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Pro- and prebiotics in pig nutrition – potential modulators of gut health?

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ABSTRACT

The stressful physiological and environmental conditions experienced in particular by young pigs promote the proliferation of pathogens in the digestive tract. Probiotics, such as lactic acid–producing bacteria, *Bacillus* spp. and yeast have been reported to improve microbial balance in the gastrointestinal tract through bacterial antagonisms, competitive exclusion and immune stimulation. Prebiotics which include non-digestible oligosaccharides may control or manipulate microbial composition and/or activity, thereby assisting to maintain a beneficial microflora that suppresses through different regulatory mechanisms the growth of pathogens. The combination of probiotics and prebiotics, also referred to as synbiotics, may improve the survival rate of probiotics during their passage through the digestive tract, thus contributing to the stabilization and/or enhancement of the probiotic effects.

KEY WORDS: pig, probiotic, prebiotic, non-digestible oligosaccharide, synbiotic, intestine

INTRODUCTION

In recent years with increasing concern over drug residues in meat products and increased occurence of pathogens resistant against therapeutically used antibiotics in animals and humans, the use of antibiotics as growth promoters has been restricted continuously. For example, a general ban of antibiotics as feed additives was implemented in Sweden and Switzerland in 1986 and 1999, respectively. Consequently, new concepts have been developed aiming to promote animal health and to secure growth performance, feed efficiency and product quality as well. Several naturally occurring compounds have been shown to affect beneficially the composition and activity of the microflora in the gastrointestinal tract of pigs such as organic acids, fermented feed, specific components of dietary fibre and probio-

tics and prebiotics as well (Jensen, 1998). In the following, alternatives to antibiotics as growth promoters in pigs nutrition will be reviewed including probiotics, prebiotics and the combination of both, also referred to as synbiotics.

DEFINITIONS OF PRO-, PRE- AND SYNBIOTICS

Probiotics

According to a widely accepted definition by Fuller (1989) probiotics can be characterised as „a live microbial feed supplement which beneficially affects the host by improving its intestinal microbial balance". The probiotic effects of lactic acid-producing bacteria have received most attention, probably due to their predominance within the microflora, the historical perception of health-links and, additionally, the observation that they are rarely pathogenic (Kelly, 1998). The microflora in the intestine of livestock in the state of eubiosis is predominantly composed of lactobacilli in addition to different species of bifidobacteria and bacteroidaceae (Gedek, 1987). The species currently being used in probiotic preparations are lactic acid-producing bacteria such as *L. bulgaricus*, *L. acidophilus*, *L. paracasei*, *Streptococcus thermophilus*, *Enterococcus faecium* and *faecalis*, bifidobacteria such as *B. pseudolongum*, *B. thermophilum*, *B. breve* and *B. bifidum* and *Bacillus* spp. such as *B. cereus*, *B. toyoi* and *B. subtilis*. Furthermore, fungal probiotics such as *Saccharomyces cerevisiae* and *S. boulardi* are also commercially available (Durst et al., 1998; Lee et al., 1999).

Mode of action of probiotics

There are many beneficial claims for probiotics, but it is not always possible to provide sufficient scientific evidence to support them. The potential benefits that can arise from the application of the probiotic concept are growth promotion as well as anti-carcinogenic, anti-pathogenic, anti-allergenic and anti-mutagenic effects. Special attention has been paid to the anti-pathogenic mechanisms which are particularly relevant to young animals and which can be categorised as direct bacterial antagonisms, competitive exclusion and immune stimulation.

Direct bacterial antagonisms are related to the production of various inhibitory substances which are produced by the commensal microflora. These substances include organic acids, hydrogen peroxide, and non-peptide or polypeptide antibiotics, also referred to as bacteriocins. They inhibit the growth of other bacteria including enteric pathogens thus assisting the animal to resist infections. The antimicrobial activities of bacteriocins involve permeabilization of the cell membrane of the target cells (Kelly, 1998).

According to Kelly (1998) competitive exclusion is the most favoured hypothetical mode of action of probiotics despite the fact that it is difficult to support this hypothesis under *in vivo* conditions. Various anti-microbial factors such as pH, hydrogen peroxide, bacteriocins, fatty acids and deconjugated bile salts may be involved in the mechanisms that affect competitive exclusion of pathogens (Fuller, 1999).

