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Bovine Colostrum as a Natural Growth Factor for Newly-Weaned Piglets: A Review

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Abstract. The aim of this review is to present the potential of bovine colostrum as growth promoter in piglet-weaner diet. The main consequence of weaning the piglet is a critical period of underfeeding of which results in the so-called "weaning growth check". Near this reduction in feed intake and growth performance, the gastro-intestinal tract and the immune system of the animal are also affected. Bovine colostrum can be used to reduce the impact of weaning by the action of its bioactive components which may be classified in two classes: the growth factors, which promote the growth and development of the newborn, and the antimicrobial factors, which provide passive immunity and protect against infection. Studies using bovine colostrum in the weaning diet showed increased growth performance and feed intake the first week post-weaning, moreover, a better feed efficiency was also reported, suggesting that the growth benefits attributed to the bovine colostrum supplementation is not due solely to the increased feed consumption. Effects were also observed on the intestinal tract (gastric pH, mucosa restoration, intestinal microflora, local immunisation) but the systemic immune responses were not altered.

Keywords: Weaned pig, Bovine colostrum, Growth performance, Feed Intake, Gastrointestinal tract, Immunity

INTRODUCTION

Weaning can be regarded as one of the most critical periods in the modern-day pork production cycle. In addition to mother-young separation, weaning involves abrupt and profound modifications of the environment, feeding habits and social interactions when litters of piglets are mixed. These changes contribute to the post-weaning "growth check", intimately associated with a range of intestinal and immunological alterations (Pluske *et al.*, 1997).

Over the last decades, antibiotic growth promoters have been used in piglet diets to reduce the production penalty associated to weaning. However, concerns about potential risks for human health due to the use and misuse of antibiotics in animal feeds (Dewey *et al.*, 1997) have led to their ban as growth-promoters throughout Europe since 1 January 2006 (Regulation EC No. 1831/2003). Initial experience of a in-feed antibiotic ban in Sweden and Denmark indicated that there was a reduced performance and increased morbidity in nursery pigs, which emphasised the therapeutic use of antibiotics in farm (Stein, 2002). This underlines the need to develop alternative strategies.

By its richness in biologically active molecules essential for specific functions, the bovine colostrum constitutes a good candidate to replace the in-feed antibiotics. The most important bioactive components in colostrum include growth and antimicrobial factors (Pakkanen and Aalto, 1997).

The aim of this review is to present the potential of bovine colostrum as growth promoter in piglet-weaner diet.

BOVINE COLOSTRUM

Colostrum is the lacteal secretion directly after parturition common to all mammals and essential for development and immune status for newborn (Scammell, 2001). More than a source of nutrients, colostrum also contains biologically active molecules which are essential for specific functions (Pakkanen and Aalto, 1997). The most important bioactive components in colostrum include immune, growth and antimicrobial factors. The Table 1 compares the concentrations of the main components of bovine colostrum and regular milk.

Table 1. Main components of bovine colostrum and bovine milk.

	Bovine colostrum (/litre)	Bovine milk (/litre)	References
DM	153-245 g	122 g	Blum and Hammon, 2000
Crude protein	41-140 g	34 g	Gopal and Gill, 2000
Lactose	27-46 g	46 g	Gopal and Gill, 2000
Crude fat	39-44 g	37 g	Gopal and Gill, 2000
Crude ash	5-20 g	7 g	Gopal and Gill, 2000
IgG1	50-90 g	0.30-0.40 g	Elfstrand *et al.*, 2002
IgG2	1,5-2 g	0.03-0.08 g	Elfstrand *et al.*, 2002
IgA	3.0-6.5 g	0.04-0.06 g	Elfstrand *et al.*, 2002
IgM	3.8-6 g	0.03-0.06 g	Elfstrand *et al.*, 2002
IL-1β	840 µg	3 µg	Hagiwara *et al.*, 2000
IL-1ra	5.2 mg	27 µg	Hagiwara *et al.*, 2000
IL-6	77 µg	0.15 µg	Hagiwara *et al.*, 2000
TNF-α	926 µg	3.3 µg	Hagiwara *et al.*, 2000
IFN-γ	260 µg	0.21 µg	Hagiwara *et al.*, 2000
IGF-I	100-2000 µg	<25 µg	Elfstrand *et al.*, 2002
IGF-II	200-600 µg	<10 µg	Pakkanen and Aalto, 1997
EGF	4-8 mg	2 µg	Scammell, 2001
TGF-β	100-300 µg	1-2 µg	Elfstrand *et al.*, 2002
Lactoferrin	1.5-5 g	0.1-0.3 g	Korhonen, 1977
Lactoperoxydase	30 mg	20 mg	Korhonen, 1977
Lysozyme	0.14-0.7 mg	0.07-0.6 mg	Korhonen, 1977

DM = dry matter ; Ig = immunoglobulin ; IL = interleukin ; TNF = tumor necrosis factor ; INF = interferon ; IGF = insulin-like growth factor ; EGF = epidermal growth factor ; TGF = transforming growth factor.

