2007 Knarreborg et al. 2002 Øverland et al. 2007	Jensen et al. 2001 Naughton & Jensen 2001 Tsiloyiannis et al. 2001a
Acetic	<i>Active against bacteria - inhibits the growth of many species of bacteria (E. coli, Salmonella spp) - a lesser extent of yeasts and moulds</i> Jensen et al. 2001	Partanen & Mroz 1999 Piva et al. 2002 Valencia 2002 Roth & Kirchgessner 1988
Propionic	<i>High spectrum of action against fungi and yeasts - Antibacterial activity: Coliforms (E. coli - ETEC strains), Salmonella spp.</i> Foegeding & Busta, 1991 Knarreborg et al. 2002 Partanen & Mroz 1999	Jensen et al. 2001 Naughton & Jensen 2001 Tsiloyiannis et al. 2001a Partanen et al. 2007 Tsiloyiannis et al. 2001a
Butyric	<i>Antibacterial activity: Coliforms (E. coli)</i> Knarreborg et al. 2002	Naughton & Jensen 2001 Mroz et al. 2000
Lactic	<i>High antibacterial activity: Coliforms (E. coli - ETEC strains), Salmonella spp. - Many moulds and yeasts can metabolize it</i> Creus et al. 2007 Jensen et al. 2001 Naughton & Jensen 2001 Tsiloyiannis et al. 2001a, b	Foegeding & Busta, 1991 Knarreborg et al. 2002 Piva & Grilli 2007 Jongbloed et al. 2000 Tsiloyiannis et al. 2001a, b
Sorbic	<i>Antibacterial activity: Coliforms (E. coli - ETEC strains), Salmonella spp. - Active against yeasts, moulds, fungi</i> Foegeding & Busta, 1991 Øverland et al. 2007	Jensen et al. 2001 Piva & Grilli 2007 Kirchgessner et al. 1995
Fumaric	<i>Antibacterial activity: (E. coli - ETEC strains, clostridia)</i> Biagi et al. 2003 Naughton & Jensen 2001 Tsiloyiannis et al. 2001a	Knarreborg et al. 2002 Owusu-Asiedu et al. 2003 Giesting et al. 1991 Lawlor et al. 2006 Owusu-Asiedu et al. 2003 Tsiloyiannis et al. 2001a Krause et al. 1994 Mroz et al. 2000 Risley et al. 1991
Malic	<i>Antibacterial activity: Coliforms (E. coli - ETEC strains) Active against yeasts -</i> Partanen & Mroz 1999	Tsiloyiannis et al. 2001a Kirchgessner et al. 1993 Tsiloyiannis et al. 2001a Krause et al. 1994
Citric	<i>Antibacterial activity: Coliforms (E. coli)</i> Foegeding & Busta, 1991 Tsiloyiannis et al. 2001a, b	Boling et al. 2000 Radcliffe et al. 1998 Tsiloyiannis et al. 2001a, b Krause et al. 1994 Risley et al. 1991
Benzoic acid	<i>Antibacterial activity: Coliforms (E. coli)</i> Papatsiros et al. 2011	Piva & Grilli 2007 Bühler 2009 Maribo et al. 2000 Kluge et al. 2006

Table 2. Activity of most common acids - Beneficial effects

2. Mechanisms of action

Benefits from the use of dietary acidifiers include positive effects on growth performance and health status (Figure 1). Proposed mechanisms of action include reduction or stabilization of gastric pH, resulting in increased activity of proteolytic enzymes and gastric retention time, and thus led to improvement of protein digestion. Organic acids may influence mucosal morphology or induce alterations in gut microflora through bacteriostatic or bactericidal actions, as well as enhance endogenous enzyme activity, stimulate pancreatic secretions, and they also serve as substrates in intermediary metabolism (Partanen & Mroz, 1999). It is also

hypothesized that acidifiers could be related to the reduction of gastric emptying rate, the energy source in intestine, the chelation of minerals, the stimulation of digestive enzymes and the provision of an energy source in the distal gastrointestinal tract. Organic acid supplementation can reduce dietary buffering capacity, which is expected to slow down the proliferation and/or colonization of undesirable microbes, e.g. *Escherichia coli*, in the gastro-ileal region, resulting in reduction of scouring (Partanen & Mroz, 1999; Partanen, 2001).

Name	Physical form	Odour	Application possible in	Beneficial effects	
Ca/ K/ Na salts				Antimicrobial activity	Improvement of growth performance
Ca salts (eg Ca-formate, Ca-propionate)	Solid	Neutral	Feed	Bosi et al. 2005, 2007 Eidelsburger et al. 1992b	Bosi et al. 2006
K salts (eg K-diformate, K-sorbate)	Solid	Neutral	Feed	Canibe et al., 2001 Øverland et al. 2000 Taube et al. 2009	Roth et al. 1996 Mroz et al. 2002 Øverland et al. 2000 Papenbrock et al. 2005 Partanen et al. 2007 Paulicks et al. 2000 Windisch et al 2001
Na salts (eg Na - butyrate, Na- benzoate, Na - formate)	Solid	acid / Neutral	Feed	Pallauf & Huter 1993 Kirchgessner & Roth 1990	Piva et al. 2002b Partanen et al. 2007 Mazzoni et al. 2008 Le Gall et al. 2009
Ammonium salts (eg. Amm. formate)	Liquid		Water, feed		Eisemann & Heugte 2007

Table 3. List of most common salts of acids and their properties

The hypothesis that lowering dietary pH with organic acids reduces gastrointestinal pH has been tested in several studies. The low pH of gastric contents is thought to kill many ingested bacteria, while the gastric pH of newly weaned piglets is notably higher than of older pigs. So in newly weaned pigs this protective action may be enhanced by any low pH which is produced by acids in the feed in comparison to the gastric pH (Ravindran & Kornegay, 1993). Moreover, weaned piglets are physiologically immature and may not produce enough hydrochloric acid (HCl) to keep stomach pH at an optimum of approximately 3.5 (Ravindran & Kornegay, 1993). Weaned piglets are physiologically immature and may not produce enough hydrochloric acid (HCl) in order to keep stomach pH at an optimum of approximately 3.5.

The purpose of adding acidifiers in feed, is to lower the pH in the stomach below pH 5, resulting in an increased activity of proteolytic enzymes, improving protein digestibility and inhibiting the proliferation of pathogenic bacteria in the gastrointestinal tract (Partanen & Mroz, 1999). At pH=3.5, digestion of proteins and populations of beneficial bacteria (lactobacilli) are maximized and harmful bacteria are inhibited. Organic acids, in a non dissociated form, are lipophilic and can diffuse across bacterial cell membranes to reach the interior of the cell. There, in the relatively high intracellular pH, organic acids dissociate and disrupt the bacterial cell function and this effect may be stronger in some bacteria than in others (Partanen, 2001). A low pH is required for conversion of pepsinogen to pepsin, which is the active form of the most important gastric proteolytic enzymes. Elevated gastric pH may lead to an ineffective gastric proteolysis as a result of limited pepsin activity, and then a greater proportion of protein may enter the small intestine intact, resulting in lower

efficiency of digestion and scouring problems (Piva et al. 2002a). In addition, the pH activity profile of pepsin seems to be more active at a low pH. Some results indicate that short-chain fatty acids have a stimulatory effect on both endocrine and exocrine pancreatic secretions in pigs; pancreatic exocrine responses are ranked as: formic acid > lactic acid > acetic acid > butyric acid > propionic acid (Harada et al. 1986).

