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## The Prophylactic Use of Acidifiers as Antibacterial Agents in Swine

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### 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	<b>Synthetically:</b> from methyl formate and formamide, by-product of acetic acid production and by laboratory methods <b>Naturally:</b> in many fruits (apples, strawberries and raspberries), honey and nettles
Acetic	Acetic Acid	CH <sub>3</sub> COOH	4.76	soluble in all proportions	Liquid Colourless, Very volatile	Pungent odour Sour taste	<b>Synthetically:</b> by various methods <b>Naturally:</b> by bacterial fermentation dietary fibre in the colon
Propionic	2-Propanoic Acid	CH <sub>3</sub> CH <sub>2</sub> COOH	4.88	soluble in all proportions	Liquid (in pure state) Oily	Pungent odour Emission of very strong smells	<b>Synthetically:</b> from ethyl alcohol and carbon monoxide <b>Naturally:</b> by bacteria of genus Propionibacterium, as the end product of their fermentation of dietary fibre in the colon
Butyric	Butanoic Acid	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> COOH	4.82	soluble in all proportions	Liquid Oily	Rancid, unpleasant odour Acrid taste, with a sweetish after taste (similar to ether)	<b>Synthetically:</b> by fermentation of sugar or starch <b>Naturally:</b> by bacterial fermentation dietary fibre in the colon
Lactic	2-Hydroxypropanoic Acid	CH <sub>3</sub> CH(OH)COOH	3.83	very soluble	Liquid (in pure state) colourless or slightly yellow	Rancid, disagreeable odour Sour milk taste	<b>Synthetically:</b> from chemicals or organically as a byproduct of corn fermentation. <b>Naturally:</b> 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 <sub>3</sub> CH:CHCH:CHCOOH	4.76	sparingly soluble	Solid white crystalline powder or granule form	Distinctive odour Midly acrid and sour taste	<b>Synthetically:</b> by several different chemical pathways <b>Naturally:</b> in certain berries
Fumaric	2-Butenedioic Acid	COOHCH:CHCOOH	3.02	sparingly soluble	Solid white crystalline powder	Odourless Tart flavour, fruit-like taste	<b>Synthetically:</b> from malic acid <b>Naturally:</b> in fumitory (Fumaria officinalis), bolete mushrooms (specifically Boletus fomentarius var. pseudo-igniarius), lichen, and Iceland moss.
Malic	Hydroxybutanedioic Acid	COOHCH <sub>2</sub> CH(OH)COOH	3.40	soluble in all proportions	Liquid / Solid white crystal or crystalline powder	Odourless Apple taste	<b>Synthetically:</b> from maleic anhydride <b>Naturally:</b> 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	<b>Synthetically:</b> by chemical reactions of maleic anhydrid <b>Naturally:</b> in many plants (particularly grapes, bananas, tamarinds)
Citric	2-Hydroxy-1,2,3-Propanetricarboxylic Acid	COOHCH <sub>2</sub> C(OH)(COOH)CH <sub>2</sub> COOH	3.13	very soluble	Solid	Odourless Pleasant sour taste	<b>Synthetically:</b> by a fermentation process <b>Naturally:</b> in a variety of fruits (most notably citrus fruits- lemons, limes) and vegetables
Benzoic acid	Benzenecarboxylic acid	C <sub>6</sub> H <sub>5</sub> COOH	4.19		Solid colorless crystalline	Highly fragrant odour	<b>Synthetically:</b> by partial oxidation of toluene with oxygen <b>Naturally:</b> 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; Kasprowicz-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                      Jensen et al. 2001 Knarreborg et al. 2002              Naughton & Jensen 2001 Øverland et al 2007                  Tsiloyiannis et al. 2001a	Canibe et al., 2005                      Eisemann et al 2007 Jongbloed et al 2000                  Mroz, et al 2000 Partanen et al. 2001a,b, 2007 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                      Roth & Kirchgessner 1988 Valencia 2002
Propionic	<i>High spectrum of action against fungi and yeasts - Antibacterial activity: Coliforms (E. coli - ETEC strains), Salmonella spp.</i> Foegeding & Busta, 1991              Jensen et al. 2001 Knarreborg et al. 2002                  Naughton & Jensen 2001 Partanen & Mroz 1999                  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                      Foegeding & Busta, 1991 Jensen et al. 2001                      Knarreborg et al. 2002 Naughton & Jensen 2001              Piva & Grilli 2007 Tsiloyiannis et al. 2001a, b	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                  Jensen et al. 2001 Øverland et al. 2007                      Piva & Grilli 2007	Kirchgessner et al. 1995
Fumaric	<i>Antibacterial activity: (E. coli - ETEC strains, clostridia)</i> Biagi et al. 2003                      Knarreborg et al. 2002 Naughton & Jensen 2001              Owusu-Asiedu et al. 2003 Tsiloyiannis et al. 2001a	Giesting et al. 1991                      Krause et al. 1994 Lawlor et al. 2006                      Mroz et al. 2000 Owusu-Asiedu et al. 2003              Risley et al. 1991 Tsiloyiannis et al. 2001a
Malic	<i>Antibacterial activity: Coliforms (E. coli - ETEC strains) Active against yeasts -</i> Partanen & Mroz 1999                  Tsiloyiannis et al. 2001a	Kirchgessner et al. 1993                  Krause et al. 1994 Tsiloyiannis et al. 2001a
Citric	<i>Antibacterial activity: Coliforms (E. coli)</i> Foegeding & Busta, 1991 Tsiloyiannis et al. 2001a, b	Boling et al. 2000                      Krause et al. 1994 Radcliffe et al. 1998                  Risley et al 1991 Tsiloyiannis et al. 2001a, b
Benzoic acid	<i>Antibacterial activity: Coliforms (E. coli)</i> Papatsiros et al. 2011                  Piva & Grilli 2007	Bühler 2009                      Kluge et al. 2006 Maribo et al. 2000