Immune factors:

Immunoglobulins: The immunological function mediated by the Igs depends on the Ig class. The most important action of IgG antibodies is the activation of complement-mediated bacteriolytic reactions. Another vital function is their ability to increase the recognition and phagocytosis of bacteria by leucocytes. IgM antibodies are considerably more efficient than IgG in regards of the above activities, especially complement-mediated lysis. IgA, in contrast, does not fix complement or opposing bacteria, but agglutinates antigens, neutralises viruses and bacterial toxins, and prevents the adhesion of enteropathogenic bacteria to mucosal epithelial cells. Moreover, this Ig is present in bovine colostrum under a secretory form (sIgA) which makes it resistant to the activities of proteolytic digestive enzymes (Korhonen *et al.*, 2000).

Cytokines: Cytokines are small peptide molecules that are important mediators in the regulation of the immune and inflammatory responses. In general, cytokines do not regulate normal cellular homeostasis, but alter cellular metabolism during times of perturbation (Playford *et al.*, 2000). Of particular interest is the role of cytokines as major regulators of epithelial cell growth and development, including intestinal inflammation and epithelial restitution following mucosal damage (Elson and Beagley, 1994).

Growth promoters:

IGF-I and –II: The most abundant growth factors of bovine colostrum are IGF-I and –II. They stimulate cell growth and differentiation and are proposed to act both as endocrine hormones through the blood and, locally, as paracrine and autocrine growth factors. Four IGF binding proteins are present in bovine colostrum in detectable levels (IGFBP-3 > IGFBP-2 ≈ IGFBP-4 > IGFBP-5). Those binding proteins are involved in the regulation and the coordination of biological activities of the IGF-I and –II (Jones and Clemmons, 1995).

EGF: EGF plays an important role in cell differentiation rather than cell proliferation in young animals, and it may be involved in stimulating mucus secretion (Schweiger *et al.*, 2003).

TGF-β: Three isoforms of TGF-β (-1, -2 and-3) are known. The forms -1 and -2 have been isolated from bovine colostrum with a predominance of the β2 form (85-95 %). TGF-β stimulates proliferation of some cells, especially in connective tissue, whereas it acts as a growth inhibitor of other cells, such as lymphocytes and epithelial cells. During injury or disease, it acts in concert with EGF to stimulate cell proliferation (Border and Noble, 1995).

Antimicrobial factors:

Lactoferrin: Lactoferrin exhibits both bacteriostatic and bactericidal activities against a range of microorganisms. The bacteriostatic activity is related to the high iron binding affinity of the protein that deprives iron-requiring bacteria of this essential growth nutrient. The bactericidal mechanism is related to its ability to cause release of lipopolysaccharide molecules from the outer membrane of the Gram-negative bacteria (Conneely, 2001).

Lactoperoxidase: It catalyses the oxidation of thiocyanate (SCN^-) in the presence of hydrogen peroxide (H_2O_2), producing a toxic intermediary oxidation product. This product inhibits bacterial metabolism via the oxidation of essential sulphydryl groups in microbial enzymes and other proteins (Pruitt and Reiter, 1985).

Lysozyme: The natural substrate of this enzyme is the peptidoglycan layer of the bacterial cell wall and its degradation results in lysis of the bacteria (Reiter, 1978).

BOVINE COLOSTRUM IN THE PIGLET WEANER DIET

Growth performance, feed intake and feed conversion ratio: studies about the effects of bovine colostrum on the performance, the feed intake and the feed efficiency of newly-weaned piglets and their main results are presented in the Table 2.

Table 2. Effects of bovine colostrum supplementation on growth performance, feed ingestion and feed conversion ratio of newly-weaned piglets.