There are considerable variations in the results of response to acidification due to possible dietary and other factors such as (Mroz, 2005):

- feed palatability,
- type / pKa / dose of supplemented acids,
- type / composition of diets and their acid-base or buffering capacity,
- level of intraluminal production of acids in particular segments of the gastrointestinal tract by inhabiting microflora,
- quantity of fermentable carbohydrate substrates in the diet for bacterial growth,
- colonization and activity resulting in acids production,
- receptors for bacterial colonization on the epithelial villi,
- maternal immunity by vaccinations against pathogens,
- age of pigs,
- hygiene and welfare standards (density/pen, ventilation intensity and area, cleaning frequency etc.)

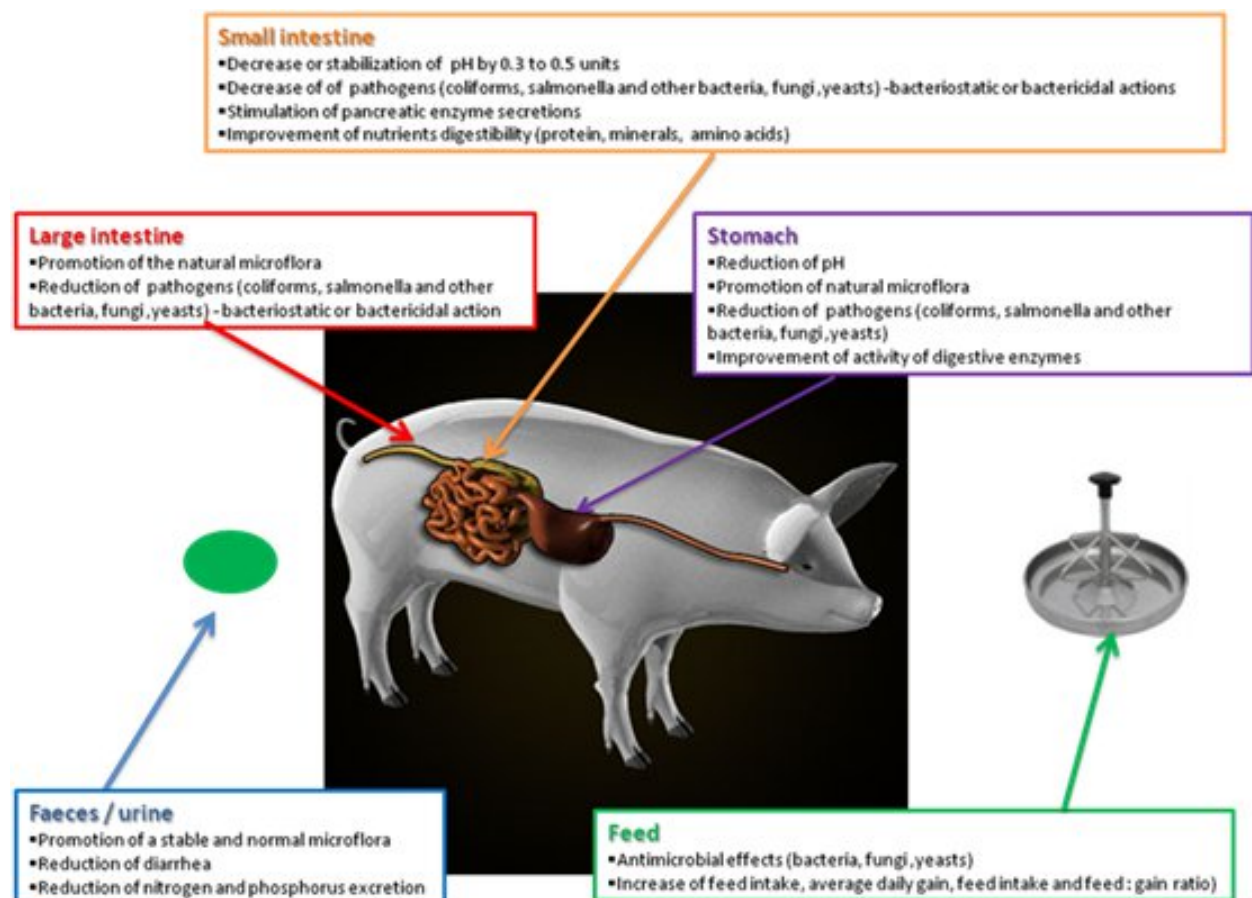


Fig. 1. Mode of action of acidifiers in pig

Dietary buffering capacity varies substantially between different feedstuffs (Bolduan et al. 1988a, 1988b). The acid-buffering capacity is lowest in cereals and cereal by-products, intermediate or high in protein feedstuffs and very high in mineral sources (Jasaitis et al. 1987). Addition of organic acids reduces dietary pH curvili nearly depending on the acid pKa value and buffering capacity (Bolduan et al. 1988a, 1988b) of the diet. The pH-lowering effect of different organic acids is reduced in the following order: tartaric acid>citric acid>malic acid> fumaric acid>lactic and formic acids>acetic acid> propionic acid. Salts of organic acids have only a small influence on dietary pH, but the addition of protein and mineral sources to the diet weakens the pH-lowering effect of the acid (Roth & Kirchgessner, 1989). It seems reasonable to assume that the buffering capacity of feed can be considerably influenced by the selection of feed ingredients, and it may in part reflect the differences in the effectiveness of acidifiers. In general, organic acids lower dietary buffering capacity, whereas certain salts of organic acids can increase it.

The greatest acidification benefits have been observed in diets formulated from cereals and plant proteins, while the growth-promoting effect in diets containing milk products is small (Giesting et al. 1991). The latter presumably holds true when lactose in milk products is converted to lactic acid by lactobacilli in the stomach, creating the desired reduction in pH and thus reducing the need for diet acidification (Easter, 1988).

2.1 Antimicrobial activity

There are several commercial products with organic acids on the market, all with their own specific chemical and functional properties. As shown in Table 1, the inclusion of organic acids can reduce pH and the feed's buffering capacity, while their antimicrobial effect can prevent the growth of bacteria (especially Gram negative bacterial species, like *Salmonella spp.* and *E. coli*), yeasts and moulds. In the stomach, the pH is decreased, reducing the concentration of all the types of bacteria. In the small intestine, only the organic acids with antibacterial activity are able to inhibit bacteria growth. This is the main reason that the use of these acids has been proposed as a way of preventing or reducing the incidence of diarrhea in young pigs (Jensen et al. 2001; Tsioloyiannis et al. 2001a, 2001b; Piva et al. 2002a; Papatsiros et al. 2011). Thus, the organic acids are divided into two large groups. In the first group are included those with indirect effect on the decrease of the bacterial population by pH reduction and acting mainly on the stomach because the animal organism has the capability of preventing the decline in the acidity in the small intestine by buffering the medium with bicarbonate (fumaric, citric, malic and lactic acids). In the other group, are involved those organic acids (formic, acetic, propionic and sorbic acid), that have the ability to reduce the pH and affect directly Gram- bacteria by interfering in the bacterial cell with complex enzymes. These enzymes destroy the cell membrane and influence the mechanism of DNA duplication which prevents bacterial reproduction (Castro, 2005).

