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DIETARY NON-PHARMACOLOGICAL ALTERNATIVES TO THE USE OF ANTIBIOTICS AS GROWTH PROMOTERS IN SWINE**

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**Plenary invited paper

Abstract: The first weeks after weaning are a critical stage for piglets characterized by high incidence of diarrhoea and low weight gain. These problems were counteracted with the use of antibiotic growth promoters that may as a side-effect induce the selection of antibiotic-resistant genes in animal and human pathogens. For this reason, the European Union decided to completely ban the antibiotics used as growth promoters as of January 2006. As a consequence of this decision, alternative strategies to modulate the piglet gastrointestinal environment have been the object of many studies. The use of non-pharmaceutical dietary supplements, such as organic acids, prebiotics, probiotics, and essential oils has been shown to improve piglet post-weaning health and growth performances but results are sometimes controversial. Moreover, the role of molecules that can influence gastrointestinal and immune development in the newly weaned piglet has been investigated. The proper choice and use of a non-pharmacological dietary supplement might improve piglet productivity but it has to be considered that dietary supplements usually increase the feed price, which means that the gains in productivity should exceed the increased costs.

Key words: piglet, weaning, antibiotics, growth promoters, non-pharmacological supplements.

Introduction

Weaning piglets at 3-4 weeks of age exposes the animals to nutritional, environmental, and social stresses that usually result in a post-weaning phase characterized by low weight gain, low feed intake and diarrhoea (*Barnett et*

al., 1989). This post-weaning lag period is mainly caused by insufficient secretions of gastric hydrocloric acid and pancreatic amylase, lipase, and trypsin (*Kidder and Manners,* 1978) as well as insufficient immune development (*Gaskins and Kelley,* 1995). These problems were counteracted with widespread use of antibiotic substances that may as a side-effect select antibiotic-resistant genes in the intestinal flora with the possibility of a transfer to human pathogens (*Phillips et al.,* 2004). Because of these concerns, the European Union decided to completely ban the antibiotics used as growth promoters as of January 2006. This review deals with some of the alternative strategies that can be used to positively modulate the piglet gastrointestinal environment after weaning.

Non-pharmacological dietary supplements

Organic acids: Organic acids are widely used as food preservatives for their antimicrobial action. In particular, it is the undissociated form of the acid that can freely diffuse through the membrane of micro-organisms into their cell cytoplasm. Once inside the cell, where pH is close to neutrality, the acid will dissociate and anions will accumulate suppressing cell enzymes (decarboxylases and catalases) and nutrient transport systems (*Russell and Diez-Gonzalez,* 1998).

There is a wide literature regarding the effect of feeding organic acids to piglets on their growth performance and health. In their review, *Partanen and Mroz* (1999) have concluded that organic acids seem to improve growth performance and feed efficiency of weaned piglets but the responses vary greatly, depending on type and dose of acid used, composition of basal diet, age of animals, and environmental conditions and hygiene (*Ravindran and Kornegay,* 1993). Among the acids tested in weaned pigs, formic, fumaric, and citric acids have been the object of several studies and seem to effectively improve animal growth performance *(Partanen and Mroz,* 1999*)*. Other acids that have shown growth-promoting effects include malic, sorbic, lactic *(Roth and Kirchgessner,* 1998*)*, and gluconic *(Biagi et al.,* 2006*)* acids. Conversely, feed supplementation with inorganic acids *(Giesting and Easter,* 1986*)* failed to improve piglet growth performance. Organic acids are used also as salts, because they are generally odourless and easier to handle in the feed manufacturing process owing to their solid and less volatile form. They are also less corrosive and often more soluble in water than the free acids.

Despite the fact that organic acids were used in the past as acidifiers, the effect of organic acids on gastric and intestinal pH seems to be marginal.

While their exact mode of action remains unclear, organic acids might improve animal growth performance by reducing feed buffering capacity, inhibiting undesirable microbes (*Tsiloyiannis et al.,* 2001*)*, and stimulating gastrointestinal development *(Gálfi and Bokori,* 1990*)* as well as pancreatic secretions.
Organic acids are usually utilized at concentrations between 5 and 10 g/kg of diet; higher inclusion levels are very likely to cause reduced feed intake and poor growth performance due to reduced feed acceptance *(Roth and Kirchgessner,* 1998*)*.