There is growing evidence that in addition to direct interactions with pathogenic bacteria probiotics may improve disease resistance of the host by modulating systemic and mucosal immunity. In studies with rats oral administration of lactic acid-producing bacteria significantly affected both the systemic and mucosa associated immune response (Perdion and Alvarez, 1992; Famularo et al., 1997).

A recently published review in which the results of probiotic supplementation to piglet diets on growth performance were summarised, showed quite variable results (Forschungsbericht Fachbereich Agrarwirtschaft Soest, 1998). Out of 23 studies, in which lactic acid-producing bacteria (n = 9) or *Bacillus* spp. (n = 11) or yeast (n = 3) were used as supplements, there were only two studies in which growth performance was significantly improved whereas in some studies even a growth depression was obtained.

There were no significant growth-promoting effects of probiotic supplementation to diets for grower-finisher pigs and the results obtained for sows were equivocal (Forschungsbericht Fachbereich Agrarwirtschaft Soest, 1998).

Prebiotics

Another approach to protect the host against infections with pathogens would be to improve the beneficial activity of the microflora through specific ingredients in the diet. In recent years, it has been recognised that certain non-digestible oligosaccharides (NDO) specifically promote the proliferation of bifidobacteria (e.g. Hidaka et al., 1986a; Hayakawa et al., 1990). Such NDO escape enzymatic digestion by host enzymes in the gastrointestinal tract and were recently defined as „non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon" (Gibson and Roberfroid, 1995). Due to the potential of certain NDO to promote a favourable intestinal microflora these authors introduced the term prebiotics.

Physiologically functional oligosaccharides are natural constituents of plants such as legume seeds (Bach Knudsen, 1997) and cereals (Henry and Saini, 1989) consisting of 2-10 sugar units. In addition, NDO can be manufactured under commercial conditions to be used as functional ingredients in feed and food. Table 1 lists some of the NDO used as prebiotics (including their chemical structure and their mode of production).

TABLE 1

Non-digestible oligosaccharides (NDO) arranged according to their chemical structure

NDO	Chemical structure	Mode of production	Trade name	Main natural origin
Inulin	Glu (fru)$_n$ n = 10-50; β 1,2		Raftiline®	Jerusalem artichoke, chicory roots, onion, garlic, banana
Oligofructose (FOS)	Glu (fru)$_n$ n = 2-10; β 1,2	Partial enzymatic hydrolysis of inulin/ transfructosylation from saccharose	Raftilose P95®	
Soybean-oligosaccharides	Stachyose (fru, gal, gal, glu) and raf- finose (fru, gal, glu)	Extraction from soyabean whey	Soya-oligo	Soyabean
Transgalacto-oligosaccharides	Glu (gal)$_n$ n = 2-5; β 1,6	Trans-galactosylation of lactose with *Aspergillus oryzae* β-galactosidase	Oligomate 50® Oligostroop®	
Isomalto-oligosaccharides	Glu (Isomaltose)$_n$ n = 2-4; α 1,6	Enzymatic hydrolysis of starch Transglucosylation of maltose	Isomalto-900® Panorup®	
Mannan-oligosaccharides	Mannose$_n$ n = 2-8; α 1,6	Enzymatic synthesis from mannose		
Xylo-oligosaccharides	Xylose$_n$ n = 2-9; ß 1,4	Enzymatic hydrolysis of xylan	Xylo-oligo	
Neosugar	Glu (fru)$_n$ n = 2-3; ß 1,2	Enzymatic synthesis from saccharose	Actilight®	
Lactulose	Gal, fru; β 1,4	Alkali isomerization	MLS/P/C	
Palatinose condensates	Glu, fru (Palatinit) various types of bonds	Enzymatic synthesis from saccharose		

compiled from data by Delzenne and Roberfroid (1994), Grizard and Barthomeuf (1999) and Van Loo et al. (1995, 1999)

Gal: galactose; glu: glucose; fru: fructose

Mode of action of prebiotics

Depending on the type of NDO in the diet, fermentation of NDO may occur in different sections of the digestive tract including stomach, small intestine, caecum and/or colon (Houdijk, 1998; Houdijk et al., 1998, 1999). As a result, NDO may display bifidogenic characteristics in different sections of the gastrointestinal tract, provided that NDO are fermented exclusively by saccharolytic bacteria. In studies by Houdijk et al. (1999) fermentation of FOS was nearly completed at the end of the small intestine of weaned pigs (initial BW 16 kg); the degradation rate exceeded 90% whereas TOS was fermented at a rate of approximately 30%. Ileal digestibilities of galacto-oligosaccharides range from 57% in velasse-based diets (Veldman et al., 1993) to 65% in pea-based diets (Canibe and Bach Knudsen, 1997) and up to nearly 90% in lupin-based diets (Gdala et al., 1997). Differences in ileal NDO digestibilities may be attributed to different rates of fermentation.