Many studies with dietary acidifiers have shown positive effects in improving growth rate, feed efficiency and acting against bacteria, yeast, fungi, moulds (Table 2), but others have found a negligible and even negative negative response (Radecki et al. 1988; Eidelsburger et al. 1992a; Manzanilla et al. 2004; Štukelj et al. 2010). It is likely that the antimicrobial effects of the organic acid ions, which act by controlling bacterial populations in the upper gastrointestinal tract, are responsible for the beneficial effects of these acids (Roth & Kirchgessner, 1998). Moreover, organic acids can also enhance the effects of antibiotics by improving their absorption (Radecki et al. 1988; Eidelsburger et al. 1992b). In addition, acidifiers can have an initial

eradicated effect on bacteria in the feed (Lueck, 1980) and remain there as a first barrier, preventing re-contamination. Even *under good conditions*, all compound feeds have a certain content of germs (bacteria, viruses, fungi and protozoa), which may be proliferate under unfavourable harvest and storage conditions (Schöner, 2001). Preservatives reduce the incidence of germs in the feed and thus the quantity of germs consumed by the animals. The hygienic quality of feed is significantly improved. The addition of organic acid lowers the pH value of the feed and also provides acid-binding capacity.

In fact, organic acids associated with specific antimicrobial activity are short-chain acids (SCFA, C1-C7) and are either simple monocarboxylic acids such as formic, acetic, propionic and butyric acids, or carboxylic acids, bearing a hydroxyl group (usually on the carbon) such as lactic, malic, tartaric, and citric acids. Four organic acids commonly used in feed - formic, acetic, propionic and lactic acid - have a specific ability to penetrate the bacterial cell wall and kill bacteria by interfering with their metabolism. These acids only pass the membrane in non dissociated form. Their primary antimicrobial action (strain-selective growth inhibition or delay) is through pH depression of the diet. However, the ability of organic acids to change from undissociated to dissociated form, depending on the environmental pH, makes them effective antimicrobial agents. When acid is in the undissociated form it can freely diffuse through the semi permeable membrane of microorganisms into their cell cytoplasm. Once inside the cell, where the pH is maintained near 7, the acid dissociates and suppress cell enzymes (decarboxylases and catalases) and nutrient transport systems (Lueck, 1980). The efficacy of an acid in inhibiting microbes is dependent on its pKa value which is the pH at which 50% of the acid is dissociated. Organic acids with higher pKa values are more effective preservatives and their antimicrobial efficacy is generally improved with increasing chain length and degree of unsaturation (Foegeding & Busta, 1991). In practice this means that the stomach pH has to be lower than 5 for optimal results. Without these specific antimicrobial acids, the pH needs to be very low to destroy bacteria. Some of the above acids' salts, have also shown to have benefits on growth performance. Other acids, such as sorbic and fumaric acid, have some antifungal activity and are short chain-carboxylic acids, containing double bonds. Organic acids are weak acids and are only partly dissociated; most of them, with antimicrobial activity, have a pKa 3 - 5.

In addition, each acid has its own spectrum of antimicrobial activity. Their antimicrobial effects vary from one acid to another, depending on concentration and pH (Chaveerach et al. 2002). For example, lactic acid is more effective in reducing gastric pH and coliforms (Jensen et al. 2001; Tsiloyiannis et al. 2001a; Øverland et al. 2007), whereas other acids, such as formic, propionic have broader antimicrobial activities and they can be effective against bacteria (e.g. coliforms, clostridia, Salmonella), fungi and yeast (Partanen & Mroz, 1999; Bosi et al. 2005; Creus et al. 2007; Øverland et al. 2007). Several reports have shown that the use of organic acids may reduce the coliform burden along the gastrointestinal tract (Bolduan et al. 1988b) and reduce scouring and piglet mortality or control postweaning diarrhea and edema disease in piglets (Tsiloyiannis et al. 2001a, 2001b; Piva et al. 2002a, Papatsiros et al. 2011). The following order of killing potency of coliform bacteria in the gastric digesta at pH 3, 4, and 5, are: propionic < formic < butyric < lactic < fumaric < benzoic were established (Naughton & Jensen, 2001; Knarreborg et al. 2002). Jensen et al. (2001) demonstrated that the potency of these acids against *Salmonella typhimurium* in gastric digesta at pH4 was in the following order: acetic < formic < propionic < lactic < sorbic < benzoic. Inconsistent results may be due to the variety of diets with different buffering capacities that were used in these

experiments. Bacteria are known to develop acid-resistance when exposed to acidic environments for some time (Mroz, 2005).

2.2 Antibacterial activity and growth promoting effects

The beneficial effects of organic acids and their salts on growth performance have been confirmed in several studies. Acidifiers added to pig diets may potentially help improve growth performance (Table 2 & 3) by improving digestive processes through several mechanisms. It is believed that acidifiers can enhance the growth performance by:

- a. Improving gut health by promoting the beneficial bacterial growth, while inhibiting growth of pathogenic microbes (through reduction of pH and buffering capacity of diets). A reduced buffering capacity of diets containing organic acids is also expected to slow down the proliferation and/or colonization of undesirable microbes, e.g. *E. coli*, *clostridia* in the gastro-ileal region (jejunum, cecum) (Partanen & Mroz, 1999; Biagi et al. 2003). In addition organic acids or their salts could not improve the animal growth performance, but they could indirectly increase cecal pH and cecal ammonia concentrations (Biagi et al. 2007).
- b. Stimulating - improving pancreatic secretions (Harada et al. 1986), which increase the digestibility, absorption and retention of protein and amino acids (Blank et al 1999, Kemme et al. 1999) and minerals (such as Ca, P, Mg and Zn - particularly Ca and P) (Jongbloed et al. 2000; Valencia, 2002; Omogbenigun et al. 2003) in the diet. Although opposite results have also been reported (Radecki et al. 1988), it is generally considered that dietary organic acids or their salts lower gastric pH, resulting in increased activity of proteolytic enzymes and gastric retention time.
- c. Influencing of gut morphology by promoting changes in the digestive function and microbial ecology and fermentation (Piva et al. 2002a; Manzanilla et al. 2004). Some organic acids act positively on microbial growth and ammonia production by pig cecal microflora. Biagi and Piva (2007) noticed that various acids (formic, acetic, propionic, lactic, butyric, sorbic, fumaric, malic, citric, benzoic) can inhibit or enhance cecal bacterial activity and can positively influence pig cecal microflora *in vitro* fermentation reducing ammonia concentrations. It is well known that short-chain fatty acids (acetic, propionic and n-butyric acid) produced by microbial fermentation of carbohydrates stimulate epithelial cell proliferation (Sakata et al. 1995) and the strength of this effect is in the following order: n-butyric>propionic>acetic acid (Sakata, 1987). Increased epithelial cell proliferation has also been observed when short-chain fatty acids are orally given or provided by intravenous or gastrointestinal infusions (Sakata et al. 1995), since dietary organic acids can influence fermentation patterns in the small intestine, and may indirectly influence intestinal morphology. Kirchgessner and Roth (1988) have proposed that organic acids may stimulate intermediary metabolism resulting in improved energy or protein/amino acid utilization.