References	BC supplementation		Piglets		Effects of BC *vs.* control treatment
	Description	g.kg^{-1} feed	n	Weaning age	
Pluske *et al.*, 1999	BC powder rich in IgG	0, 50 and 100 during 10 d	131	28 d	↗ADG Week 1 and 2 PW ≈ ADFI and FCR ↘ Days to slaughter
King *et al.*, 2001	Spray-dried BC	0 and 60 during 7 d	110	28 d	≈ ADG and FCR ↗ADFI Week 1 PW
Dunshea *et al.*, 2002	Freeze-dried BC	0 and 60 during 7d	24	14 d	≈ ADG, ADFI and FCR
Le Huërou-Luron *et al.*, 2004	Freeze-dried BC	0 and 40 during 11 d in uncleaned pens	150	28 d	↗ADG Week 1 and 2 PW ↗ADFI Week 1 PW ↘ FCR Week 1 PW
		0, 20 and 40 during 14 d in clean pens	12	21 d	↗ADG d5-d7 PW ≈ ADFI and FCR
Boudry *et al.*, 2008	Freeze-dried BC whey	0 and 20 during 10 d, then 0 and10 until 28 d	48	26 d	↗ BW on d 7 PW ↗ADG and ADFI Week 1 PW ↘ FCR Week 1 PW
Le Huërou-Luron *et al.*, 2008	Freeze-dried BC	0 and 30 during 12 d	60	28 d	↗ADG and ADFI Week 1 PW ↘ FCR Week 1 PW
	LM of BC	LM of 30 g of BC during 12 d			↗ADG and ADFI Week 1 PW ↘ FCR Week 1 PW
	SM of BC	SM of 30 g of BC during 12 d			≈ ADG, ADFI and FCR
Boudry *et al.*, 2009	Freeze-dried BC whey	0, 10 and 20 during 28 d	39	24 d	↗ BW on d 7 PW ↗ADG and ADFI Week 1 PW ↘ FCR Week 1 PW No effect of the dose of BC
	Freeze-dried BC whey vs. defatted BC	10 of milk, 10 of BC whey and 10 of defatted BC	36	26 d	↗ADG on d4-d7 PW with the defatted BC ↗ADFI on d4-d7 and on d11-14 PW with the defatted BC ≈ FCR

↗ increase, ↘ reduction, ≈ no effect

BC = bovine colostrum, LM = large molecules, SM = small molecules, ADG = average daily gain, ADFI = average daily feed intake, FCR = feed conversion ratio, PW = post-weaning.

Globally, we may conclude from these results that the bovine colostrum has an effect on the growth performance and feed intake of the piglets the first week post-weaning. The better feed efficiency measured in 4 of the 9 studies presented indicates that the higher feed intake is not solely responsible for the higher performances. The study of Le Huërou-Luron *et al.* (2008) shows that similar effects are obtained with bovine colostrum and the fraction of bovine colostrum containing the large molecules, mainly immunoglobulins. Finally, Le Huërou-Luron *et al.* (2004) measured higher effects of bovine colostrum in an uncleaned environment suggesting that the effects of bovine colostrum may result from an improved sanitary status of the piglets by a direct effect of the colostrum on gut health and/or immunity.

Effect of bovine colostrum on the gastro-intestinal tract: Effects of bovine colostrum on the gastro-intestinal tract are presented in the Table 3.

Table 3. Effects of bovine colostrum supplementation on the gastro-intestinal tract of newly-weaned piglets.

References	BC supplementation		Piglets		Effects of BC *vs.* control treatment
	Description	$g.kg^{-1}$ feed	n	Weaning age	
Le Huërou-Luron *et al.*, 2003	Defatted BC	BC provided 5 µg IGF-I and 21 mU insulin kg^{-1} BW d^{-1} during 5 d	6	7 d	↗duodenal VH ↗duodenal protein synthesis ≈ SI mucosa weight and protein content ≈ SI lactase and aminopeptidase N activities
Huguet *et al.*, 2006	Freeze-dried defatted BC	0 and 50 during 14 d	12	21 d	↘gastric pH on d7 and d14 ↗ duodenal *lactobacilli:coliform* ≈ duodenal mucosal structure, crypt cell proliferation, migration index, digestive enzyme activities
Huguet *et al.*, 2007	Freeze-dried defatted BC	0 and 50 during 14 d	12	21 d	≈ duodenal mucosa/muscularis ratio ↗duodenal villi perimeter ≈ duodenal crypt size and crypt cell proliferation
King *et al.*, 2007	Spray-dried BC	0 and 75 during 19 d	7	21 d	↗ proximal and mid jejunal VH ↘ proximal and mid jejunal and distal ileal CD ↗VH:CD in distal ileum ↗epithelial cell height in mid jejunum
King *et al.*, 2008	Freeze-dried BC	0 and 50 during 14 d	6	14 d	↗ jejunal and ileal VH ↘ jejunal and ileal CD ↗VH:CD in jejunum and ileum ≈ epithelial cell height

↗ increase, ↘ reduction, ≈ no effect

BC = bovine colostrum, BW = body weight, SI = small intestine, VH = villi height, CD = crypts depth.