NDO such as FOS and TOS will primarily stimulate the production of acetate and lactate (Wang and Gibson, 1993). Due to the low pKa of these acids, it was found in studies with human subjects that the population of bacteroides, clostridia and fusobacteria in faeces decreased (Gibson et al., 1995). According to Macfarlane and Macfarlane (1993), NDO may increase the barrier effect against infections by enteric pathogens through stimulation of lactic acid production in the small intestine and, particularly, through production of short chain fatty acids in the large intestine. Table 2 shows the molar ratios of acetate, propionate and butyrate from fermentation of several NDO by mixed faecal bacteria from humans and pigs.

There is growing evidence that NDO are not fermented by saccharolytic bacteria only. Wang and Gibson (1993) claimed that after fermentation of FOS by human faecal inocula succinate, propionate and butyrate could be detected, origina-

TABLE 2

Molar ratios of acetate, propionate and butyrate produced from carbohydrate fermentation by mixed faecal bacteria of humans[1] and pigs[2]

Substrate	Acetate	Propionate	Butyrate
Inulin[1]	72 ± 6	19 ± 5	8 ± 2
Oligofructose[1]	78 ± 4	14 ± 2	8 ± 2
Lactulose[1]	81 ± 5	12 ± 4	7 ± 2
Lactitol[1]	85 ± 4	9 ± 2	6 ± 2
Maltitol[1]	57 ± 6	26 ± 6	17 ± 1
Mannanoligosaccharide[2]	60 ± 4	30 ± 6	10 ± 3

compiled from data by Wang and Gibson (1993) and Duda et al. (2000)

ting from direct fermentation of FOS by non-saccharolytic bacteria or indirect fermentation of endproducts produced by lactobacilli and bifidobacteria. In addition, studies by Hartemink and Rombouts (1997) revealed that a significant proportion of different sources of NDO were fermented by other species than bifidobacteria including species such as clostridia, enterobacteria and *E. coli*. None of the NDO that were tested were selective for bifidobacteria (Table 3).

TABLE 3

Bacterial fermentation of non-digestible oligosaccharides

Bacterial group/species	FOS[1]	INU	TOS	IMO	LAT	LAC
Bacteroides distasonis	+	+	+	+	+	+
B. fragilis	+	+	+	+	+	+
B. ovatus	+	+	+	+	+	
B. thetaiotaomicron	+	+	+	+		+
B. vulgatus	+	+	+	+	+	
Bifidobacterium spp.	+	+	+	+	+	+,-
Clostrium butyricum		-	-	-	+	+
Cl. clostridioforme	+,-	-		-	-	+
Cl. perfringens	+,-	-,+	-,+	+	+	+
Cl. ramosum	+	+		+	+	+
Escherichia coli	-,+	-	+	-	+,-	-
Eubacterium lentum	-	-		-	-	
Eu. Limosum	-	-	-	-	-	
Lactobacillus acidophilus-group	+,-	+	+	+,-	+	+
Lb. Casei	+,-	+	+	-	+	+

[1] FOS: fructo-oligosaccharides, INU: inulin, TOS: transgalacto-oligosaccharides, IMO: isomalto-oligosaccharides, LAT: lactulose, LAC: lactitol (Hartemink and Rombouts, 1997)

Synbiotics

According to Roberfroid (1998) a synbiotic is defined as „a mixture of probiotic and prebiotic that beneficially affects the host by improving the survival and the implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria".