The use of some organic acids has been found to reduce the formation of biogenic amines (such as cadaverine and putrescin) that are produced particularly in high protein feeds and in feeds, containing added synthetic amino acids. Biogenic amines have unfavourable effects on growth and feed conversion. The growth stimulation effects of formic, acetic and propionic acids are partly caused by their inhibitory effect on biogenic amines (Eckel et al. 1992). However, a clear mode of action has not been fully described yet and the magnitude and consistency of the response may vary, depending on inclusion rate and other dietary factors.

The use of acidifiers appears to be most beneficial in the early period after weaning. Studies demonstrating the improved feed conversion ratio, weight gain and growth-promoting effects of acidifiers indicated that the effect was greater in young pigs than older pigs (Radcliffe et al. 1998; Øverland et al. 2000; Partanen et al. 2007), but there is some evidence that they may be beneficial for improvement of daily gain and feed efficiency in growing-finishing pigs (Øverland et al. 2000; Partanen et al. 2001a; Gauthier 2002; Canibe et al. 2005).

The results of trials including the addition of inorganic acids in pig diets has indicated positive responses on growth performance (Walsh et al. 2007; Stein, 2007), especially during the period after weaning (Mahan et al. 1996, 1999). However, the use of other inorganic acids, such as sulfuric acid, has not shown positive effects on growth performance (Ravindran & Kornegay, 1993). In addition, salts of organic acids, such as formates and diformates can be used to significantly improve growth rate and feed conversion in pigs (Table 3). However, there are also studies with no responses (Biagi et al. 2007) or involving risk factors (Pallauf & Huter, 1993; Øverland et al. 2000). For example, calcium formate decreased feed intake and daily gain (Pallauf & Huter, 1993; Øverland et al. 2000).

3. Risk factors of acidifier use

The use of organic acids in feed appears two main problems:

- a. Acidifiers may have a negative effect on diet palatability, when they are added at excessive levels, resulting in lower feed intake or feed refusal (Partanen & Mroz, 1999). Certain acids, e.g. tartaric and formic acids have a strong odour and flavour, and an increasing dietary acid level, which is generally associated with a dramatic decrease in feed intake, as reflected by lower daily gains (Eckel et al. 1992; Kirchgessner et al. 1993). Addition of excessive amounts of formates to the diet may also disturb the acid-base status of pigs leading to metabolic acidosis, which results in decreased feed intake and slower growth (Giesting et al. 1991; Eckel et al. 1992; Eidelsburger et al. 1992e). Organic acids metabolized via the citric-acid cycle, e.g. fumaric and citric-acids, do not seem to cause acidosis, irrespective of their dietary inclusion (Eidelsburger et al. 1992c).
- b. Acids at high levels in feed are corrosive to cement and galvanized steel in pig housing, resulting to pose handling and equipment issues to the feed manufacturer. For example, formic acid is the most corrosive for the equipment and it is dangerous to handle, while fumaric acid is easy to handle (Mateos et al. 1999). Salts of organic acids are generally odorless and less corrosive than their acid forms, making them easier to handle in the feed manufacturing process (Jacela et al. 2009).
- c. The use of organic acids in their free form, at levels that have been proven to be efficacious, can cause palatability problems (Partanen, 2001), damage the stomachal and duodenal mucosae (Argenzio & Eisemann, 1996), as well as cause bone demineralization (Partanen & Mroz, 1999) and an acidic stress, inducing a resistance mechanism towards organic acids in certain bacteria (Bearson et al. 1997).

In order to minimize these effects, the natural buffering capacity of feeds (related to mineral and protein content) should be evaluated to determine the minimum effective amount of acid to use (Best, 2000). Another strategy to extend the effectiveness of acid supplements and reduce corrosion damage to housing materials is the use of a slow-release form of acids. It consists on the use of organic acids with fatty acids and mono- and diglycerides mixed to form microgranules. A study by Cerchiarri (2000) showed that use of these granules, as compared to use of free acids, results in greater feed intake and growth.

4. Conclusion

Due to consumers' concern about the possibility of drug resistance of pathogenic bacteria, there is an urgent need to search for growth promoters other than antibiotics. Dietary acidifiers can actually become the most common and efficacious alternative solution to antibiotics, in order to improve health status and performance of pigs. The use of organic acids in pig production could be part of a general nutritional strategy focusing on a better gastrointestinal health; the goal is better productivity and better meat quality.

5. References

- Argenzio, R.A. & Eisemann, J. (1996). Mechanisms of acid injury in porcine gastroesophageal mucosa. *American Journal of Veterinary Research* Vol. 57, No. 4, pp. 564-573, ISSN 0002-9645.
- Bearson, S.; Bearson, B. & Foster, J.W. (1997). Acid stress responses in enterobacteria. *FEMS Microbiology Letters*, Vol. 147, No. 2, pp. 173-180, ISSN 1574-6968.
- Best, P. (2000). Adding acids to swine diets. *Feed Management*, Vol. 51, No. 5, pp. 19-22, ISSN: 0014-956X.
- Biagi, G. & Piva, A. (2007). In vitro effects of some organic acids on swine cecal microflora. *Italian Journal of Animal Science* Vol. 6, No. 4, pp. 361-374, ISSN 1594-4077.
- Biagi, G.; Piva, A.; Hill, T.; Schneider, D.K. & Crenshaw, T.D. (2003). Low buffering capacity diets with added organic acids as a substitute for antibiotics in diets for weaned pigs, *Proceedings of the 9th International Symposium on Digestive Physiology in Pigs*, pp. 217-219, (Ball R, ed.) University of Alberta, Department of Agriculture, Food and Nutritional Science, Edmonton, Banff, Alberta, Canada, May 14-17, 2003.
- Biagi, G.; Piva, A.; Moschini, M.; Vezzali, E. & Roth, F. (2007). Performance, intestinal microflora, and wall morphology of weanling pigs fed sodium butyrate. *Journal of Animal Science*, Vol. 85, No. 5, pp. 1184-1191, ISSN 0021-8812.
- Blank, R.; Mosenthin, R.; Sauer, W.C.; & Huang, S. (1999). Effect of fumaric acid and dietary buffering capacity on ileal and fecal amino acid digestibilities in early weaned pigs. *Journal of Animal Science*, Vol. 77, No. 11, pp. 2974 - 2984, ISSN 0021-8812.
- Bolduan, G.; Jung, H.; Schneider, R.; Block, J. & Klenke, B. (1988a). Influence of propionic and formic acids on piglets. *Journal of Animal Physiology and Animal Nutrition*, Vol. 59, No. 2, pp. 72-78, ISSN 1439-0396.
- Bolduan, G.; Jung, H.; Schneider, R.; Block, J. & Klenke, B. (1988b) Influence of fumaric acid and propanediol formate on piglets. *Journal of Animal Physiology and Animal Nutrition* 59, No. 1-5, pp. 143 - 149, ISSN 1439-0396.
- Boling, S.D.; Webel, D.M.; Mavromichalis, I.; Parsons, C.M. & Baker, D.H. (2000). The effects of citric acid on phytate-phosphorus utilization in young chicks and pigs. *Journal of Animal Science* 78, No. 3, pp. 682-689, ISSN 0021-8812.
- Bosi, P.; Mazzoni, M.; Filippi De, S.; Trevisi, P.; Casini, L.; Petrosino, G. & Lalatta-Costerbosa, G. (2006). Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions. A Continuous Dietary Supply of Free Calcium Formate Negatively Affects the Parietal Cell Population and Gastric RNA Expression for H1/K1-ATPase in Weaning Pigs. *Journal of Nutrition*, Vol. 136, No. 5, pp. 1229-1235, ISSN 1541-6100.
- Bosi, P., Sarli, G., Casini, L., De Filippi, S., Trevisi, P., Mazzoni, M. & Merialdi, G. (2007). The influence of fat protection of calcium formate on growth and intestinal defence in *Escherichia coli* K88-challenged weanling pigs. *Animal Feed Science and Technology*, Vol. 139, No. 9, pp. 170-185, ISSN ISSN: 0377-8401.