The studies presented in the Table 3 show that bovine colostrum help to preserve intestinal integrity after weaning by maintaining higher villi and reduced crypt depth the first week post-weaning. Moreover, Le Huërou-Luron *et al.* (2003) showed an increase in the duodenal protein synthesis.

An effect of bovine colostrum-supplemented diets was also observed on the intestinal microflora by Huguet *et al.* (2006), who showed an improved *Lactobacilli:Coliform* ratio in bovine colostrum treated weaned piglets, compared to weaned piglets receiving a control diet without colostrum (1.63 *vs*. 1.19). This effect was mainly caused by lower C*oliforms* counts whereas *Lactobacilli* counts were identical between colostrum treated and control piglets. This observation confirms the higher effects of bovine colostrum reported by Le Huërou-Luron *et al.* (2004) in an "unclean" environment and indicates the positive contribution of bovine colostrum in the improvement of gut health around weaning in piglets.

Another effect of importance observed by Huguet *et al.* (2006) in the gastro-intestinal tract is the lower gastric pH in bovine colostrum treated piglets. This strengthened the effects of colostral antibacterial components and may also be at the origin of the *Coliform* population reduction, the later being less resistant to low pH than *Lactobacilli*.

Effect of bovine colostrum on the immune system: the effects of bovine colostrum on the immune system of the newly-weaned piglets are presented in the Table 4.

Table 4. Effects of bovine colostrum supplementation on the immune system of newly-weaned piglets.

References	BC supplementation		Piglets		Effects of BC *vs.* control treatment
	Description	$g.kg^{-1}$ feed	n	Weaning age	
Boudry *et al.*, 2007	Freeze-dried BC	0, 1 or 5 g/d during 21 d	7	21 d	↗ MC in the ileal PP on d21 ↘ B cells in the ileal PP on d 21 ↗ SI of ileal PP MC ↗ serum total IgA on d 21 ↗ local anti-colostral IgM, IgG and IgA ↗ cytokine Th1 and Th2 in the GALT
Boudry *et al.*, 2008	Freeze-dried BC	0 and 20 during 10 d, then 0 and10 until 28 d	48	26 d	↘ serum Tc cells on d 7 PW ↗ serum total IgA on d 7 PW
King *et al.*, 2008	Freeze-dried BC	0 and 50 during 14 d	6	14 d	↗ mid jejunal Tc and Th cells

↗ increase, ↘ reduction

BC = bovine colostrum, PP = Peyer Patch, MC = mononuclear cells, SI = stimulation index, GALT = Gut associated lymphoid tissue

In the study of Boudry *et al.* (2007), the different measures on the blood, the spleen and the gut-associated lymphoid tissues indicate a local immunisation to bovine colostrum with a marked Th2 immune response. In the ileal Peyer patch, the bovine colostrum ingestion induces a reduction of the number of cells, especially the B-cell, in an isotype manner and the study of the cytokine expression showed a more marked Th2 immune response.

Furthermore, the increase in systemic IgA concentrations and the reduction of the Tc cells observed in the studies of Boudry *et al.* (2007 and 2008) may both be the consequence of a Th2 immune response.

The results of the cytokine expression (Boudry *et al.*, 2007) suggest an immuno-modulatory effect of bovine colostrum targeting mainly the gut-associated lymphoid tissues, which respond by producing both Th1 and Th2 cytokines. This bipolarity is important in the context of exposure to a wide range of antigens associated with pathogens, with commensal bacteria and with food. It includes the ability to generate tolerance to food and commensal bacterial antigens as well as to activate the immune response to pathogens.

King *et al.* (2008) reported a moderate expansion of T lymphocytes subsets in the lamina propria of weaned piglets consuming a bovine colostrum enriched diet. They associated this expansion to an induction of the immunological tolerance to the numerous novel proteins present in bovine colostrum.

CONCLUSION

From the results presented in this review, it appears clearly that bovine colostrum supplementation improves the growth performance and the sanitary status of piglets during the early post-weaning period. These beneficial effects are explained by an increase in feed intake, a better feed efficiency and a likely direct effect on gut health (preservation of gut integrity and reduction of the *coliform* population) the first days post-weaning.

However, bovine colostrum is not yet used in pig production because of the high processing costs for the preparation of freeze-dried colostrum (60 €/kg). Further investigations are needed to evaluate the economical impact of its use.

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