Prebiotics: A prebiotic has been defined as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health" (*Gibson and Roberfroid,* 1995). Degradation of non-digestible oligosaccharides (NDO) occurs at the terminal ileum and in the hindgut. Some NDO have been tested in trials with pigs. When fed to pigs, galacto-oligosaccharides (GOS; *Tzortzis et al.,* 2005) and fructo-oligosaccharides (FOS; *Howard et al., 1995*) increased bifidobacteria and reduced the presence of pathogens. Moreover, NDO can help the gastrointestinal development in new-born animals as they are fermented to short-chain fatty acids, and butyrate is the main energy source for the colonocytes. As a drawback to the use of NDO, it must be considered that high levels of dietary NDO might result in gastrointestinal bloating, pain, and reduced feed intake. Despite the positive influence that NDO can have on animal intestinal health, there is still a lack of evidence that prebiotics can significantly improve animal growth performance.

Probiotics: Recently, *Schrezenmeir and de Vrese* (2001) have defined a probiotic as "a preparation or product containing viable, defined micro-organisms in sufficient numbers, which alter the microflora of the host intestine and by that exert beneficial health effects on the host". Currently, only a few probiotic strains are authorized for farm animals within the European Union; these are *Bacillus, Lactobacillus, Enterococcus, Pediococcus* strains as well as two fungal strains, *Saccharomyces cerevisiae* and *Kluyveromyces marxianus-fragilis*. To be able to exert their beneficial effect, probiotics must be resistant to several factors such as gastric acidity, bile salts, and, to some extent, technological treatments. When used in farm animals, the beneficial claims for probiotics include growth-promotion, anti-pathogenic (*Zeyner and Boldt,* 2006), and immune-stimulant (*Shu et al., 2001*) effects but these are not always consistent. In fact, many factors can

affect the efficacy of probiotics fed to farm animals, including the probiotic strain used, age of animals, dietary ingredients and supplements, environmental conditions, feed processing, and feeding technique.

Probiotics can be used together with prebiotics that selectively favor the probiotic strains and this association is called a synbiotic (*Schrezenmeir and de Vrese,* 2001). Some trials with pigs seem to suggest that the proper combination of a probiotic strain with a NDO might increase the probiotic efficacy (*Bohmer et al.,* 2005*; Piva et al.,* 2005)

Essential oils: Essential oils are very complex mixtures of volatile, lipophilic compounds that are extracted from some aromatic plants. When ingested, essential oils stimulate the secretion of digestive enzymes and increase gastric and intestinal motility (*Platel and Srinivasan,* 2001). Moreover, many essential oils show strong in vitro antioxidant and antibacterial properties (*Faleiro et al.,* 2005), but at present there is little evidence of action against microbes in the gastrointestinal tract. Different plant extracts (particularly those obtained from oregano and thymus) have been tested as dietary supplements for weanling pigs but results were often inconclusive (*Manzanilla et al.,* 2004; *Namkung et al.,* 2004).

Glutamine: Feeding glutamine to newborn pigs has been shown to have a trophic effect on the intestinal mucosa (*Domeneghini et al.,* 2006) and reduce the incidence of bacterial diseases (*Yi et al.,* 2005). Because glutamine is an energy source also for lymphocytes and macrophages, feeding glutamine to weaned piglets might also improve their immune status (*Johnson et al.,* 2006).

Other dietary strategies: other strategies that might help piglets to overcome the post-weaning phase related problems include reducing feed buffering capacity (*Biagi et al.,* 2003) as well as feeding specific enzymes (*Gill et al.,* 2000) and mannanoligosaccharides (*Hang et al.,* 2006).

Conclusion

Several dietary supplements are available to be fed to piglets in the post-weaning phase in order to improve animal intestinal health and growth performance. Despite the fact that non-pharmacological dietary supplements do not reach the efficacy of antibiotics as growth promoters, the proper choice and use of a dietary supplement can improve piglet productivity. Nevertheless, it has to be considered that dietary supplements usually

increase the feed price, which means that the gains in productivity should exceed the increased costs.

NEFARMAKOLOŠKE ALTERNATIVE KORIŠĆENJU ANTIBIOTIKA U OBROCIMA KAO PROMOTERA PORASTA KOD SVINJA

G. Biagi

Rezime

Prve nedelje nakon odbijanja predstavljaju kritičan period za Prasad koji odlikuje pojava proliva i slabog prirasta težine. Ovi problemi su dovedeni u vezu sa upotrebom antibiotika kao promotera porasta koji kao sporedni efekat mogu izazvati selekciju gena rezistentnih na antibiotike kod životinskih i ljudskih patogena. Iz tog razloga, Evropska Unija je odlučila da zabrani u potpunosti antibiotike iz upotrebe kao promotera rasta od januara 2006. godine. Kao posledica ove odluke, cilj mnogih istraživanja su postale alternativne strategije za moduliranje gastrointestinalne sredine kod prasadi.