- Bosi, P.; Sarli, G.; Casini, L.; De Filippi, S.; Trevisi, P.; Mazzoni, M. & Merialdi, G. (2005). Effect of dietary addition of free or fat-protected calcium formate on growth, intestinal morphology and health of *Escherichia coli* k88 challenged weaning pigs. *Italian Journal of Animal Science*, Vol. 4, No. 2, pp. 452-454, ISSN 1594-4077.
- Bühler, K.; Bucher B.; Wenk, C. & Broz, J. (2009). Influence of benzoic acid in high fibre diets on nutrient digestibility and VFA production in growing/finishing pigs. *Archives of Animal Nutrition*, Vol. 63, No. 2, pp. 127-136, ISSN 1477-2817.
- Canibe, N.; Højberg, O, Højsgaard S. & Jensen B.B. (2005). Feed physical form and formic acid addition to the feed affect the gastrointestinal ecology and growth performance of growing pigs. *Journal of Animal Science*, Vol. 83, No. 6, pp. 1287-1302, ISSN 0021-8812.
- Canibe, N.; Steien, S.H.; Overland M. & Jensen, B.B. (2001). Effect of K-diformate in starter diets on acidity, microflora, and the amount of organic acids in the digestive tract of piglets, and on gastric alterations. *Journal of Animal Science*, Vol. 79, No. 8, pp. 2123 - 2133, ISSN 0021-8812.
- Castro, M. (2005). Use of additives on the feeding of monogastric animals. *Cuban Journal of Agricultural Science* 39, p. 439, ISSN 0253-5815.
- Cerchiari, E. (2000). Active matrix technology making more of acids. *Pig Progress*, Vol. 16, No. 4, pp. 34-35, ISSN 0031-9775.
- Chaveerach, P; Keuzenkamp, D.A; Urlings, H.A.P; Lipman, J.A. & van Knapen, F. (2002). In vitro study on the effect of organic acids on *Campylobacter jejuni* /*coli* populations in mixtures of water and feed. *Poultry Science*, Vol. 81, No. 5, pp. 621-628, ISSN 1537-0437.
- Corpet, D.E. (1996). Microbiological hazards for humans of antimicrobial growth promoter use in animal production. *Veterinary Medical Review*, Vol. 147, No. 12, pp. 851-862, ISSN 0341-9851.
- Creus, E.; Perez, J.F.; Peralta, B.; Baucells, F. & Mateu, E. (2007). Effect of acidified feed on the prevalence of *Salmonella* in market-age pigs. *Zoonoses and Public Health*, Vol. 54, No. 8, pp. 314-319, ISSN 1863-2378.
- Easter, R.A. (1988). *Acidification of diets for pigs*. In *Recent Advances in Animal Nutrition*, ISBN 0-407-01162-5, pp. 61-71 (Haresign W & Cole DJA, eds). London, Butterworths, UK.
- Eckel, B.; Kirchgessner, M, & Roth, F.X. (1992). Influence of formic acid on daily weight gain, feed intake, feed conversion rate and digestibility. *Journal of Animal Physiology and Animal Nutrition*, Vol. 67, No. 2, pp. 93-100, ISSN 1439-0396.
- Eidelsburger, U.; Kirchgessner, M. & Roth, F.X. (1992a). Influence of formic acid on daily weight gain, feed intake, feed conversion rate and digestibility. *Journal of Animal Physiology and Animal Nutrition*, Vol. 68, No. 2, pp. 82-92, ISSN 1439-0396.
- Eidelsburger, U.; Kirchgessner, M. & Roth, F.X. (1992b). Influence of formic acid, calcium formate and sodium hydrogen carbonate on dry matter content, pH value, concentration of carbonic acids and ammonia in different segments of the gastrointestinal tract. *Journal of Animal Physiology and Animal Nutrition*, Vol. 68, No. 2, pp. 20-32, ISSN 1439-0396.
- Eidelsburger, U.; Kirchgessner, M. & Roth, F.X. (1992c). Influence of fumaric acid, hydrochloric acid, sodium formate, tylosin and toyocerin on acid-base status. 13. Nutritive value of organic acids in piglet rearing. *Journal of Animal Physiology and Animal Nutrition*, Vol. 68, No. 3, pp. 165- 173, ISSN 1439-0396.
- Eidelsburger, U.; Roth FX, & Kirchgessner, M. (1992e). Influence of formic acid, calcium formate and sodium bicarbonate on acid-base status. 9. Effect of organic acids in