Several NDO including xylo-oligosaccharides (Suwa et al., 1988), inulo-oligosaccharides (Hidaka et al., 1986b), mannan-oligosaccharides (Kumprecht and Zobac, 1998) as well as TOS, FOS and soyabean oligosaccharides (Rowland, 1992) have been used to promote the proliferation of probiotics. Recent results in piglets revealed synergistic effects of the combination of different probiotics and prebiotics (NDO) in terms of improved growth performance (Kumprecht and Zobac,

1998), decreased mortality rate (Nousiainen and Setälä, 1993) and increased counts of total anaerobes, aerobes, lactobacilli and bifidobacteria in faecal samples of young pigs (Nemcová et al., 1999). A study with Wistar rats showed 14 days after daily oral administration of over 10^9 live cells of probiotic strains and/or 5% (w/w) of oligofructose in the diet, that the composition of the intestinal microflora was almost not affected, except for bifidobacteria. In comparison to the control group, the bifidobacteria live cell numbers in the gut content increased by 0.6 log cfu/g in groups of rats receiving *B. longum*, by 1.6 log cfu/g in groups fed oligofructose and by 1.4 log cfu/g in animals receiving a combination of both (synbiotics) (Bielecka et al., 2000).

CONCLUSIONS

It is evident that in many cases the enhanced saccharolytic activity in the small intestine of NDO-fed pigs could not be maintained throughout the large intestine due to the fast rate of fermentation of these NDO in the upper tract. Combinations of easily fermentable NDO with slowly fermentable carbohydrates may maintain a constant saccharolytic activity throughout the whole digestive tract.

Pairing NDO and probiotic strains that have the metabolic potential of fermenting the supplied NDO at a competitive rate compared to the indigenous microflora, is likely to be a successful strategy in controlling the intestinal ecosystem. The expected benefits are an improved survival rate during the passage of the probiotic bacteria through the upper intestinal tract and a more efficient implanta-

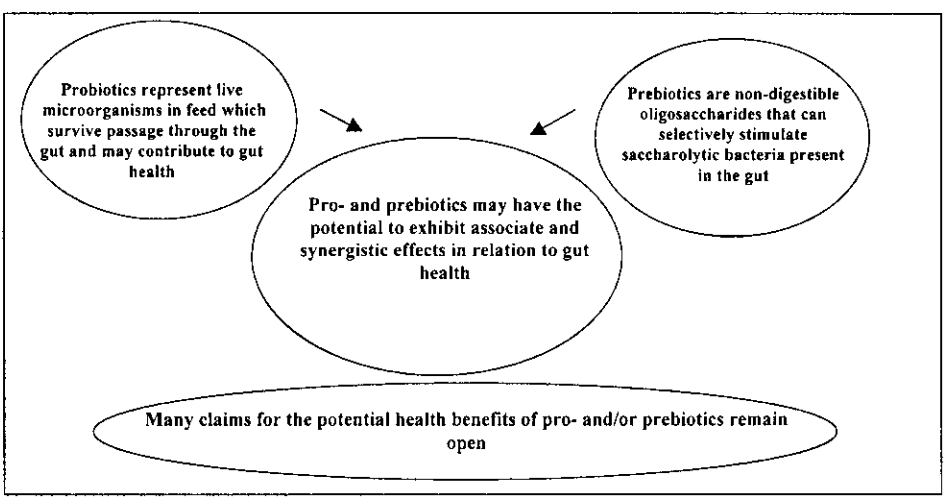

Figure 1. General aspects for the use of pro- and prebiotics in pig nutrition

tion in the colonic microbiota together with a stimulating effect of the NDO on the growth and/or activity of both the exogenous (probiotic) and endogenous bacteria. In Figure 1 general aspects for the use of pro- and prebiotics in pig nutrition are presented. Future research should be directed towards elucidating the synbiotic mechanisms in more detail.

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STRESZCZENIE

Pro- i prebiotyki w żywieniu świń – modulatory zdrowotności przewodu pokarmowego?

Stresogenne fizjologiczne i środowiskowe warunki, na które narażone są szczególnie młode prosięta, przyczyniają się do namnażania organizmów chorobotwórczych w przewodzie pokarmowym. Uznano, że probiotyki, takie jak bakterie produkujące kwas mlekowy, *Bacillus* spp. i drożdże poprawiają spektrum mikrobiologiczne w przewodzie pokarmowym poprzez antagonizmy między bakteriami, eliminację na zasadzie współzawodnictwa i stymulację odpornościową. Prebiotyki, które zawierają niestrawne oligosacharydy, mogą kontrolować lub zmieniać spektrum i/lub aktywność mikroflory, która poprzez różne mechanizmy regulujące, powstrzymuje rozwój organizmów chorobotwórczych. Kombinacja probiotyków i prebiotyków, nazywana także synbiotykami, może poprawić przeżywanie probiotyków w czasie ich przechodzenia przez przewód pokarmowy, przyczyniając się do stabilizacji i/lub wzmocnienia działania probiotyków.