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.)

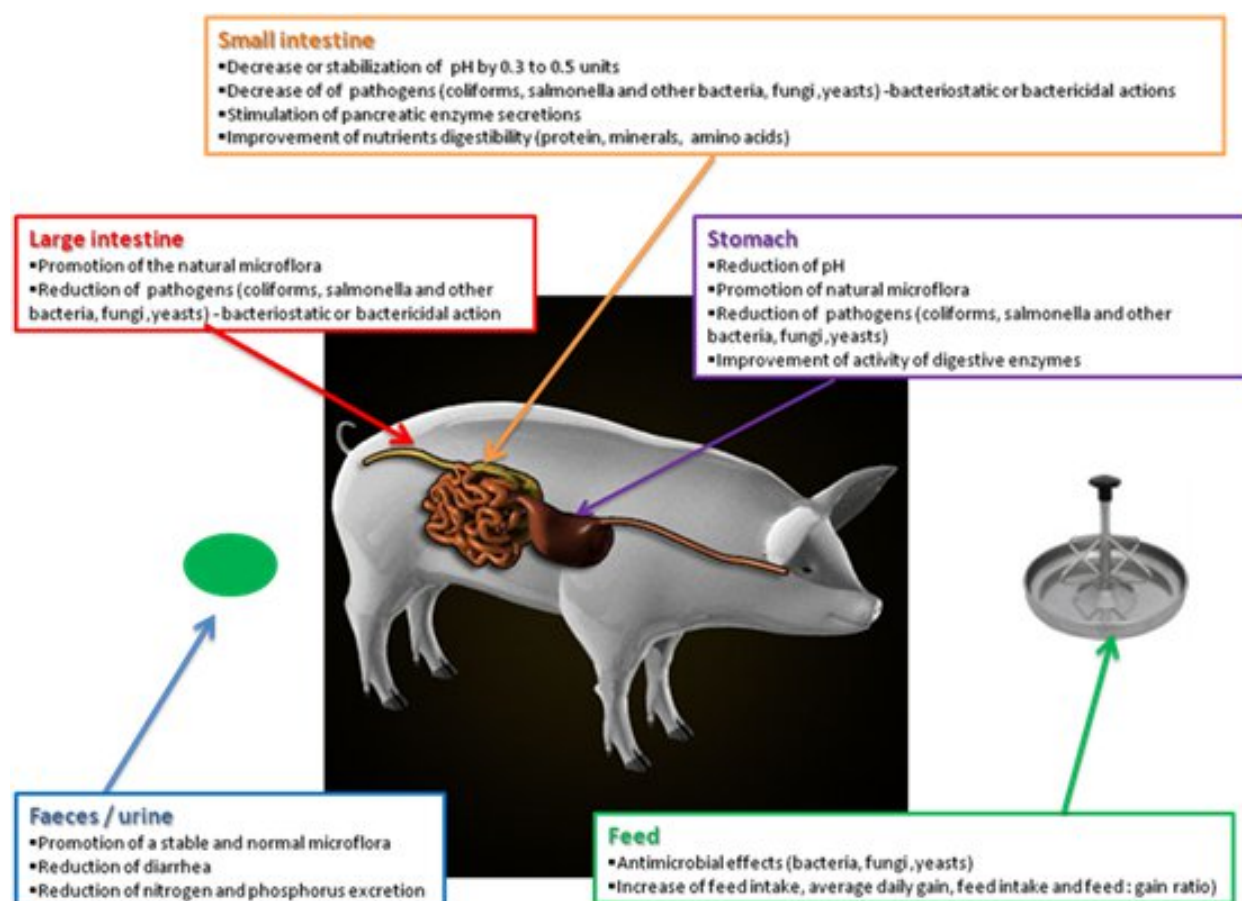


Fig. 1. Mode of action of acidifiers in pig

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 micro-organisms 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 mucosas (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 Cerchiari (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.

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