- piglet rearing. *Journal of Animal Physiology and Animal Nutrition*, Vol. 68, pp. 33- 42, ISSN 1439-0396.
- Eisemann, J.H. & van Heugten, E. (2007). Response of pig dietary inclusion of formic acid and ammonium formate. *Journal of Animal Science*, Vol. 85, No. 6, pp. 1530-1539, ISSN 0021-8812.
- Foegeding, P.M. & Busta F.F. (1991). *Chemical food preservatives*. In: Disinfection, Sterilization and Preservation, ISBN 0812113640, pp. 802- 832 (Block SS, ed). Lea & Febiger, Malvern, Philadelphia, PA.
- Franco, L.D.; Fondevila, M.; Lobera, M.B. & Castrillo, C. (2005). Effects of combinations of organic acids in weaned pig diets on microbial species of digestive tract contents and their response on digestibility. *Journal of Animal Physiology and Animal Nutrition*, Vol. 89, No. 3-6, pp. 88-93, ISSN 1439-0396.
- Gauthier, R. (2002). *The mode of action of acidifiers and the interest they generate in the growing-finishing phase*. In: Current Developments in Pig Production, French Association of Swine Practitioners, p. 16, Maisons-Alfort, France.
- Giesting, D.W.; Ross, M.A. & Easter, R.A. (1991). Evaluation of the effect of fumaric acid and sodium bicarbonate addition on performance of starter pigs fed diets of different types. *Journal of Animal Science*, Vol. 69, No. 6, pp. 2489 – 2496, ISSN 0021-8812.
- Gustafson, R.H., Bowen, R.E. (1997). Antibiotic use in animal agriculture. *Journal of Applied Microbiology*, Vol. 83, No. 5, pp. 531-541, ISSN: 1365-2672.
- Harada, E.; Niiyama, M. & Syuto, B. (1986). Comparison of pancreatic exocrine secretion via endogenous secretin by intestinal infusion of hydrochloric acid and monocarboxylic acid in anesthetized piglets. *Japanese Journal of Physiology*, Vol. 36, No. 5, pp. 843- 856, ISSN 1881-1396.
- Hardy, B. (2002). The issue of antibiotic use in the livestock industry. What have we learned? *Animal Biotechnology*, Vol. 13, No. 1, pp. 129-147, ISSN 1049-5398.
- Hunter, P.A.; Dawson, S.; French, G.L.; Goossens, H.; Hawkey, P.M.; Kuijper, E.J.; Nathwani D.; Taylor, D.J.; Teale, C.J.; Warren, R.E.; Wilcox, M.H.; Woodford, N.; Wulf, M.W. & Piddock L.J.V. (2010). Antimicrobial-resistant pathogens in animals and man: prescribing, practices and policies. *Journal of Antimicrobial Chemotherapy*, Vol. 65, No. 1, pp. 3-17, ISSN 1460-2091.
- Jacela, J.Y.; DeRouchey, J.M.; Tokach, M.D.; Goodband, R.D.; Nelssen, J.L.; Renter, D.G. & Dritz S.S. (2009). Feed additives for swine: Fact sheets – acidifiers and antibiotics. *Journal of Swine Health and Production*, Vol. 17, No. 5, pp. 270-275, ISSN 1066-4963.
- Jasaitis, D.K.; Wohlt, J.E. & Evans, J.L. (1987). Influence of feed-ion content on buffering capacity of ruminant feedstuffs in-vitro. *Journal of Dairy Science*, Vol. 70, No. 7, pp. 1391-1403, ISSN 0022-0302.
- Jensen BB, Mikkelsen LL, Canibe N, & Høyberg O (2001). *Salmonella in slaughter pigs*. Annual Report 2001 from the Danish Institute of Agricultural Sciences, p.23, Research Centre Foulum, Tjele, Denmark.
- Jongbloed, A.W.; Mroz, Z.; van der Weij-Jongbloed, R. & Kemme, P.A. (2000). The effects of microbial phytase, organic acids and their interaction in diets for growing pigs. *Livestock Production Science*, Vol. 67, No. 1/2, pp. 113-122, ISSN 1871-1413.
- Kasproicz-Potocka, M.; Frankiewicz A.; Selwet, M. & Chilomer, K. (2009). Effect of salts and organic acids on metabolite production and microbial parameters of piglets' digestive tract. *Livestock Production Science*, Vol. 126, No. 1-3, pp. 310-313, ISSN 1871-1413.
- Kemme, P.A.; Jongbloed, A.W.; Mroz, Z.; Kogut, J. & Beynen, A.C. (1999). Digestibility of nutrients in growing-finishing pigs is affected by *Aspergillus niger* phytase,

- phytate and lactic acid levels 1. Apparent ileal digestibility of amino acids. *Livestock Production Science*, Vol. 58, No. 2, pp. 107-117, ISSN 1871-1413.
- Kirchgessner, M. & Roth F.X. (1988). Energy value of organic acids in the rearing of piglets and the fattening of pigs. *Übersichten zur Tierernährung*, Vol. 16, pp. 93-108, ISSN 0303-6340.
- Kirchgessner, M. & Roth, F.X. (1990). Nutritive effect of calcium formate in combination with free acids in the feeding of piglets. *Agribiological Research* 43, No. 1, pp. 53- 64, ISSN 0938-0337.
- Kirchgessner, M.; Roth, F.X., & Eidelsburger, U. (1993). Nutritive efficiency of tartaric acid and malic acid in the rearing of piglets. *Journal of Animal Physiology and Animal Nutrition*, Vol. 70, No. 4-5, pp. 216-224, ISSN 1439-0396.
- Kirchgessner, M.; Roth, F.X. & Paulicks, B.R. (1995). Nutritive value of sorbic acid in piglet rearing. *Journal of Animal Physiology and Animal Nutrition* 74, No. 4/5, pp. 235 - 242, ISSN 1439-0396.
- Kluge, H.; Broz J.; & Eder, K. (2006). Effect of benzoic acid on growth performance, nutrient digestibility, nitrogen balance, gastrointestinal microflora and parameters of microbial metabolism in piglets. *Journal of Animal Physiology and Animal Nutrition*, Vol. 90, No. 7-8, pp. 316-324, ISSN 1439-0396.
- Knarreborg, A.; Miquel, N.; Granli, T. & Jensen, B.B. (2002). Establishment and application of an in vitro methodology to study the effects of organic acids on coliform and lactic acid bacteria in the proximal part of the gastrointestinal tract of piglets. *Animal Feed Science and Technology*, Vol. 99, No. 1-4, pp. 131-140, ISSN: 0377-8401.
- Krause, D.O.; Harrison, P.C. & Easter, R.A. (1994). Characterization of the nutritional interactions between organic acids and inorganic bases in the pig and chick. *Journal of Animal Science*, Vol. 72, No. 5, pp. 1257-1262, ISSN 0021-8812.
- Lawlor, P.G.; Lynch, P.B. & Caffrey, P.J. (2006). Effect of fumaric acid, calcium formate and mineral levels in diets on the intake and growth performance of newly weaned pigs. *Irish Journal of Agricultural and Food Research* 45, No. 1, pp. 61-71, ISSN 0791-6833.
- Le Gall, M.; Gallois, M.; Sève, B.; Louveau, I.; Holst, J.J.; Oswald, I.P.; Lallès, J.P. & Guilloteau, P. (2009). Comparative effect of orally administered sodium butyrate before or after weaning on growth and several indices of gastrointestinal biology of piglets. *British Journal of Nutrition*, Vol. 102, No. 9, pp. 1285-1296, ISSN 1475-2662
- Lueck, E. (1980). *Antimicrobial Food Additives*, ISBN 354-0100- 563, Springer-Verlag, Berlin.
- Mahan, D.C.; Newton, E.A. & Cera, K.R. (1996). Effect of supplemental sodium phosphate or hydrochloric acid in starter diets containing dried whey. *Journal of Animal Science* 74, No. 6, pp. 1217 -1222, ISSN 0021-8812.
- Mahan, D.C.; Wiseman, T.D.; Weaver, E. & Russell, L. (1999). Effect of supplemental sodium chloride and hydrochloric acid added to initial diets containing sprayed-dried blood plasma and lactose on resulting performance and nitrogen digestibility of 3-week-old weaned pigs. *Journal of Animal Science* 77, No. 11, pp. 3016-3021, ISSN 0021-8812.
- Manzanilla, E.G.; Perez, J.F.; Martin, M.; Kamel, C.; Baucells, F. & Gasa, J. (2004). Effect of plant extracts and formic acid on the intestinal equilibrium of early-weaned pigs. *Journal of Animal Science* 82, No. 11, pp. 3210-3218, ISSN 0021-8812.
- Maribo, H.; Jensen, B.B. & Hedemann, M.S. (2000). *Different doses of organic acids to piglets*. Danish Bacon and Meat Council, Report no. 469, Copenhagen, Denmark.
- Mateos, G.G.; Salado S, & Gracia, M.I. (1999). *Uso de aditivos como mejorantes de la calidad de las dietas para monogástricos: enzimas y acidificantes*. V Encuentro Regional de Producción de animales Monogástricos. Universidad de Maracay, Venezuela.