Organske kiseline imaju široku primenu kao konzervansi zbog svoje antimikrobiološke aktivnosti i mogu poboljšati rezultate porasta kod životinja kada se dodaju u obrok za prasadmeđu kiselinama koje su testirane kod odbijene prasadi, mravlja kiselina, fumarna i limunska kiselina su bile predmet nekoliko studija i čini se da efikasno poboljšavaju rezultate porasta kod životinja. Ostale kiseline koje su pokazale svoje dejstvo u poboljšanju porasta uključuju jabučnu kiselinu, sorbinsku, mlečnu i glukonsku kiselinu. Suprotno tome, dopuna obroka neorganskim kiselinama nije imala pozitivan uticaj na porast kod prasadi.

Prebiotik je definisan kao “nesvarljivi sastojak hrane koji ima pozitivan uticaj na domaćina tako što selektivno stimuliše porast i/ili aktivnost jedne ili ograničenog broja bakterija u debelom crevu i time poboljšava zdravlje domaćina”. Nesvarljivi oligosaharidi mogu imati pozitivna uticaj na intestinalno zdravlje prasadi povećavajući broj korisnih bakterija kao što su bakterije mlečne kiseline i bifido bakterije. Međutim, još uvek nema dovoljno dokaza da prebiotici mogu signifikantno da poboljšaju porast kod odbijene prasadi.

Probiotik je definisan kao “preparat ili proizvod koji sadrži žive, definisane mikro organizme u dovoljnom broju, koji mogu da promene mikrofloru u crevima domaćina in a taj način imaju korisno dejstvo na zdravlje domaćina”. Kada se koristi kod domaćih životinja, korisno dejstvo probiotika uključuje i uticaj na poboljšanje porasta, anti-patogeno i imuno-stimulativno dejstvo ali oni nisu uvek konzistentni. U stvari, mnogi faktori mogu da utiču na efikasnost probiotika uključujući i to koji je soj/vrsta probiotika korišćena, uzrast životinja, sastav hraniva i dodaci/dopune hranivima, uslovi sredine, prerada hraniva itehnika/način ishrane. Probiotici se mogu koristiti zajedno sa prebioticima koji selektivno preferiraju sojeve/vrste probiotika i simbiotika.

Esencijalna ulja predstavljaju veoma kompleksne međavine isparljivih, lipofillna jedinjenja koja su ekstrahovana iz nekih aromatičnih biljki. Kada se konzumiraju esencijalna ulja stimulišu izlučenje digestivnih enzima i povećavaju gastričnu i intestinalnu pokretljivost. Takođe, mnoga esencijalna ulja pokazuju snažna in vitro antioksidantska i antibakterijska svojstva, ali trenutno nema puno dokaza o dejstvu protiv ikroba u gastrointestinalnom traktu. Različiti biljni ekstrakti (posebno oni dobijeni od oregano i timijana) su testirani kao dopune hranivima za ishranu odbijene prasadi ali rezultati su često bili neubedljivi.

Ishrana novorpđene prasadi glutaminom je pokazala trofni uticaj na intestinalnu mukozu i smanjuje pojavu bakterijskih oboljenja. Zato što je glutamin izvor energije takođe i za limfocite i makrofage, ishrana odbijene prasadi glutaminom može popraviti njihov imunološki status.

Ostale strategije koje bi mogle da doprinesu da prasad savlada probleme u periodu posle odbijanja uključuju smanjenje puferskog kapaciteta hraniva kao i ishrana koja sadrži specifične enzime i mananoligosaharide.

Postoji nekoliko dopuna hranivima koja su dostupna i mogu s ekoristiti u ishrani prasadi u fazi nakon odbijanja kako bi se poboljšalo intestinalno zdravlje i porast. Uprkos činjenici da nefarmakološki dodaci hranivima neamju efikasnost/delotvornost antibiotika kao promotera porasta, pravi izbor i korišćenje dopuna hranivima može poboljšati produktivnost kod prasadi. Međutim, mora se uzeti u obzir da dopune hranivima obično povećavaju cenu hraniva, što znači da povećanje produktivnosti mora da bude veće od uvećanih troškova.

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