- Mathew, A.G.; Cissell, R., & Liamthong, S. (2007). Antibiotic Resistance in Bacteria Associated with Food Animals: A United States Perspective of Livestock Production. *Foodborne Pathogens and Disease*, Vol. 4, No. 2, pp. 115-133, ISSN 1535-3141.
- Mazzoni M.; Le Gall, M.; De Filippi, S.; Minieri, L.; Trevisi, P.; Wolinski, J.; Lalatta-Costerbosa, G.; Lallès, J.P.; Guilloteau P. & Bosi P. (2008). Supplemental sodium butyrate stimulates different gastric cells in weaned pigs. *Journal of Nutrition* 138, No. 8, pp.1426-1431, ISSN 1541-6100.
- Mroz, Z. (2005). Organic Acids as Potential Alternatives to Antibiotic Growth Promoters for Pigs. *Advances in Pork Production*, Vol. 16, pp. 169 -182, ISSN 1489-1395.
- Mroz, Z.; Reese, D.E.; Overland, M.; van Diepen, J.T. & Kogut, J. (2002). The effects of potassium diformate and its molecular constituents on the apparent ileal and fecal digestibility and retention of nutrients in growing-finishing pigs. *Journal of Animal Science*, Vol. 80, No. 3, pp. 681-690, ISSN 0021-8812.
- Mroz, Z.; Jongbloed, A.W.;Partanen, K.H.; Vreman, K.; Kemme, P.A. & Kogut, J. (2000). The effects of calcium benzoate in diets with or without organic acids on dietary buffering capacity, apparent digestibility, retention of nutrients, and manure characteristics in swine. *Journal of Animal Science*, Vol. 78, No. 10, pp. 2622-2632, ISSN 0021-8812.
- Naughton, P.J. & Jensen, B.B. (2001). A bioreactor system to study survival of Salmonella typhimurium in pig gut content. *Berliner und Münchener Tierärztliche Wochenschrift*, Vol. 114, No. 1, pp. 1-4, ISSN: 0005-9366.
- Omogbenigun, F.O.; Nyachoti, C.M. & Slominski, B.A. (2003). The effect of supplementing microbial phytase and organic acids to a corn-soybean based diet fed to early-weaned pigs. *Journal of Animal Science*, Vol. 81, No. 7, pp. 1806-1813, ISSN 0021-8812.
- Øverland, M.; Granli, T.; Kjos, N.P.; Fjetland, O.; Steien, S.H. & Stokstad, M. (2000). Effect of dietary formates on growth performance, carcass traits, sensory quality, intestinal microflora, and stomach alterations in growing-finishing pigs. *Journal of Animal Science*, Vol. 78, No. 7, pp. 1875-1884, ISSN 0021-8812.
- Øverland, M.; Kjos, N.P.; Borg, M. & Sørum, H. (2007). Organic acids in diets for entire male pigs. *Livestock Production Science*, Vol. 109, No. 1-30, pp. 170-173, ISSN 1871-1413.
- Owusu-Asiedu, A.; Nyachoti, C.M.; & Marquardt, R.R. (2003). Response of early-weaned pigs to an enterotoxigenic escherichia coli (K88) challenge when fed diets containing spray-dried porcine plasma or pea protein isolate plus egg yolk antibody, zinc oxide, fumaric acid, or antibiotic. *Journal of Animal Science*, Vol. 81, No. 7, pp. 1790-1798, ISSN 0021-8812.
- Pallauf, J. & Huter J. (1993). Studies on the influence of calcium formate on growth, digestibility of crude nutrients, nitrogen balance and calcium retention in weaned piglets. *Animal Feed Science and Technology*, Vol. 43, No. 1-2, pp. 65-76, ISSN 1365-2052.
- Papatsiros, V.G.; Tassis, P.D.; Tzika, E.D.; Papaioannou, D.S.; Petridou, E.; Alexopoulos, C.; & Kyriakis, S.C. (2011). Effect of benzoic acid and combination of benzoic acid with probiotic containing *Bacillus cereus var. Toyoi* in weaned pig nutrition. *Polish Journal of Veterinary Science*, Vol. 14, No. 1, pp. 117-125, ISSN 1505-1773.
- Papenbrock, S.; Stemme, K.; Amtsberg, G.; Verspohl, J. & Kamphues, J. (2005). Investigations on prophylactic effects of coarse feed structure and/or potassium diformate on the microflora in the digestive tract of weaned piglets experimentally infected with Salmonella Derby. *Journal of Animal Physiology and Animal Nutrition*, Vol. 89, No. 3-6, pp. 84-87, ISSN 1439-0396.
- Partanen, H.K. & Mroz, Z. (1999). Organic acids for performance enhancement in pig diets. *Nutrition Research Reviews*, Vol. 12, No. 1, pp. 117-145, ISSN 1475-2700.

- Partanen, K. (2001). *Organic acids - Their efficacy and modes of action in pigs*. In: Gut Environment of Pigs, Piva, A., Bach Knudsen K.E. and Lindberg, J.E. (Eds), pp. 201-218, ISBN ISBN, 978-1-897676-77-6, Nottingham University Press, Nottingham, UK.
- Partanen, K.; Siljander-Rasi, H.; Alaviuhkola, T.; Suomi, K. & Fossi, M. (2001a). Performance of growing-finishing pigs fed medium- or high-fibre diets supplemented with avilamycin, formic acid or formic acid-sorbate blend. *Livestock Production Science*, Vol. 73, No. 2-3, pp. 139-152, ISSN 1871-1413.
- Partanen, K.; Jalava, T.; Valaja, J.; Perttila, S.; Siljander-Rasi, H. & Lindeberg, H. (2001b). Effect of dietary carbadox or formic acid and fibre level on ileal and faecal nutrient digestibility and microbial metabolite concentration in ileal digesta of the pig. *Animal Feed Science and Technology*, Vol. 93, No. 3, pp.137-155, ISSN 1365-2052.
- Partanen, K., Siljander-Rasi, H., Pentikäinen, J., Pelkonen, S., & Fossi, M. (2007). Effects of weaning age and formic acid-based feed additives on pigs from weaning to slaughter. *Archives of Animal Nutrition*, Vol. 61, No. 5, pp. 336-356, ISSN 1477-2817.
- Paulicks, B.R.; Roth, F.X. & Kirchgessner, M. (2000). Effects of potassium diformate (Formi® LHS) in combination with different grains and energy densities in the feed on growth performance of weaned piglets. *Journal of Animal Physiology and Animal Nutrition*, Vol. 84, No. 3-4, pp. 102-111, ISSN 1439-0396.
- Piva, A. & Grilli, E. (2007). Role of benzoic, lactic and sorbic acid in vitro swine cecal fermentation. *Veterinary Research Communications*, Vol. 31, No. 1, pp. 401-404, ISSN: 1573-7446.
- Piva, A.; Casadei, G. & Biagi, G. (2002a) An organic acid blend can modulate swine intestinal fermentation and reduce microbial proteolysis. *Canadian Journal of Animal Science*, Vol. 82, No. 4, pp. 527-532, ISSN 1918-1825.
- Piva, A.; Morlacchini, M.; Casadei, G., Gatta, P.P.; Biagi, G. & Prandini, A. (2002b). Sodium butyrate improves growth performance of weaned piglets during the first period after weaning. *Italian Journal of Animal Science*, Vol. 1, No. 1, pp. 35-41, ISSN 1594-4077.
- Radcliffe, J.S.; Zhang, Z. & Kornegay, E.T. (1998). The effects of microbial phytase, citric acid, and their interaction in a corn-soybean meal-based diet for weanling pigs. *Journal of Animal Science*, Vol. 76, No. 7, pp. 1880-1886, ISSN 0021-8812.
- Radecki, S.V.; Juhl, M.R. & Miller, E.R. (1988). Fumaric and citric acids as feed additives in starter pig diets: Effect on performance and nutrient balance. *Journal of Animal Science*, Vol. 66, No. 10, pp. 2598-2605, ISSN 0021-8812.
- Ravindran, V. & Kornegay E.T. (1993). Acidification of weaner pig diets: A review. *Journal of the Science of Food and Agriculture*, Vol. 62, No. 4, pp. 313-322, ISSN 1097-0010.
- Risley, C.R.; Kornegay E.T.; Lindemann, M.D. & Weakland, S.M. (1991). Effects of organic acids with and without a microbial culture on performance and gastrointestinal tract measurements of weanling pigs. *Animal Feed Science and Technology*, Vol. 35, No. 3, pp. 259-270, ISSN 1365-2052.
- Roth, F.X. & Kirchgessner, M. (1988). Use of acetic acid in pig nutrition. *Landwirtschaftliche Forschung*, Vol. 41, No. 3-4, pp. 253-258, ISSN 0023-8147.
- Roth, F.X. & Kirchgessner M. (1989). Significance of dietary pH and buffering capacity in piglet nutrition. 1. pH and buffering capacity in diets supplemented with organic acids. *Landwirtschaftliche Forschung*, Vol. 42, No. 2-3, pp. 157-167, ISSN 0023-8147.
- Roth, F.X. & Kirchgessner, M. (1998). Organic acids as feed additives for young pigs—nutritional and gastrointestinal effects. *Journal of Animal Feed Science*, Vol. 7, No. 1, pp. 25-33, ISSN 0377-8401.
- Roth, F.X.; Kirchgessner, M. & Paulicks, B.R. (1996). Nutritive use of feed additives based on diformates in the rearing and fattening of pigs and their effects on performance.

- Agribiological Research Zeitschrift für Agrarbiologie-Agrikulturchemie-Ökologie*, Vol. 49, No. 4, pp. 307-317, ISSN 0938-0337.
- Sakata, T. (1987). Stimulatory effect of short-chain fatty acids on epithelial cell proliferation in the rat intestine: a possible explanation for trophic effects of fermentable fibre, gut microbes and luminal trophic factors. *British Journal of Nutrition*, Vol. 58, No. 1, pp. 95-103, ISSN 1475-2662.
- Sakata, T.; Adachi, M.; Hashida, M.; Sato, N. & Kojima, T. (1995). Effect of n-butyric acid on epithelial cell proliferation of pig colonic mucosa in short-term culture. *Deutsche Tierärztliche Wochenschrift*, Vol. 102, No. 4, pp. 163-164, ISSN 0341-6593.
- Schöner, F.J. (2001). Nutritional effects of organic acids. *Cahiers Options Méditerranéennes*, Vol. 54, 55-61, ISSN 0253-1542.
- Stein, H. (2007). *Feeding the pig's immune system and alternatives to antibiotics*, Proceedings of London Swine Conference pp. 65-82, ISBN 978-0-9688770-6-7, London, Ontario, Canada.
- Štukelj, M.; Valencak, Z.; Krsnik, M. & Svete, A.N. (2010). The effect of the combination of acids and tannin in diet on the performance and selected biochemical, haematological and antioxidant enzyme parameters in grower pigs. *Acta Veterinaria Scandinavica*, Vol. 52, No. 1, p. 19, ISSN 1751-0147.
- Taube, V.A.; Neu, M.E.; Hassan, Y., Verspohl, J.; Beyerbach, M. & Kamphues, J. (2009). Effects of dietary additives (potassium diformate/organic acids) as well as influences of grinding intensity (coarse/fine) of diets for weaned piglets experimentally infected with Salmonella Derby or Escherichia coli. *Journal of Animal Physiology and Animal Nutrition*, Vol. 93, No. 3, pp. 350-358, ISSN 1439-0396.
- Tsiloyiannis, V.K.; Kyriakis, S.C.; Vlemmas, J. & Sarris, K. (2001a). The effect of organic acids on the control of porcine post-weaning diarrhoea. *Research in Veterinary Science*, Vol. 70, No. 3, pp. 287-293, ISSN 0034-5288.
- Tsiloyiannis, V.K.; Kyriakis, S.C.; Vlemmas, J. & Sarris, K. (2001b). The effect of organic acids on the control of post-weaning oedema disease of piglets. *Research in Veterinary Science*, Vol. 70, No. 3, pp. 281-285, ISSN 0034-5288.
- Valencia, Z. (2002). Phytase and acetic acid supplementation in the diet of early weaned piglets: effect on performance and apparent nutrient digestibility. *Nutrition Research*, Vol. 22, No. 5, pp. 623-632, ISSN 0271-5317.
- Walsh, M.C.; Sholly, D.M.; Hinson, R.B.; Saddoris, K.L.; Sutton, A.L.; Radcliffe, J.S.; Odgaard, R.; Murphy J. & Richert, B.T. (2007). Effects of water and diet acidification with and without antibiotics on weanling pig growth and microbial shedding. *Journal of Animal Science*, Vol. 85, No. 7, pp. 1799-1808, ISSN 0021-8812.
- Weber, T.E. & Kerr, B.J. (2008). Effect of sodium butyrate on growth performance and response to lipopolysaccharide in weanling pigs. *Journal of Animal Science*, Vol. 86, No. 2, pp. 442-450, ISSN 0021-8812.
- Windisch, W.M.; Gotterbarm, G.G. & Roth, F.X. (2001). Effect of potassium diformate in combination with different amounts and sources of excessive dietary copper on production performance in weaning piglets. *Archiv für Tierernährung*, Vol. 54, No. 2, pp. 87-100, ISSN 0003-942X.

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen